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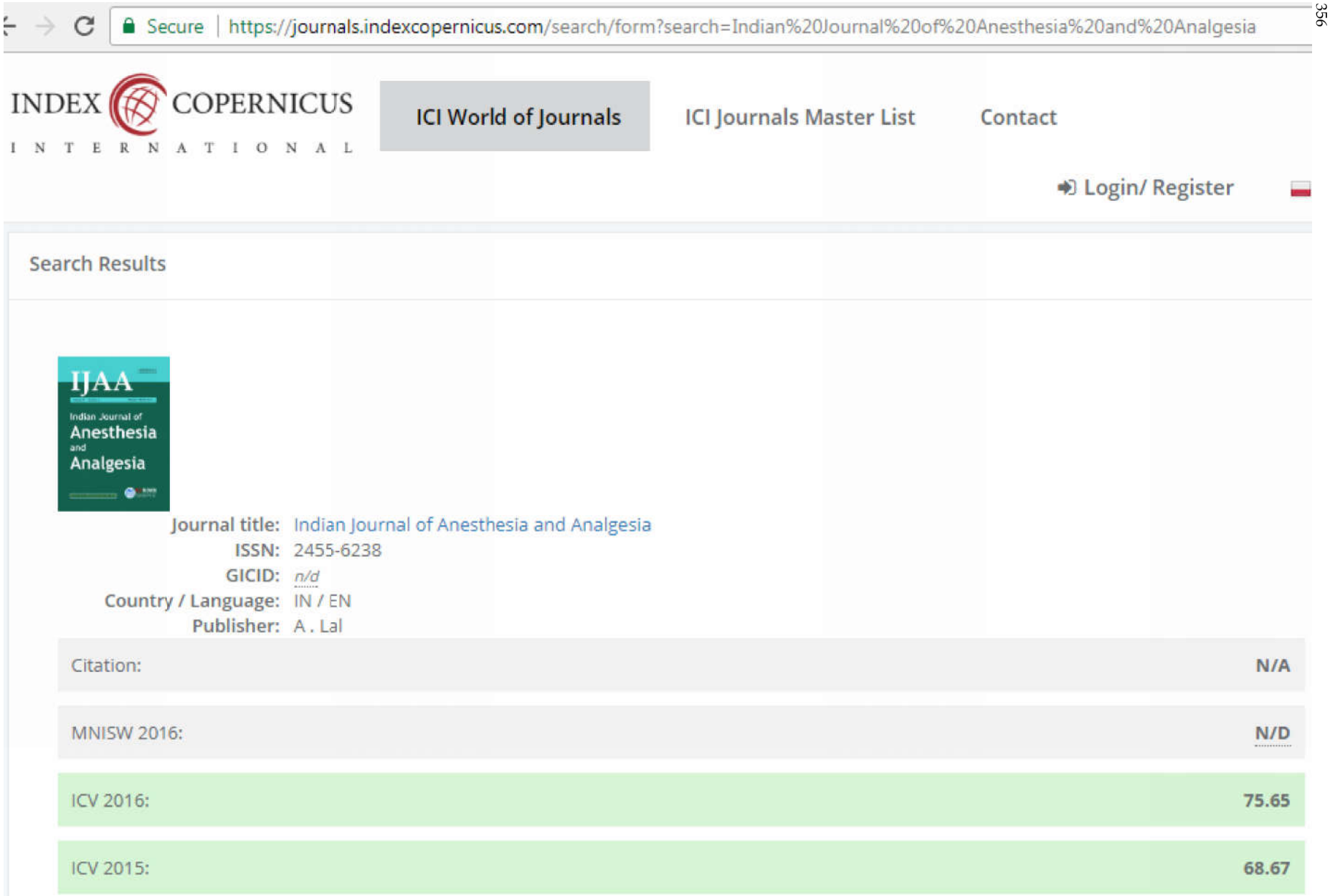
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A Comparison of the Effect of 0.9% Saline versus Balanced Salt Solution (Plasma Lyte-A) on Acid Base Equilibrium, Serum Osmolarity and Serum Electrolytes in Supratentorial Neurosurgical Procedures Requiring Craniotomy

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Abstract

Background: The most commonly used isoosmolar fluid in neurosurgery is 0.9% saline, which is known to produce hyperchloraemic metabolic acidosis. A balanced salt solution, like PlasmaLyte A, is not only isoosmolar, but also maintains acid –base balance and is stated to produce less serum chloride changes. Our aim was to study the effects of PlasmaLyte-A on acid base balance, serum osmolarity and serum electrolytes in neurosurgical procedures. *Methodology:* 70 patients posted for elective supratentorial craniotomies were randomly allocated to two groups, to receive either 0.9% saline or PlasmaLyte A as the sole intravenous fluid. Arterial Blood Gas Samples were analysed at regular intervals and the variables noted were: serum osmolarity, pH, base deficit or excess, serum chloride, serum lactate, serum sodium, serum potassium, serum calcium, and glucose levels. Intergroup data was analysed statistically by student's T test (continuous) and chi-square test (categorical) while repeated ANNOVA and post-hoc Tukey Kramer test was used to analyze data within each group using NCSS statistical software version 9.0. *Results:* Towards the end of the surgery, pH was found to be low in the normal saline group (7.334±0.05 and 7.275±0.05) as compared to the plasmalyte group (7.402±0.03 and 7.406±0.03), this difference being statistically highly significant ($p<0.0001$). The difference in base deficit was also highly significant at the same time intervals. Chloride levels were significantly higher in the normal saline group in comparison to the study group at different time intervals (112.8±8.002 and 103.63±6.17) and (115.77±9.84 and 103.15±2.95) (p value<0.0001) while serum electrolytes and serum osmolarity was found to be comparable in both the groups. *Conclusion:* We conclude that 0.9% saline when used as sole intravenous fluid in neurosurgical procedures, causes significantly higher chloride levels and significant acidosis when compared to plasmalyte A used for the same purpose.

Keywords: Neurosurgery; Craniotomy; Acid-Base Equilibrium; Osmolarity; Electrolytes; Fluid Therapy.

Introduction

Fluid therapy in neurosurgical procedures poses a challenge to the attending anaesthesiologist. A majority of these patients receive perioperative diuretic therapy which causes a lot of electrolyte imbalance. In addition to these changes, peripheral vasodilatation due to general anaesthesia, excessive blood loss, and inadequate secretion of ADH, complicate the homeostasis of the patient resulting in the need of an ideal intravenous replacement fluid which is iso-osmolar, does not alter the acid base balance and also replenishes lost electrolytes.

In the presence of an intact blood brain barrier, even a small drop in plasma osmolarity (<5%) can potentially increase brain water content and intracranial pressure [1]. The use of hypo-osmolar solutions like 0.45% saline and 5% glucose, for the same reason is avoided in neurosurgical procedures to ensure a better postoperative outcome [2]. Thus, the necessity to preferably choose only an iso-osmolar fluid for perioperative use arises, leaving the anaesthesiologist with only a few options.

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The most commonly used intravenous fluid in craniotomies is 0.9% saline which is iso-osmolar (308 mosm/l), has a high chloride content (154meq/l), is documented to produce acidosis [3] and does not contain potassium. A balanced salt solution, e.g. Plasmalyte A (multiple electrolytes injection, Type 1, USP, Baxter healthcare India Pvt Ltd) on the other hand, is not only isoosmolar (294mosm/l), but also contains additional electrolytes (potassium 5meq/l, magnesium, acetate, gluconate), has chloride content same as in plasma (98meq/l) and has been reported to produce less acid base disturbances [4,5]. Sodium hydroxide and other acid buffers are used in this product to maintain a physiologic pH of 7.4 [6].

Plasmalyte A has been used and compared before with other iso-osmolar fluids in trauma care, diabetic ketoacidosis, and abdominal surgery [7-9]. Its use in neurosurgery has not been reported in the available literature so far.

We carried out this prospective randomized study with the primary objective to determine whether balanced salt solution (plasmalyte A) produces any changes in acid base balance when compared to 0.9% saline as the sole intravenous fluid in neurosurgical procedures requiring craniotomy. The secondary objectives were to compare changes in serum osmolarity and serum electrolytes after using the two intravenous fluids.

Methodology

After approval from the institutional ethics committee, a prospective, randomized, clinical investigation was carried out in 70 adult consenting patients scheduled to undergo elective supratentorial craniotomies within a period of 12 months.

Sample Size Calculation

A total sample size of 70 (35 in each group) was calculated on the basis of a similar study conducted by Hafizah M , Liu C, Ooi J, et al in 2015, considering changes in pH as the study parameter (mean values of 7.44±0.2 for plasmalyte and 7.39±0.8 for 0.9% normal saline). We used the software G power 3.1 (Universitat Dusseldorf, Germany) to derive the sample size using an effect size of 0.85, α error of 0.05 and power (1-β error probability) of 0.90.

An informed consent was taken, a routine preanaesthetic checkup done and preoperative investigations were carried out which included haemogram and serum electrolytes in particular. History related to treatment with diuretics, coagulopathy, and blood transfusion was taken into account and noted.

Our exclusion criteria were extremes of ages (<20years and >60 years), those with renal dysfunction, patients with severe electrolyte imbalance, a haematocrit of <30 or haemoglobin <10g/dl, and those with known hypersensitivity to plasmalyte. Surgeries involving excessive blood loss (>1.5 liters), longer surgeries (> 6hours), raised intracranial pressure or tense brain/bulging brain, and cases with haemodynamic instability requiring use of intraoperative vasopressors were also excluded from this study.

All the remaining ASA grade 1 or 2 patients were randomly divided into two groups of 35 each using a computer generated randomization table (Microsoft excel 2010, Microsoft corporation, Washington USA).

The two groups received

Group N (n=35): 0.9% saline as the sole intravenous fluid (exclusive of blood and blood products)

Group P (n=35): Plasmalyte-A as the sole intravenous fluid (exclusive of blood and blood products)

The rate of infusion of either fluid was maintained at a range of 8 -10 $ml.kg^{-1}.hr^{-1}$ in both the groups.

Routine neuroanaesthetic management as per our institutional protocol was carried out in each patient which included Fentanyl citrate(2µg/kg), glycopyrrolate (4mcg/kg), pantoprazole (0.8mg/kg) as premedication, thiopentone (5-7mg/kg) and atracurium besylate (0.4mg/kg) for induction, scalp nerve block with bupivacaine 30 ml of 0.25% for suppression of haemodynamic response during Mayfield pin holder insertion, fentanyl-atracurium infusion (both at 0.3mg/kg/h) and sevoflurane at a MAC of 0.8 -1.2% for maintenance, ondansetron (8mg) and dexamethasone (0.08mg/kg) as antiemetics and phenytoin as per requirement. The dose of mannitol was kept constant for all the patients at 0.4g/kg intravenously over 10 minutes. Acetaminophen (15mg/kg) intravenous infusion was given to reduce postoperative pain.

Invasive monitoring (arterial blood pressure and central venous pressure) was carried out along with other noninvasive monitors, including capnography, pulse oximetry, electrocardiography, end tidal exhaled gases, MAC, spirometry, systolic pressure variation, core temperature, urine output, and blood loss. A mean arterial pressure between

50-70mm Hg, Central venous pressure (8-13 mmHg) etCO2 (28-32 mm Hg), and SPV <12 was maintained in all the cases. Total intravenous fluids infused, total blood loss, urine output, number of blood transfusions given if any, and total duration of surgery was noted at the end of each case.

Serial Arterial Blood Gas Samples were analysed at the following time intervals

1. Baseline (T1)
2. At the time of dural opening (T2)
3. One hour after dural opening (T3)
4. At skin closure (T4)
5. One hour postoperatively (T5)

The following observations were made at these five time intervals, serum pH, Serum sodium, serum potassium, serum calcium, serum chloride, serum osmolarity, base deficit, serum lactate, haemoglobin, and glucose. All the deviations in these parameters outside the normal range were meticulously treated. Serum pH values of less than 7.35 were promptly treated with intravenous sodium bicarbonate after careful calculation of the requirement from the base deficit values.

The observations were analyzed statistically using student's T test (continuous data), chi-square test (categorical data) and repeated ANOVA test with post-hoc Tukey Kramer for data within the group and in between the two groups, using NCSS software version 9.0. All values have been expressed in mean±SD, and ratio for categorical data. Probability values of less than 5% were taken as significant.

Results

No patient was excluded. Both the groups were comparable and found to be normally distributed in terms of age, weight, height, gender distribution, total intravenous fluids infused, total blood loss, duration of surgery, and total urine output (Table 1).

pH values were seen to be comparable in both the groups at time intervals T1,T2 and T3. However, at T4 (skin closure) and T5 (1 hour postoperatively), there was a highly significant difference in pH between the groups, with the values in the control group being on the lower side. Similar observations were seen with changes in base deficit, where the groups were comparable at T1and T2, but had highly significant difference in mean base deficit at T3, T4 and T5. (Table 2) (Graph 1)

Intragroup data analysis (ANOVA with post – hoc Tukey kramer) revealed a significant fall in mean ph value and base deficit from baseline (T1) in Group N at T3, T4 and T5 with no significant change at all time intervals in group P. (p value for change from baseline (T1) in control group were T3 (0.02)*, T4 (0.00)** T5 (0.00)** .

Serum chloride levels were similar in both groups at T1 and T2, however there was a highly significant increase in mean chloride levels in the normal saline group towards the end of surgery (at T4 and T5) (Table 3) (Graph 2). Intra-group analysis showed a highly significant rise in mean serum chloride level in Group N at T3 (0.002**)T4 (0.001**)T5 (0.00**) from baseline (T1).

An overall rise in serum lactate was seen in both the groups from baseline group N p=0.04* (T2), p=0.04*(T3) p=0.02*(T4) p=0.01**(T5), and group P p=0.02* (T2), p=0.032*(T3) p=0.02*(T4) p=0.01**(T5) which was comparable between the groups at all time intervals except at T3 (1 hour after dural opening) where the difference was significant (p=0.02*).

Changes in serum sodium, potassium, calcium, blood glucose, serum lactates and serum osmolarity were comparable in both the groups (Table 5). Intragroup comparison of mean values from

Table 1: Demographic and intraoperative data

	Demographic and Intra-operative Data		
	Group N	**Group P**	**P value**
Age (years)	50.25±13.73	46.88±10.95	0.5
Weight (kg)	62.48±9.39	58.42±8.70	0.325
Gender (M:F)	15:20	19:16	0.5
BMI (kg/m²)	22.08±0.9	24.03±2.2	0.8
Height (cm)	159.91±5.88	159.14±6.09	0.20
Fluids infused(ml)	2437.14±525.9	2271.42±320.27	0.69
Blood loss (ml)	551.42±212.99	372.57±22.26	0.54
Urine output (ml)	82±64.52	72.87±61.27	0.78
Duration (min)	275.71±87.22	248.11±117.29	0.07

n=35, values in mean±SD, p<0.05=significant*, p<0.01=highly significant**

Table 2: Changes in pH and base deficit (BD)

Time interval	Changes in pH and base deficit (BD) Group N	Group P	P value
T1 (pH)	7.432±0.04	7.406±0.06	0.0652
T1 (BD)	-0.871±0.80	-0.954±0.140	0.672
T2 (pH)	7.407±0.05	7.403±0.04	0.753
T2 (BD)	-1.36±1.092	-1.023±0.625	0.063
T3 (pH)	7.393±0.05	7.394±0.03	0.915
T3 (BD)	-2.028±1.004	-0.974±0.706	0.00**
T4(pH)	7.334±0.05	7.402±0.03	0.00**
T4(BD)	-2.474±1.169	-1.046±0.831	0.00**
T5 (pH)	7.275±0.05	7.406±0.03	0.00**
T5 (BD)	-3.682±2.124	-1.438±1.093	0.00**

n=35, values in mean±SD, p<0.05=significant*, p<0.01=highly significant**

Table 3: Changes in serum chloride

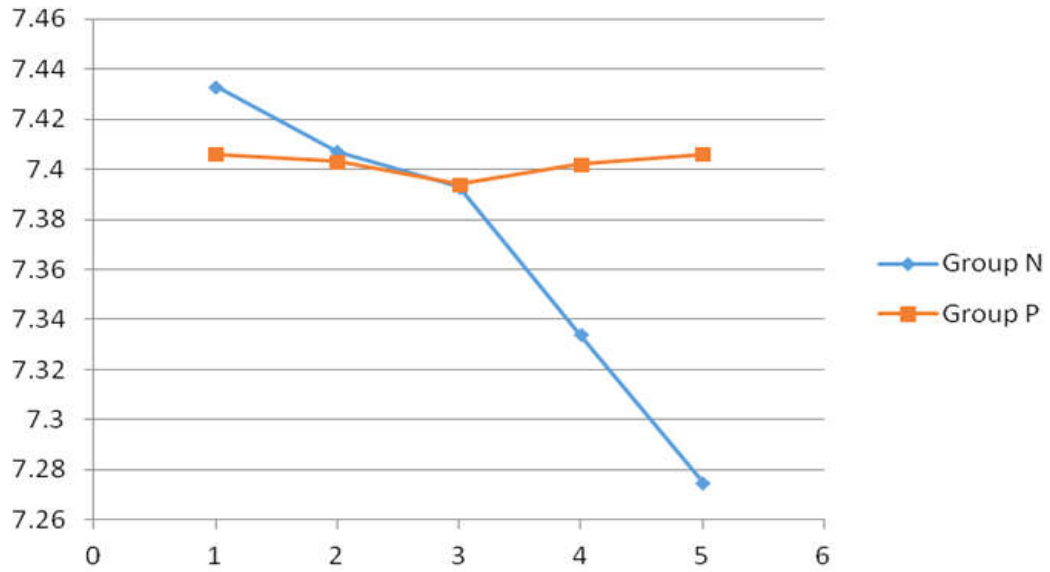
Time interval	Changes in serum chloride Group N	Group P	P value
T1	107.5±3.32	102.8±6.06	0.472
T2	105.228±6.188	100.348±6.625	0.063
T3	109.8±1.008	102.571±5.202	0.062
T4	112.8±8.002	103.63±6.17	0.00**
T5	115.77±9.849	103.151±2.952	0.00**

n=35, values in mean ±SD, p<0.05=significant*, p<0.01=highly significant**

Table 4: Changes in serum lactate

Time interval	Changes in serum lactate Group N	Group P	P value
T1	1.097±0.632	1.108±0.595	0.372
T2	1.941±0.772	2.06±0.625	0.631
T3	2.527±1.008	2.362±0.815	0.02*
T4	3.198±1.201	2.905±0.977	0.267
T5	3.598±0.923	4.054±1.141	0.07

n=35, values in mean ±SD, p<0.05=significant*, p<0.01=highly significant**

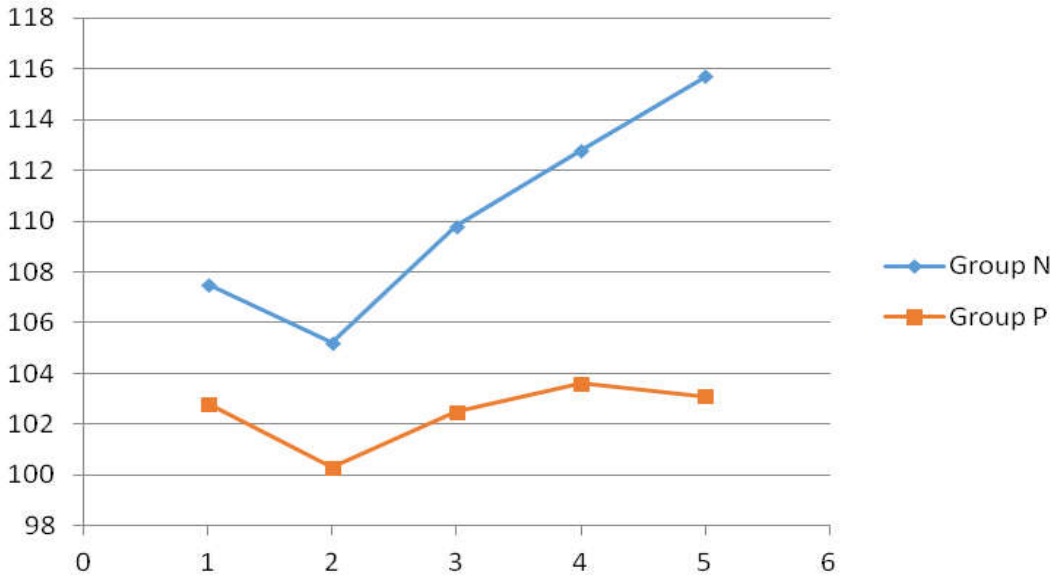


Graph 1: Graph showing changes in ph at different time intervals in both the groups with pH values on y axis and time intervals (T1 to T5) on x axis.

Table 5: Comparison of changes in serum electrolytes, serum osmolarity and blood glucose

Parameter	Time interval	Group N	Group P	P value
Serum sodium	T1	134.97±3.27	135.24±4.05	0.754
	T2	136.12±3.14	136.28±4.04	0.853
	T3	137.21±3.88	137.13±3.82	0.926
	T4	137.2±3.37	137.78±3.55	0.517
	T5	137.11±3.87	138.48±3.47	0.124
Serum potassium	T1	3.58±0.231	3.67±0.261	0.095
	T2	3.68±0.245	3.68±0.356	0.953
	T3	3.67±0.29	3.66±0.321	0.910
	T4	3.72±0.378	3.74±0.339	0.819
	T5	3.75±0.41	3.72±0.389	0.817
Serum calcium	T1	0.85±0.133	0.94±0.144	0.10
	T2	0.90±0.149	0.87±0.134	0.389
	T3	0.89±0.241	0.87±0.117	0.797
	T4	0.98±0.296	0.87±0.138	0.052
	T5	0.95±0.264	0.91±0.130	0.445
blood glucose	T1	106.05±25.246	114.54±27.320	0.181
	T2	123.0±34.534	129.55±43.515	0.289
	T3	134.71±34.119	129.71±48.611	0.11
	T4	141.02±32.482	138.90±52.325	0.07
	T5	151.37±38.677	142.52±45.077	0.06
Serum osmolarity	T1	275.90±3.087	276.82±4.296	0.07
	T2	276.47±5.648	277.81±6.464	0.21
	T3	278.92±4.970	281.22±17.750	0.61
	T4	277.44±5.221	280.31±4.501	0.267
	T5	278.89±5.344	281.33±5.060	0.07

n=35, values in mean±SD, p<0.05=significant*, p<0.01=highly significant**



Graph 2: Graph showing changes in serum chloride levels at different time intervals in both the groups (time intervals T1 –T5 on x axis)

baseline with regards to all the above parameters showed no significant difference p>0.05.

None of the patients in either of the groups presented with any adverse reaction to the intravenous fluid infused. There was no hypersensitivity reaction reported.

Discussion

Intravenous fluids with an osmolarity of around 300mosm per liter tend to remain in the intravascular compartment, reducing the possibility of increased brain water and raised intracranial

pressure, with or without an intact blood brain barrier [10,11]. The iso-osmolar fluid most widely used in neurosurgery is 0.9% normal saline (308mosm/L), which is easily available and has a long term safety record as fluid therapy. However large volumes of 0.9% normal saline (NS) tend to cause hyperchloraemic metabolic acidosis (HMA) with a normal anion gap [3]. Significant increases in chloride levels and HMA have been observed in various surgeries like intraabdominalsurgery [9], Gynecological surgery [12], and kidney replacement post-operative fluid therapy [13]. HMA tends to impede recovery [14].

Plasmalyte-A contains organic acid buffers like sodium hydroxide, acetate and gluconate, and is physiologically similar to plasma (pH 7.4) [6]. It is more similar to body fluid composition than NS, making it less likely to lead to HMA.

In our study, we observed that acid base changes with the use of plasmalyte –A and normal saline were initially comparable over a period of time, after which as the duration of infusions prolonged, significant acidosis in the control group started to set in. Similar findings have been reported by other authors in studies where normal saline was compared to plasmalyte-A [7,9,13]. We also observed a significant increase in serum chloride levels with normal saline, towards the end of the surgery, a finding similar to many other authors [4,8,16,17].

A literature search revealed that another iso-osmolar crystalloid stereofundin ISO has also been compared to 0.9% normal saline in neurosurgical procedures [18], where the authors have reported better control of acid base balance, sodium and chloride levels with stereofundin than normal saline. The chloride content in stereofundin (127meq/L) is still higher than plasmalyte-A(98 meq/L), further lowering the possibility of hyperchloraemia with our study fluid.

The available literature so far, indicates that there is very little and inconclusive evidence, as far as the association of acidosis and postoperative outcome is concerned [19]. However, Hyperchloraemia, has been shown to influence renal function in the perioperative period by altering tubular chloride reabsorbtion and renal vasoconstriction [16]. Similarly, hyperchloraemia is also stated to cause coagulation abnormalities which have been studied by thromboelastography and platelet aggregometry [20]. Moreover acidosis following hyperchloraemia is known to increase inflammatory markers in the serum [21]. All these factors when compounded together carry the potential to adversely affect the postoperative outcome of a neurosurgical patient, in whom ,renal function is already affected by the use of diuretics and electrolyte disturbances, and in whom haemostasis is a major determinant of prognosis.

Serum osmolarity did not show any significant change in both groups. Maitenance of serum osmolarity is one of the prime concerns in neurosurgical anaesthesiology as even a small fall in the same can increase brain water content [11]. In our study both the fluids maintained serum osmolarity well, thus indicating that they were comparable in this aspect. Similarly, changes in serum sodium, potassium, calcium and glucose were comparable in both groups, an observation similar to other studies [7,8].

We therefore suggest that the positive effect of plasmalyte A on acid base equilibrium and particularly on chloride levels, and its subsequent prospective effect on patient recovery and outcome marginally outweighs its only disadvantage of being available at a higher cost when compared to normal saline.

Our study was not devoid of limitations. We could not use the benefit of blinding, due to technical reasons, which would have otherwise made our study methodologically stronger. Secondly, we did not continue our study in the postoperative period for more than an hour after extubation. By doing the same we would, perhaps, have also been able to provide evidence related to the effect on postoperative outcome of the patient after using plasmalyte-A. Another reason why we chose to refrain ourselves from commenting on the effect of these changes on postoperative outcome, is the fact that neurological outcome in brain tumour surgery necessarily has a multifactorial causation [22]. Factors like, anatomical site of tumor, its size, structures involved, histopathology, vascularity are only a few of them. Attributing a postoperative outcome only to intraoperative acid-base changes or chloride levels thus, is difficult to justify. Our limitations leave scope for further research in this area.

Conclusion

We thus conclude that, 0.9% normal saline when used as sole intravenous fluid in neurosurgical procedures involving craniotomy, has a potential to cause significant acidosis and significant hyperchloraemia when compared to plasmalyteA used for the same purpose. Hyperchloraemia can

potentially prove to be harmful for neurologic outcome in neurosurgical procedures.

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Original Research Article

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Study of Efficacy and Safety of Dextmedetomidine Vs Midazolam in Gynacological Laproscopic Surgery

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Abstract

Background: Laparoscopic surgeries under are associated with unique hemodynamic changes thus a basic need is felt among the anaesthesiologist fraternity for the desired availability of a drug that effectively suppresses all the hazardous responses to obnoxious stimuli with a maximum safety margin. Dexmedetomidine due to its distinct sedation, analgesia and sympatholytic properties can be used as an anaesthetic adjuvant in anaesthesia for Laparoscopic surgeries. Thus we undertook this double blind, prospective comparative study. *Methods*: Fifty women undergoing Laparoscopic gynaecological Surgeries divided randomly by a computer generated table into two groups of 25 each. D group - Dexmedetomidine loading dose 1µg/kg followed by maintenance infusion of Dexmedetomidine at 0.4µg/kg/hr M Group – Midazolam loading dose 0.03 mg/kg followed by maintenance infusion of saline. Both the group were given Fentanyl citrate 1ug/kg. We undertook this double blind, prospective comparative study to evaluate efficacy and safety and its effect on sedation, hemodynamic, anaesthesia and analgesia requirement and recovery characteristics. *Results*: Baseline Mean degree of sedation was same but after 5 min study drug it was 2 for group D compared to group M -1.32 and postoperative 1.16 for group D and 1.08 for group M. Mean heart rate was 73.84 for group D and 74.52 for group M. Mean blood pressure was 100.84 for group D and 102.56 for group M. Same trend observed at the time of induction, intubation, mean during pneumoperitonium and mean value in PACU. Mean dose of fentanyl required was less 65µg compared to 93.4µg in group M. *Conclusion*: This randomised, double blind study demonstrated that when compared to Midazolam Dexmedetomidine is more effective anaesthetic adjuvant that causes adequate sedation without respiratory depression, decreases requirement of anaesthetic and opioid, attenuate sympathoadrenal response, maintains stable haemodynamics perioperatively at the same time provide excellent recovery profile without any adverse events but continuous monitoring for hypotension and bradycardia is essential during first two hours of postoperative period if higher infusion rate are used.

Keywords: Midazolam Dexmedetomidine; Anaesthesia; Laparoscopic Surgeries.

Introduction

There are many class of drugs that can be used for to relieve anxiety and provide sedation. Among these most frequently used drugs are benzodiazepines like Midazolam and opioids like Fentanyl. Dextmedetomidine is alpha 2 receptors agonist are being increasingly used in anaesthesia as they not only decrease sympathetic tone and attenuate stress response to anaesthesia and surgery but also cause sedation and analgesia and attenuates sympathoadrenal response to noxious stimuli encountered during anaesthesia and surgery thus providing improved haemodynamics, metabolic, and hormonal stability [1,2]. Laparoscopic surgeries under anaesthesia are associated with unique hemodynamic changes in the form of increased systemic vascular resistance leading to hypertension thus a basic need is continuously felt among the anaesthesiologist fraternity for the desired availability of a drug that effectively suppresses all

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the hazardous responses to obnoxious stimuli with a maximum safety margin [3].

General anaesthesia with Midazolam as sedation agent and Fentanyl as opioids is standard practice of anaesthesia for Laparoscopic surgeries in our institution. Dexmedetomidine due to its distinct sedation, analgesia and sympatholyticproperties we undertook this double blind, prospective comparative study to evaluate efficacy and safety of Dexmedetomidine verses Midazolam in Gynaecological Laparoscopic surgery. We studied its effect on sedation, hemodynamic, anaesthesia and analgesia requirement and recovery characteristics.

Materials and Methods

After institutional medical ethics committee approval written informed consent was obtained from all patients. Patient were included in study if they are between18-40, ASA1 and ASA 2, Gynaecological laparoscopy procedurs of anticipated duration < 2hrs and patient requiring one day post-op stay in hospital. patient excluded from study if ASA 3 and more, body weight ≥ 25% of recommended height, contraindication to the use of Dexmedetomidine e.g. Liver, kidney and cardiac disorder, History of severe adverse reaction or allergy to any drug, if patient has taken any sedative analgesic within 24hrs. This study was carried out in 50 women undergoing Laparoscopic gynaecological Surgeries like chromopertubation, Ovariancystectomy, ovarian drill and other short procedure. They will be divided randomly by a computer generated table into two groups of 25 each.

D group - Dexmedetomidine loading dose 1µg/kg followed by maintenance infusion of Dexmedetomidine at 0.4µg/kg/hr M Group – Midazolam loading dose 0.03 mg/kg followed by maintenance infusion of saline.

Double Blind Design Employed as Follows

Drug was prepared in two syringes by senior anaesthetist who was not a part of the anaesthesia team and not the investigator. patient randomized into 2 groups – group Dexmedetomidine (D) and Midazolam (M) by using a computer generated randomization. In group M loading dose of drug was prepared in 20cc syringe with normal saline containing Midazolam 0.03mg/kg and group (D) loading dose of drug was prepared in 20cc syringe with normal saline containing Dexmedetomidine 1ug/kg. Each syringe contained a fixed volume of 20cc. Intraoperative maintenance infusion drugs were prepared in 20cc syringe with only normal saline in group M and Dextmedetomidine in group D Dexmedetomidine infusion was prepared in normal saline in the concentration of 0.4µg/cc. Maintenance drip rate was adjusted as per Dexmedetomidine 0.4µg/kg/hr. Two syringes were handed over to the investigator as loading dose and maintenance infusion. Decoding was done at end of study for statistical analysis A complete history obtained from the patient. Basic routine and specific investigation as per history and clinical finding were carried out. Patients ASA physical classification was determined. As per Inclusion and exclusion criteria patients enrolled in study and written valid informed consent taken from each patient posted for surgery B) Patient preparation: Baseline monitor like electrocardiogram (ECG), Pulse oximetry, Non invasive blood pressure (NIBP) were attached. Baseline value of systolic, diastolic and mean blood pressure, Heart rate, Respiratory rate by inspection. Two intravenous lines were secured one for routine fluid and other exclusively for Dexmedetomidine using 20 gauge cannulas. Every 5 min pulse, BP, SpO_2, RR noted. Degree of sedation monitored using the six point scale described by Ramsay andcolleagues. Ramsay Sedation score noted as baseline, 5min after loading dose of study drug postoperative every 15 mins for period of 2 hrs. In group D patients given Dexmedetomidine 1µg/kg iv over 10 min using a infusion pump. In group Midazolam, patient received normal saline with Midazolam 0.03mg/kg. Over 10 mins. After loading dose, then infusion was changed to maintenance infusion. After noting the sedation score after loading dose of study drug patients in both the group were given Fentanyl citrate 1µg/kg. Pulse, BP, SpO_2, RR recorded for every 5 min before induction. 3 mins after giving Fentanyl citrate Patient preoxygenated with 100% O_2 for 3 min. Induction was done with Inj Thiopentone sodium (3-5mg/kg) in graded doses till loss of eyelash reflexes and Inj Succinylcholine1.5mg/kg was given to facilitate endotracheal intubation. After intubation pulse, BP, SPO_2 monitored for every 10 minute. Patient maintained on O_2+N_2O+Isoflurane (0.3%) inspired concentration using closed circuit. $ETCO_2$ attached and monitored and maintained below 35-40 mmhg by adjusting tidal volume and respiratory rate. Intraoperative anaesthetic requirement was decided on basis of haemodynamics. Increase in HR, increase in SBP 20% from the baseline patient were given Fentanyl

in dose of 0.5µg/kg increment once dose of Fentanyl exceeded 2µg/kg, Propofol top up of 10 mg given when needed. In addition to hemodynamic sign of anaesthetic depth we look for other signs of lightness such as sweating lacrimation, swallowing or movement. HR, BP noted down at the time of induction, intubation, during pneumoperitonium, the time of extubation and in PACU. Time from creation of pneumoperitonium to release of pneumoperitonium taken as duration of pneumoperitonium. All patients received intravenous Ringer lactate solution at the rate of 5 ml/kg/hr as maintenance fluid. NM block was maintained Vecuronium bromide 0.02mg/kg. CO_2 was insufflated to create pneumoperitonium + abdominal pressure (IAP) monitored intraoperatively and kept below 15 mmhg Adversehaemodynamics monitored perioperativly Hypotension (systolic BP <90 treated with rapid infusion of 250ml of glucose salt solution followed by Ephedrine 2.5mg in repeated doses if systolic BP did not increase above 90 mmhg within 2 min. Bradycardia treated with inj atropine 0.01mg/kg if pulse rate less than 50.Maintainance infusion was decided to stop if hypotension, bradycardia persisted inspite of above. Maintenance drip of study drug was stopped when trocar was removed also Isoflurane and Propofol stopped at the same time. Then time of awakening and responding to verbal command from the end of drip was noted. Diclofenac sodium 75mg added to iv fluid for postoperative analgesia. Requirement of additional Fentanyl and Propofol noted down. Patients were reversed and extubated when they fulfilled criteria for extubation like sustained head lift and then patient were transferred to PACU. In recovery patient observed for Ramsay sedation score and vitals including blood pressure, heart rate, and respiratory rate for a minimum of 2hrs duration. No of patient requiring analgesia (inj. Tramadol 50mg) and amount of analgesia needed noted. Haemodynamics parameters monitored during perioperatively are Blood pressure and heart rate baseline,at the time of induction, at the time of Laryngoscopy, mean value during pneumoperitonium, at the time of Extubation, Mean value in PACU.

Results

Study reveals that mean duration of surgery was **70.52 mins** in Group D group which was comparable to 70.20mins in Group M

Table 1:

Groups	Mean Dose of Induction Thiopentone (mg) ($\overline{X}$ ± SD)
Group D	262.40 ± 32.68
Group M	334.36 ± 39.51
p value	*0.001

By Student't' test *Significant

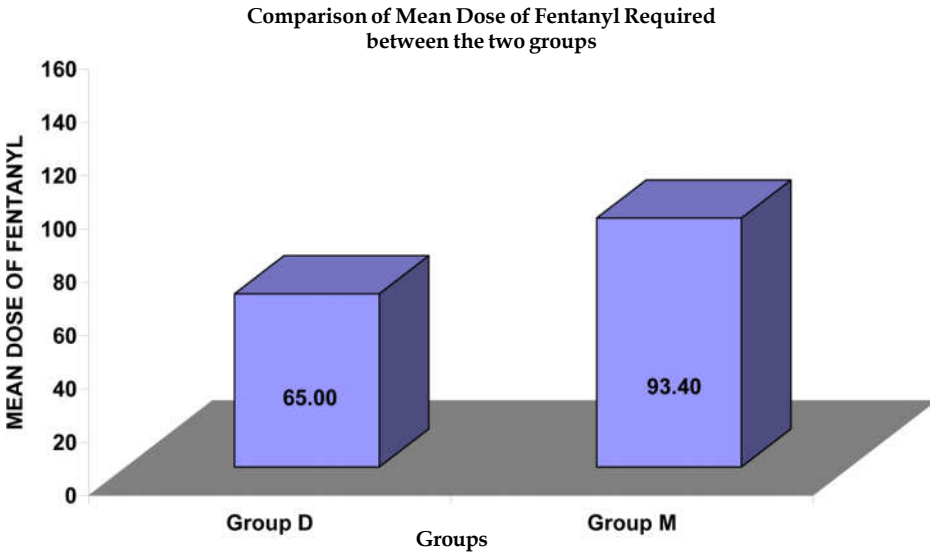

Fig. 1: Comparison of mean degree of sedation

Mean anesthesia recovery time for Group D group was 8.78 mins which was comparable to 8.65 mins in Group M.Data revealed that Mean PACU discharge time for Group D group was 100.76 mins which was more as compared to 93.0 mins in Group M.

- As per this data, at baseline Mean Degree of sedation wassame i.e. 1.00 for Group D group and Group M group 5mins after loading study drug and postoperative Mean Degree of sedation was significantly more as compared to M group. Mean Heart rate at baseline was 73.84 beats/min in Group D group which was comparable to 74.52 beats/min Group M. Same observed intraoperative period and in PACU.

Data reveals mean SBP at baseline was 134.56mmHg in Group D group which was comparable with 132.96mmHg for Group M.At 5mins after 122.96mmHg for Group D which significantly less as compared 133.60mmHg for Group M. Same trend observed intraoperative period and Mean value in PACU.

Mean DBP at base line was 84.96mmHg in Group D which was 87.36mmHg for Group M, mean MBP at baseline was 100.84mm Hg in Group D which was comparable with 102.56mm Hg for Group M. At 5mins after infusion, that was 91.92mmHg for Group D which was significantly less as compare 103.47mmHg.

Comparison of Mean Heart Rate between the Two Groups

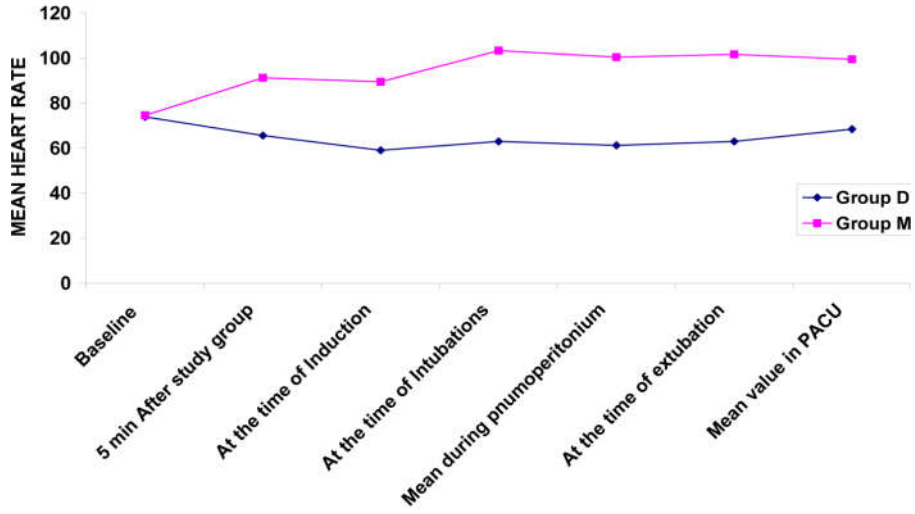

Fig. 2:

Comparison of Average Mean Blood Pressure between the Two Groups

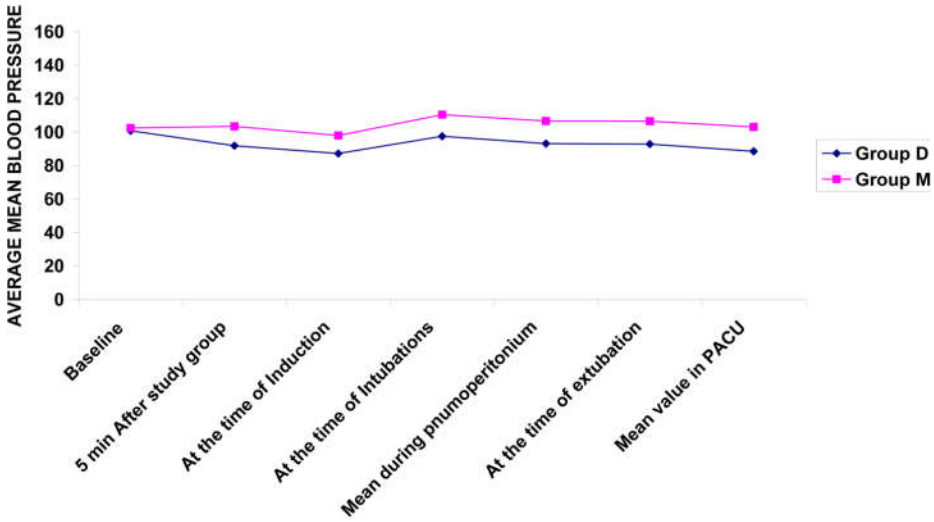

Fig. 3:

Table 2: Between the two groups

Duration	Mean Degree of sedation ($\bar{X}$ ± SD)		P value
	Group D (N=25)	Group M (N=25)	
Baseline	1.00±0.00	1.00±0.00	1.000(NS)
5mins after loading Study drug	2.00±0.00	1.32±0.48	*0.001
Postoperative	1.16±0.37	1.08±0.28	0.3929(NS)

By Student't' test *Significant NS = Not Significant

Discussion

Dexmedetomidine is gaining popularity for its sedative, hypnotic, anxiolytic and sympatholytic properties without significant respiratory depression. In recent studies, Dexmedetomidine has been shown to have clinically significant effects on anaesthetic requirements, haemodynamics responses induced by anaesthesia and surgery in patients [4]. It also produces sedation and diminishes the intraoperative requirement of analgesics. The major sedative and antinociceptive effects of Dexmedetomidine are attributable to its stimulation of α2 A subtype located in locus ceruleus [5].

Dexmedetomidine potentiate anaesthetic effect of all intraoperative anaesthetic, regardless of method of administration. The profound decrease in anaesthetic requirement shown to be mediated through central α adrenergic receptor. Laparoscopic surgery offers intraoperative stress during pneumoperitonium by increasing systemic vascular resistance and BP and at same time producing nociception [3].

Carbon dioxide (CO_2) is usually used to produce pneumoperitonium during laparoscopic surgical procedures [6,7]. Both CO_2 and pneumoperitonium causes adverse cardiovascular and renal effects [8]. Some of these effects are related to CO_2 and some to elevated intra abdominal pressure. Immediately after creation of pneumoperitonium, plasma level of Norepinephrine, Epinephrine and plasma Renin activity increases [9]. Increased catecholamine level activates the renin–angiotensin–aldosterone–system. All these changes together contribute to elevated arterial pressure, increased systemic and pulmonary vascular resistance and reduced cardiac output [10].

Dexmedetomidine significantly reduces release of catecholamine and almost completely reduces norepinephrine release and attenuate the increase in systemic vascular resistance.

This unique property of Dexmedetomidine renders it suitable as anaesthetic adjuvant for analgesia during the perioperative period in especially in laparoscopic surgery [11]. General anaesthesia with Midazolam as sedative and Fenatanyl as analgesic Opioids is standard practice of anaesthesia for laparoscopic surgeries in our institution. There are very few studies comparing Dexmedetomidine with Midazolam as perioperative sedation in general anaesthesia. Therefore we conducted this study.

In the study of Gulay [12], et al for comparison of Dextmedetomidine in dose of 1μg/kg with 3 different doses of Midazolam is 0.02 and 0.04 and 0.06mg/kg in preoperative sedation. Dexmedetomidine and Midazolam in dosage 0.04 and 0.06 mg/kg cause statistically significant difference in Ramsay sedation score and VAS as compared to baseline values.

Though Dexmedetomidine and 0.06 mg/kg Midazolam were equally sedative. The decrease in SpO2 levels was more evident and resultant hypoxemia was more frequent in 0.06 mg/kg Midazolam group. He also concluded that though Dexmedetomidine leads to depressant effect on haemodynamics parameters at dose of 1 μg/kg but it did not reach level of severe impairment and its effect on respiration was definitely lower as compared to Midazolam

Thus in our study we have taken Midazolam as 0.03 mg/kg because Fentanyl (1μg/kg) added in the study as Midazolam has no analgesic properties and this combination is conventionally used for premedication in our institution.

Hypotension and bradycardia has been observed with Dexmedetomidine in studies done earlier [4,13,14]. These effects are known to be related to dose, route of administration and infusion rate. In intravenous Dexmedetomidine administration report of its use state that α2 agonist effect is observed but not α1 effect on administration of low and moderate dosage and slow rate infusion consequently peripheral vasoconstriction and hypertension would not be expected in these instances [15,16].

Taking these data into account we elected to use Dexmedetomidine in dosage of 1 μg/kg and gave it in infusion over 10 min so as to avoid side effect associated with high dose and infusion rate Tanskanen [17], *et al*. in their study showed that intraoperative infusion of Dexmedetomidine at a rate of 0.4 μg/kg/hr maintains heart rate and blood pressure in acceptable range for a longer duration as compared to placebo group. .We thus kept intraoperative maintenance drip rate of Dexmedetomidine 0.4 μg/kg/hr and kept it constant to avoid many intraoperative variable.

It has also shown that Dexmedetomidine potentiate analgesia caused by Fentanyl and reduces its dose requirement in human during surgery while Midazolam does not have analgesic properties. Therefore we gave both groups Fentanyl as analgesic but in dose of 1μg/kg [18]. We gave both the group fixed concentration 0.3% inspired Isofluraneformaintenance of anaesthesia with O_2:N_2O as 50:50.We would have preferred giving end tidal Isoflurane for more accuracy but we do not have this facility in our institution.

Following pneumoperitonium with carbon dioxide, ventilation was adjusted to maintain normocapnia. Still Pneumoperitonium produces significant hemodynamic derangements which may be detrimental and needs to be prevented. In our study we considered both these factors altering hemomodynamics and were controlled in both groups.

Then we compared efficacy and safety of the drug on the following parameter.

Degree of sedation was observed 5 mins after end of loading dose of drug. As this time corresponds approximately to peak effect of Midazolam and Dexmedetomidine. Sleepiness appears within 5 mins after intravenous administration of Dexmedetomidine and reaches its maximum within 15 min [4].

In our study,5 min after receiving loading dose of drug, patient in Dexmedetomidine group were oriented and tranquil with mean sedation score of 2 as compared to Midazolam group where mean sedation score was 1.32. Few patients in both group there was fall of saturation to 95-96% which returned to normal on asking them to take deep breath. Similar sedation without any adverse event of hypoxia obtained with similar dose of Dexmedetomidine in study by keniya [19] et al and Bajwa [20] et al.

In the study by Gulay Eren [12] et al shown that sedative effect of Midazolam at the dose of 0.02 mg/kg was not adequate, started later, and lasted shorter. They also noted that prevalence of hypoxia SpO_2 <90% was significantly higher with Midazolam 0.06mg/kg than in other group and two patient in that group needed O_2 support with mask. This suggests Dexmedetomidine causes better sedation without respiratory depression.In our study mean dose of induction agent Thiopentone required was 262.40 mg for Dexmedetomidine group which was less as compared to 334.36 mg in Midazolam group and the difference was statistically significant.

Similar were finding of study by V. Keniya [19] et al who observed 30% decrease in dose requirement of Thiopentone for induction in Dexmedetomidine group as compared to control group when same dose of Dexmedetomidine as ours was used. In our study dose of Propofol required intra-operatively in Dexmedetomidine group was (32mg) much less as compared to Midazolam(194 mg) group. Our results were comparable to that of Ghodki [6] et al .

Intra-operative requirement of Fentanyl (65±15.21μg) was significantly reduced as compared (93.4±30.98μg) to Midazolam group. Similar results were observed in study by Bajwa [20] et al in whom mean Fentanyl dose required was 1.2 μg/kg in Dexmedetomidine as against 2.6±1.2 in control group. This suggested that opioid sparing property of Dexmedetomidine in perioperative period.

On comparing hemodynamic parameter in Midazolam group HR, SBP, DBP, MAP increased from baseline with loading dose and persisted after induction, intubation and during entire period of pneumoperitonium, at extubation and even in PACU while in Dextmedetomidine group heart rate systolic, diastolic, and mean BP fell from baseline with loading dose and after that minimal change was observed at induction, intubation, during entire perioperative period of pneumoperitonium, at extubation and even in PACU.

The similar result obtained with Chiragpatel [22] et al Dexmedomidine as compared to Midazolam group effectively controlled vasopressor response during laryngoscopy intubation and sympathoadrenal response occurring with pneumoperitonium. This hemodynamic stability shown by Dexmedetomidine is due to decreased central sympathetic outflow and thereby attenuating increase in serum epinephrine and norepinephrine from baseline [23].

Only one patient in Dexmedetomidine group developed hypotension which responded to fluid therapy similar result were obtained by Feld [24] et

al, Ghodkiet al, M Aho et al. Various studies have used Dexmedetomidine in various dosage and shown that significant incidence of bradycardia and hypotension are definitely associated with rapid bolus or higher dosage.

Mean Ramsay sedation score in our patient was 1.16 in Dexmedetomidine group while 1.08 in Midazolam group. Bajwa et al observed significantly better sedation score in group Dexmedetomidine, attributed it to lower requirement of inhalational agent and other anaesthetic drug and analgesia as compared to control group but Chirag Patel [22] et al observed higher sedation score in Dexmedeto-midine group may be due to higher infusion rate and attributed it to sedative property of Dexmedetomidine however they found no difference in both group at end of 2 hour. PACU discharge time was slightly longer in Dexmedetomidine group as compared to Midazolam group similar finding was noted by Chirag Patel [22] et al Because lack of reliable and easily monitored clinical indices to determine anaesthesia depth we used haemodynamic end point because unavailability of EEG dependant indices in our institution Other limitation was we also carried out study in surgical procedure of short duration (<2 hrs) and in small no of patients, studied in ASA I/II, so larger study, long duration of surgery. Studies focusing its effect on more debilitated patients are needed.

In conclusion this randomised, double blind study demonstrated that when compared to Midazolam Dexmedetomidine is more effective anaesthetic adjuvant that causes adequate sedation without respiratory depression, decreases requirement of anaesthetic and opioid , attenuate sympathoadrenal response, maintains stable haemodynamicsperioperatively at the same time provide excellent recovery profile without any adverse events but continuous monitoring for hypotension and bradycardia is essential during first two hours of postoperative period if higher infusion rate are used.

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An Observational Study to Compare Intrathecal Midazolam and Clonidine for Post Operative Analgesia in Patients Undergoing Elective Hernia Surgeries

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Abstract

Background and Objectives: This observational study is designed to compare the intrathecal preservative free midazolam and clonidine, used as an adjuvant with hyperbaric bupivacaine for post operative analgesia in patients undergoing elective hernia surgeries. *Material & Methodology:* The observational study was conducted on 60 patients (using formula for Estimation of mean difference) of ASA grade I/II aged between 20 and 55 years posted for elective hernia surgeries under spinal anaesthesia. Group BM (midazolam group)– 15mg 0.5% hyperbaric bupivacaine+2mg preservative free midazolam made 3.5 ml with normal saline and Group BC (clonidine group) –15mg 0.5% hyperbaric bupivacaine +30µg preservative free clonidine made 3.5ml with normal saline. Onset and duration of sensory and motor blockade, Duration of Analgesia, Hemodynamic changes, Postoperative analgesic consumption in 24 hrs, Side effects/Complications (if any) were recorded. *Results:* There was a statistically significant difference in onset of sensory & motor block (pvalue< 0.01), and Duration of sensory & motor block (p value< 0.01) in BM group than BC group. Duration of analgesia was significantly prolonged in BM group (351.6±39.1min) as compared to BC group (252.5±21.1 min) (p value<0.01). *Conclusion:* Addition of 2mg midazolam (preservative free) to 0.5% hyperbaric Bupivacaine as an adjuvant intrathecally leads to early onset of sensory and motor block, prolongation of duration of sensory and motor blockade and prolongation of duration of analgesia as compared to 30 µg clonidine (preservative free) without any side effects in both the groups.

Keywords: Bupivacaine; Intathecal; Clonidine; Midazolam.

Introduction

Spinal anaesthesia with local anaesthetic is a favourable technique during both emergency and elective surgeries [1] but only local anaesthetics provide shorter duration of action. Hence many adjuvant are used to hasten the onset and to prolong duration of post operative analgesia.

Clonidine is used as an adjuvant in spinal anaesthesia to improve the quality and duration of post-operative analgesia [2].

Midazolam has been used in both animal [3,4] and humans [5,6], as an adjuvant intrathecally without any adverse effect.

This study is designed to compare the intrathecal midazolam (preservative free) and clonidine (preservative free) when used as adjuvant with hyperbaric bupivacaine for post operative analgesia in patients undergoing elective hernia surgeries.

Material & Methods

This study was conducted in Dhiraj general hospital in Department of Anaesthesiology, after institutional ethical committee approval on 60 patients aged between 20 and 55 years of both gender scheduled for undergoing elective hernia surgeries under spinal anaesthesia.

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Patients were divided into 2 groups with 30 patients in each group. Group BM (Midazolam group)– received 15mg 0.5% hyperbaric bupivacaine +2mg preservative free midazolam made 3.5 ml with normal saline and Group BC (clonidine group) –received 15mg 0.5% hyperbaric bupivacaine + 30µg preservative free clonidine made 3.5ml with normal saline.

Sample size is calculated using formula below:

$$n = \frac{f(a,b)\times 2\times(SD1 - SD2)^2}{(d1 - d2)^2}$$

Where

n= sample size required in each group

SD1 = 2.21 hours is standard deviation of reference study for duration of analgesia of 2mg midazolam

SD2 = 0.87 hours is standard deviation of reference study for duration of analgesia of 30 µg clonidine

d1= 6.52 hours is mean of reference study for duration of analgesia of 2mg midazolam

d2= 4.94 hours is mean of reference study for duration of analgesia of 30 µg clonidine

ASA I & ASA II patients undergoing spinal anaesthesia and patients in the age range 20-55 years were included in the study.

Patients with systemic diseases, anaemia, severe hypovolemia, shock, septicemia, hypertension, coagulation disorders or on anticoagulant therapy, local infection at the site of proposed puncture for spinal anaesthesia, spinal deformities, known allergy to the trial drug and those who are not willing for spinal anaesthesia were excluded from the study.

Pre–anaesthetic check up was done one day prior to the surgery. Patient was evaluated for any systemic diseases and laboratory investigations were recorded. The procedure of spinal anaesthesia was explained to the patients and written and informed consent obtained. All patients were kept NBM for atleast 8 hours.

On the day of surgery, the patient was shifted to the operating room. On arrival in the operating room standard monitoring was applied; ECG, non invasive arterial blood pressure, pulse rate and arterial oxygen saturation were monitored. Baseline vitals were recorded – Pulse, B.P, SpO_2. IV line was secured and preloading was done with 10ml/kg of ringer lactate. Patient was premedicated with Inj. Glycopyrrolate 0.2mg IV and Inj. Ondansetron 4 mg IV. Patient was positioned in the sitting position. Painting & draping of patients back was done with povidine iodine solution, study drug was injected in L3-L4 intervertebral space with 23 G spinal needle after free flow of cerebrospinal fluid. The patient was placed supine immediately after injection.

All Patients of Both Groups were Monitored for

Sensory block: Onset, level using pinprick test, Motor block: Onset and duration of block using modified Bromage scale, pulse rate, systolic blood pressure, diastolic blood pressure, SpO_2, were monitored at: 0, 5, 10, 15, 20, 30, 45, 60, 75, 90, 120 minutes.

When the sensory block reached at T_8 level surgeon was allowed to start the surgery. Data was collected regarding the onset of sensory block (Time taken from intrathecal injection to loss of pinprick sensation at T_8) and duration of sensory block (Time from intrathecal injection to 2 segment regression) Motor block was tested by Bromage scale, time of onset (Time from intrathecal injection to grade 3 motor block) and duration of motor block (Time from intrathecal injection to grade 0 motor block) was recorded.Side effects/complications were noted and treated. Bradycardia was defined as pulse rate < 60/min and treated with IV atropine sulfate 0.6mg. Hypotension was defined as systolic BP less than 20% of the basal value and treated with IV mephentermine 6mg.

After completion of surgery patient was shifted to recovery room and watched for pulse,blood pressure, sensory level and duration of motor blockade. Pain score was assessed by prince henry's visual rating scale in postoperative period. Duration of analgesia was calculated from the time of intrathecal injection to the time when visual rating scale was 2. Total number of analgesics required in the first 24 hours were recorded.

Observation & Results

The distribution of patients with respect to age, height, weight, gender, ASA was statistically not significant in both the groups (p value > 0.05).

The mean time from intrathecal injection to onset of sensory analgesia at T8 level was 5.13±0.62 minutes in group BC and 4.28±1.28 minutes in group BM. The onset of sensory analgesia was significantly earlier in group BM as compared to group BC, which was highly significant (p value < 0.01).

The mean duration of sensory block was 154.46± 20.41 minutes in group BC & 199.66±15.80 minutes in group BM. It was significantly prolonged in Group BM as compared to Group BC (P<0.01)

The mean time from intrathecal injection to onset of motor block was 4.90 ± 0.75 minutes in group BC & 3.06±0.63 minutes in group BM . It was significantly faster in Group BM as compared to Group BC which was highly significant (p<0.01)

The mean duration of motor block was 164.86± 25.89 minutes in Group BC and 217.90±19.60 minutes in Group BM. It was significantly prolonged in Group BM as compared to Group BC which was highly significant (p<0.01).

There was statistically no significant difference in pulse rate between the two groups (p value > 0.05), at any interval of time during intraoperative and post-operative period.

There was statistically no significant difference in systolic and diastolic blood pressure and SpO_2 between the two groups (p >0.05) at any time interval intra as well as post operative period.

Table 1: Mean Duration of analgesia

Duration of analgesia	Group BC (mean ±SD)	Group BM (mean ±SD)	P value
Time interval (min)	252.50 ±21.16	351.66 ±39.11	< 0.01

Table 2: Postoperative analgesic consumption in 24 hours

Analgesic consumption (24 hours)	Group BC (mean±SD)	Group BM (mean±SD)	P value
Number	2.35 ±0.48	1.23 ±0.43	< 0.01

The mean duration of analgesia was 252.50 ± 21.16 minutes in Group BC and 351.66±39.11 minutes in Group BM. It was significantly prolonged in Group BM as compared to Group BC which was statistically highly significant (p<0.01).

Analgesic consumption for 24 hours postoperatively was less in Group BM as compared to Group BC which was statistically highly significant (p< 0.01).

No side effects were observed in either of the group.

Discussion

One of the mainstay of balanced anaesthesia is relief of pain during operation and in postoperative period. "Postoperative pain relief" is a growing concern for an anaesthesiologist, as an uneventful postoperative period makes all surgery comfortable proposition for surgical patients.

Spinal anaesthesia using local anaesthetics alone has shorter duration of action with early requirement of analgesia for postoperative pain relief.

So, many adjuvants have been used along with local anaesthetics "to hasten the onset of sensory & motor block and to improve quality and duration of postoperative analgesia, reducing postoperative analgesic requirements, without significant side effects, facilitating early ambulation & reducing the hospital stay of the patient".

In Our study, we had observed that the difference in demographic data (Age, Height, Weight, Gender distribution, American Society of Anaesthesiologists status) were statistically not significant among both groups. (p>0.05)

Similarly, *Agrawal Nidhiet al (2005)* [7], *Suchita A. Joshi et al (2012)* [8] observed no significant difference between the two groups with respect to age, weight, height, gender of the patient and ASA status.

Racle et al (1987) [9]: used 150 µg of clonidine interathecally with isobaric bupivacaine for hip surgery. He observed more episode of hypotension.

Shah BB et al (2012) [10]: used 60µg, 30µg and 15µg clonidine in spinal anaesthesia for caesarian section & observed that addition of 60µg clonidine to intrathecal bupivacaine provided longer duration of postoperative analgesia than 15µg or 30 µg clonidine but with more sedation than 15µg or 30

µg clonidine, so 15µg or 30 µg clonidine as a preferred option when sedation is not desirable. Duration of analgesia was significantly higher in 30µg clonidine than 15µg clonidine ($p<0.05$).

In our study, we used 30 µg of clonidine intrathecally with hyperbaric bupivacaine as150 µg of clonidine causes more hypotension and duration of analgesia was less with 15 µg as observed in above studies. 30µg was safer dose with minimal side effect. In our study, we had added 2mg of midazolam to hyperbaric bupivacaine.

Kim M.H. (2001) [11] used 1 mg and 2 mg of midazolam with bupivacaine intrathecallyand he found dose dependent effect of intrathecal midazolam. *Bharti N et al (2003)* [12] *and Yegin A et al (2004)* [13] administered 2 mg midazolam with bupivacaine intrathecally.

The dose of 2 mg midazolam was chosen because this was the optimal dose to relieve pain without producing negligible side effects.

In our study, we observed the onset of sensory block was statistically highly significantly early in Group BM as compared to Group BC ($p < 0.01$) and duration of sensory block was statistically highly significantly longer in group BM as compared to group BC. ($P<0.01$)

Vaswani RK et al (2002) [14]: observed same result as in our study regarding onset and duration of sensory block. ($p< 0.01$)where as *Yegin A et al (2004)* [13]: observed no statistically significant difference in the onset and duration of sensory block in both groups. In our study, we observed the onset of motor block was statistically highly significantly early in Group BM as compared to Group BC ($p < 0.01$) and duration of motor block was statistically highly significantly longer in group BM as compared to group BC.($P<0.01$).

Bharti N et al (2003) [12] observed same result as in our study regarding onset and duration of motor block. ($p< 0.01$) whereas *Yegin A et al (2004)* [13]*:* observed no statistically significant difference in the onset and duration of motor block in both groups.

In our study, we observed duration of analgesia was statistically highly significantly prolonged in Group BM as compared to Group BC ($p < 0.01$).

Suchita A. Joshi et al (2012) [8]: observed same result as in our study regarding duration of analgesia ($p< 0.01$).

In our study, there was no statistically significant change in mean pulse rate, systolic blood pressure, diastolic blood pressure and SpO_2, in both groups intraoperatively and post operatively ($p>0.05$).

Suchita A. Joshi et al (2012) [8]: observed same result as in our study regarding mean pulse rate, systolic blood pressure, diastolic blood pressure and SpO_2, in both groups intraoperatively and post operatively. ($p>0.05$).

In our study, complications like nausea, vomiting, rigors, hypotension, bradycardia were not detected with either agent in any patient.

Nidhi Agrawal et al (2005) [7] observed no episodes of bradycardia, hypotension, sedation and dizziness, vomiting and neurological deficit in both groups.

In our study, the mean postoperative analgesic consumption in 24 hours was statistically highly significantly less in group BM than in group BC ($p<0.01$).

Vaswani RK et al in (2002) [14]: observed same result as our study regarding mean postoperative analgesic consumption in 24 hours in both groups ($p<0.01$).

Conclusion

Addition of 2mg midazolam (preservative free) to 0.5% hyperbaric Bupivacaine as an adjuvant intrathecally leads to early onset of sensory and motor block, prolongation of duration of sensory and motor blockade and prolongation of duration of analgesia as compared to 30 µg clonidine (preservative free) without any side effects in both the groups.

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Original Research Article

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A Comparative Study between 10µg and 15µg of Dexmedetomidine as an Adjuvant to Intrathecal 0.75% Isobaric Ropivacaine in Patients undergoing Total Abdominal Hyterectomy

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Abstract

Introduction: Dexmedetomidine is being increasingly used to prolong the duration of subarachnoid block. Various doses of dexmedetomidine are in practice. Isobaric Ropivacaine for its reduced cardiotoxicity and early motor recovery has gained edge over bupivacaine for subarachnoid block. *Aims and objectives:* To assess the efficacy and safety of two different doses of dexmedetomidine i.e 10µg and 15µg as an adjuvant to 0.75% isobaric ropivacaine intrathecally for abdominal hysterectomy surgeries. *Materials and Methods:* This prospective randomized and double blind study was conducted in 60 female ASA I and II patients scheduled for hysterectomy surgeries were randomized into two groups A and B. Group A received 2.5ml of 0.75% isobaric ropivacaine and 10µg dexmedetomidine whereas group B received 2.5ml of 0.75%isobaric ropivacaine and 15 µg dexmedetomidine. Onset and duration of sensory and motor block, hemodynamic variables were recorded and compared between the two groups. *Results:* The mean onset time of sensory and motor block of group A was 5.52±0.28mins and 6.95±0.22mins respectively whereas in group B was 4.48±0.35 and 6.1±0.28 mins which was statistically significant ($p<0.0001$). Duration of sensory and motor blockade in group A was 423±12.85 and 382±9.25mins respectively whereas in group B was 587±10.83 and 530±15.78 mins which was statistically significant ($p<0.0001$). There was no significance in hemodynamic and side effects between two groups. *Conclusion:* Our study showed that 15µg of Dexmedetomidine provided rapid onset and prolonged duration of subarachnoid block with isobaric 0.75% ropivacaine without significant side effects.

Keywords: Dexmedetomidine; Isobaric Ropivacaine; Subarachnoid Block.

Introduction

Subarachnoid block with Bupivacaine has been the choice of anesthesia for many decades for abdominal hysterectomy surgeries. Its S-enantiomer Ropivacaine has gained popularity for its early motor recovery, less cardiotoxicity and higher threshold for central nervous system toxicity (CNS) compared to bupivacaine [1]. Intrathecal isobaric (glucose-free) 0.75% ropivacaine in the dose of 15 and 22.5 mg produced a sensory block of variable extent with a proportion of patients requiring general anesthesia because of inadequate duration of block [2]. Various adjuvants like clonidine, fentanyl or dexmedetomidine were used along with isobaric ropivacaine. Intrathecal dexmedetomidine has been used in the dose of 3 µg, 5 µg , 10 µg and 15 µg along with bupivacaine and in the dose of 5 µg and 10 µg as an adjuvant to plain ropivacaine.(3) So we compared 10 µg and 15µg of Dexmedetomidine with isobaric ropivacaine for subarachnoid block.

Materials and Methods

This prospective, randomized, double-blinded study was conducted in Narayana Medical college, Nellore from April 2017 to January 2018 with institutional ethical committee approval. After

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obtaining written informed consent, 60 female patients aged 20–60 years with American Society of Anesthesiologists (ASA) Physical Status class I–II who were scheduled for elective abdominal hysterectomies under subarachnoid block were divided into two groups A and B. Exclusion criteria included patient refusal for subarachnoid block, local sepsis at the site of proposed puncture, coagulation disorders, raised intracranial pressure, allergic reactions to study drug, patients on anticoagulants, bleeding diathesis, spinal anatomical deformities, uncooperative patients like with psychiatry diseases etc.

All the patients received tab.Alprazolam 0.5mg as premedication on the previous night. Standard fasting guidelines were followed. On the day of surgery in the operation theatre after securing wide bore i.v cannula, patients were preloaded with 15ml/kg of Ringers lactate solution. Standard monitors like heart rate(HR), noninvasive blood pressure(NIBP), pulse oxymeter and electro cardiography were connected. Subarachnoid block was performed in lateral position in L2,3 space intervertebral space with 25G quincke babcock spinal needle.

Group A patients received 2.5ml (18.75mg) of isobaric ropivacaine (0.75%) plus 10µg Dexmedetomidine (0.4ml) .

Group B patients received 2.5ml (18.75mg) of isobaric ropivacaine (0.75%) plus 15µg Dexmedetomidine (0.4ml).

Onset and duration of sensory block was assessed by pinprick method. Motor block was assessed using bromage scale. Haemodynamic variables like heart rate,mean arterial pressure were measured at 0, 3, 5, 10, 15, 30, 60, 90, 120, 150, 180 mins. Side effects like hypotension, bradycardia, sedation, nausea and vomiting were noted. Hypotension (defined as a decrease in systolic blood pressure > 30% of the baseline value or systolic blood pressure < 90 mm hg) was treated with intravenous boluses of 3 mg mephentermine. Bradycardia defined as heart rate of < 50 beats/min was treated with boluses of 0.6 mg atropine.

Statistical Analysis

All recorded data were entered using MS Excel software and analysed using SPSS 20 version software for determining the statistical significance. Results were presented as mean+standard deviation. Proportions were compared using Chi-square test. Statistical difference between both the study groups was determined by student 't' test. p <0.0005 was taken as statistically significant, p value of <0.0001 was considered as extremely statistically significant.

Results

Sixty patients scheduled for abdominal hysterectomy in the two groups were statistically comparable in age, weight, height, operative time (Table 1) Onset of sensory blockade in group B (4.48±035 mins) compared to group A (5.5±028mins) was significantly shorter which was extremely statistically significant (p<0.0001). Onset of motor blockade in group B (6.1 mins) compared to group A was shorter (6.95 mins) which was statistically extremely significant (p<0.0001) (Table 2 Figure 1). Duration of sensory blockade in group B (587 mins) was significantly prolonged compared to group A (423mins) which was statistically extremely significant (p<0.0001). Duration of motor blockade

Table 1:

Demographic Variables among the groups	Group D	Group M	P Value
Age in years (Mean±SD)	39.18±12.13	38.87±10.12	0.954
Height in cms (Mean±SD)	166.88±66	164.32±2.10	0.63
Weight in kgs (Mean±SD)	58.45±3.26	60.32±7.22	0.52
Duration of Surgery (Mean±SD)	104±4.32	103±5.61	0.58

Table 2:

	Group A	Group B	P Value
Onset of Sensory	5.52±0.28	4.48±0.35	P<0.0001
Onset of Motor	6.95±0.22	6.1±0.28	P<0.0001
Duration of Sensory	423±12.85	587±10.82	P<0.0001
Duration of Motor	382±9.25	530±15.78	P<0.0001
Side Effects			
Hypotension	5(16.60%)	11(36.66%)	P=0.774
Bradycardia	4(13.33%)	9(30%)	P=0.109

in group B (530 mins) was again significantly prolonged compared to group A (382 mins) which was statistically extremely significant ($p<0.0001$) (Table 2 Figure 2). There was no statistically significant difference in hemodynamic variables like heart rate, Mean arterial pressure though there was initial fall in heart rate and mean arterial pressure in both the groups (Figure 3, 4). Side effects were also comparable between both the groups (Table. 2, Figure 5).

Fig. 1:

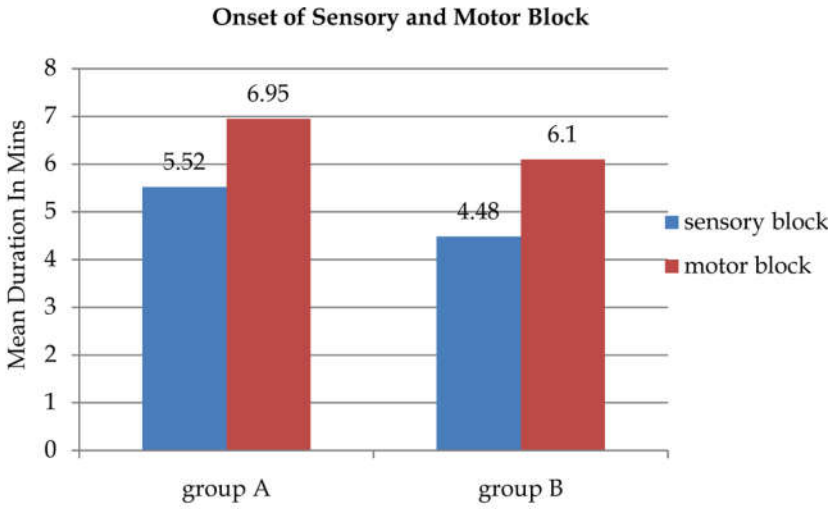


Fig. 2:

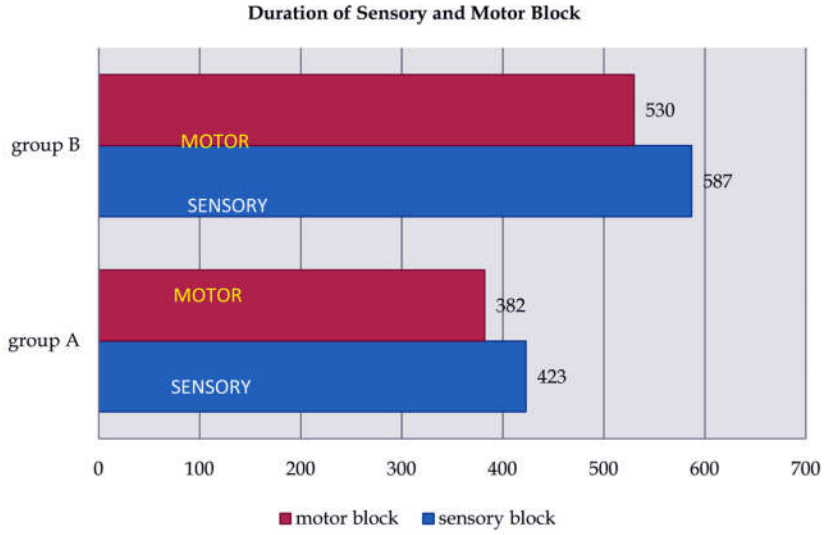
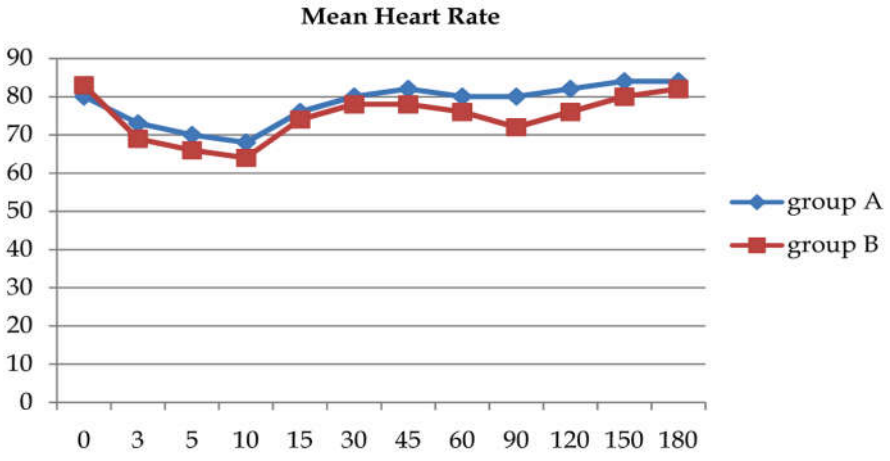


Fig. 3:



Discussion

The main limitation of local anesthetics when used alone for subarachnoid block was the shorter duration of the block they produce [4]. which prompts the anesthesiologists to use various analgesics very early in the postoperative period. Traditionally, Bupivacaine is the most commonly used local anesthetic for spinal anesthesia. Adjuvants like fentanyl, ketamine, tramadol, clonidine and Dexmedetomidine etc were added to bupivacaine to prolong the duration and reduce the postop requirement of analgesics.

Ropivacaine, a newer amide local anesthetic, has forayed into anesthetic practice and is substituting bupivacaine because of its less cardiotoxicity, early motor recovery and duration of anesthesia similar to bupivacaine. Akin to Bupivacaine many adjuvants have been added to isobaric ropivacaine to increase its duration. Addition of fentanyl, clonidine [5] and Dexmedetomidine [3] to isobaric 0.75%ropivacaine have been studied to prolong the duration of both sensory and motor blockade.

Intrathecal alpha-2 adrenergic agonists have a thorough synergistic effect with local anesthetics because both have different mechanism of action. The local anesthetics act by blocking sodium channels, whereas the alpha 2 adrenergic agonists act by binding to presynaptic c-fibers and postsynaptic dorsal horn neurons [6,7]. Intrathecal Dexmedetomidine when joined with spinal local anesthetics prolongs the sensory block by depressing the release of c-fibers transmitters and by hyperpolarization of postsynaptic dorsal horn neurons.

Motor block prolongation by alpha 2 adrenergic agonist may be due to attachment of alpha 2 agonists to motor neuron in the dorsal horn of the spinal cord [8] intrathecal alpha2 agonists possess antinociceptive action for both somatic and visceral pain [9]. Hence, use of Dexmedetomidine as an adjuvant to isobaric ropivacaine causes significant prolongation in duration of analgesia [10,11].

Previous literature shows a 1:10 equivalence dose ratio between Dexmedetomidine and clonidine, with a maximally effective dose of intrathecal clonidine equating to 150µg [12]. Considering the dose ratio, theoretically maximal effective dose of Dexmedetomidine comes out to be 15µg. Hence we choose 15mcg Dexmedetomidine in our study and compared it with 10µg dexmedetomedine which was more frequently studied compared to 15µg.

Singh, et al evaluated the efficacy of two different doses of dexmedetomidine i.e 5 or 10 µg to 0.75% isobaric ropivacaine and concluded that Dexmedetomidine appears to augment the efficacy of intrathecal ropivacaine in a dose dependent manner without associated increase in the incidence of associated adverse effects [13].

Naithani, etal have studied 0.5% isobaric ropivacaine (15 mg) with dexmedetomidine (3 µg or 5 µg) for spinal anesthesia which did not show much promise for abdominal hysterectomy as one third cases required analgesic supplementation [14].

Very few studies were done on 15µg of Dexmedetomidine with Ropivacaine. So we compared 10 and 15µg of Dexmedetomidine added to isobaric 0.75% Ropivacaine. We have observed that 15µg of Dexmedetomidine (Group B) provided faster onset and prolonged duration of sensory and motor block compared to 10µg dexmedetomidine (group A).

Though 16% of patients in group A and 36% in group B developed hypotension, the difference was not statistically significant. Similarly 10% of patients in group A and 30% in group B developed Bradycardia which was not significant statistically. None of the patients developed nausea vomiting, shivering and respiratory depression.

Conclusion

We conclude that intrathecal Dexmedetomidine in dose of 15 µg as an adjuvant to isobaric ropivacaine significantly hastens the onset of action of sensory and motor block and increases the duration of sensory and motor block when compared to intrathecal Dexmedetomidine 10mcg without any associated adverse effects.

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A Comparison of General and Spinal Anaestheia for Elective Lower Lumbar Spine Surgeries in Lateral Position

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Abstract

Introduction: General anesthesia (GA) is the common mode of anesthesia for spine surgery. However, with spine surgeries being increasingly performed in lateral, as against prone position, spinal anaesthesia (SA) is becoming more acceptable. This study was conducted to compare general and spinal anaesthesia in lumbar spine surgeries performed in lateral position. *Materials and Methods:* Patients with ASA I-II, planned to undergo single level lumbar laminectomy in lateral position were randomized into GA and SA group by computer generated random numbers. The former were given GA with endotracheal intubation as per standard protocols and latter were given SA with 3.2mL 0.5% hyperbaric bupivacaine. Surgery was performed in lateral position. Intra-operative hemodynamic events, post-operative sedation score, pain status, surgeon satisfaction, total time and complications were recorded and analysed. *Results:* 79 patients were studied. Mean heart rate and blood pressure were lower in SA group at various stages during surgery. Total time in operation room was 119 minutes in GA while only 94 minutes in SA group. VAS score was higher in GA group at 2 and 12 hrs post-operatively (5.2 v/s 2.4 and 4.0 v/s 2.7 respectively). Total consumption of tramadol in 24 hrs was higher in GA as compared to SA group, (mean ampoules, 3.12 v/s 2.19). Sedation score (mean grade, 1.18 v/s 0.06) and blood loss > 400 mL were higher and surgeon satisfaction lower in GA group. *Conclusion:* Spinal anaesthesia is a better alternative to general anaesthesia for lower lumbar spine surgeries when operated in lateral position.

Keywords: Spinal Anaesthesia; Spine Surgery in Lateral Position.

Introduction

General Anaesthesia (GA) has been the usual mode of anesthesia for spine surgeries, but regional anaesthesia is lately being evaluated as a possible alternative for lower lumbar spine surgeries [1,2]. Hence, choice of anaesthesia has become a topic of intense debate [3]. In a vast majority of patients, spinal anaesthesia (SA) would compare favorably with GA on several parameters. Hemodynamic stability, low intra and post-operative cardiac events, low blood loss and better post-operative pain control are some of the obvious advantages of SA over GA. Other advantages of SA is the ability for the patient to reposition their extremities and chest as needed to avoid nerve injury, brachial plexus palsy or pressure necrosis to the face and pressure over the eye.

Yet, a need for prone position is the main concern against the use of SA. Incikara et al [4] feels that even though anaesthesiologists would consider SA more preferable, experience shows that prolonged operations in prone position under SA increases anaesthesiologist's stress. Particularly owing to potential challenges in the event of an apnea, providing airway access and placing an ETT which are extremely difficult in prone position.

In recent times however, surgeons themselves are preferring lateral position for lumbar spine surgeries. Suhail Afzal [5] et al explained the

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advantages they gain as surgeons by operating in lateral position: Lateral position is favorable for both anterior and posterior approach to spine, less pressure on anterior abdominal wall and reduced venous engorgement resulting in reduced bleeding, easy change of positions between kyphosis and lordosis just by altering hip and knee positions etc. In addition, the complications often encountered with prone positions [6,7] are avoided. Compression of abdomen and inferior venacava resulting in hemodynamic changes, pressure necrosis, brachial plexopathy, ophthalmic complications including permanent blindness are some of the more dreaded complications that can be avoided by resorting to SA. These complications are more frequent and far more severe in prone as compared to complications that are specific to lateral position.

This changing scenario of spine surgeries being increasingly performed in lateral positions [5,8] is thus an opportunity to make good use of regional anesthesia and exploit all its advantages over GA. For that, it is hence necessary to evaluate if SA is acceptable or even more desirable as compared to GA in objective terms as applied to both the anesthesiologist and surgeon's view. Despite there being numerous studies [9-15] that have compared GA with SA in spine surgeries, the same in exclusively lateral position has not been undertaken. It is common understanding that conditions vary considerably while operating in lateral position, with respect to operative ease, hemodynamic stability, complications and risk factors. Hence, the present study was conducted to compare SA and GA in lower lumbar surgeries when performed in lateral position.

Materials and Methods

Study Design

The study was conducted in a tertiary care teaching hospital in northern India. The study design was a non-blinded prospective randomized control trial. Ethical committee clearance was taken. Written informed consent was taken from all the patients. All procedures were performed by same surgeon; anesthesia was managed by anesthesiologists of a single unit working on a common protocol.

Sample Size Estimation

A pilot study conducted at our institute in patients undergoing spinal surgery under general anaesthesia revealed a 24 hr postoperative VAS score of 6.5 with a standard deviation of 2.34. We postulated that a VAS at 2 hr will be reduced to 4.5 by using central neuraxial blockade. For the study to have a power of 90% with an alpha- error of <0.05, a minimum of 29 patients were to be registered in each group. To compensate for the dropouts, we decided to take around fourty patients in each group.

Inclusion/ Exclusion Criteria

Consecutive willing patients between 18 and 60 years of age who were scheduled for single level lumbar laminectomy with or without discectomy at levels L2 and below were selected. Only ASA-PS I or II were included. Patients with history of seizure, intracranial hypertension, contraindication for spinal anesthesia (patient refusal, coagulopathy, infection at site of needling, hypovolemia), severe spinal stenosis, infectious process, patients with hepatic or renal disease, severe cardiac disease, or bleeding abnormalities, drug or alcohol abuse were excluded. Also those undergoing revision surgery or requiring surgical stabilization or fusion were excluded from the study.

Group Allocation

Group GA: Patients were given General Anaesthesia with Endotracheal Intubation as per standard protocols.

Group SA: Patients were given Spinal Anaesthesia with 3.2 cc 0.5% hyperbaric bupivacaine

Tecnique of Anaesthesia

Patient profile, diagnosis, plan of treatment, ASA grade and patient neurological deficits were recorded. Patients were randomized using computer generated random numbers into two groups. In GA group, all patients received as premedication a intravenous dose of midazolam 1.5 mg , glycopyrolate 0.2 mg, ondansetron 4 mg and fentanyl 2mcg.kg^{-1}. Patients were induced on the operating table with IV propofol 2mg.kg^{-1}. Endotracheal intubation was facilitated with rocuronium (0.9 mg.kg^{-1} IV). Anesthesia was maintained with dial setting of 1 vol% sevoflurane and nitrous oxide 50% in oxygen. Subsequently, the patients were placed in lateral position, with pillow in between the arms to protect them from brachial plexus injury. For prevention of pressure on globe of the eyes and ears, the head was placed on a soft pad.

The heart rate, mean arterial non invasive blood pressure and oxygen saturation were monitored every 15 minutes during surgery using ECG, noninvasive blood pressure monitoring and pulse oximetry. After termination of operation, patient was returned to supine position. Anesthetic drugs were discontinued and 100% oxygen was given. Neuromuscular blockade was reversed with neostigmine ($0.05mg.kg^{-1}$) and glycopyrrolate ($0.01mg.kg^{-1}$). Extubation was done and the patient transferred to the postanesthesia care unit (PACU) after ensuring spontaneous respiration, oxygen saturation of 95% or more, end-tidal carbon dioxide 35-40 mmHg, respiratory rate less than 30 per minutes, and tidal volume more than 5 $mL.kg^{-1}$.

In SA group, patients were preloaded with 10 $mL.kg^{-1}$ lactated ringer's solution over 10-15 minutes. Sub-arachnoid block was performed using a 25-gauge Quinke spinal needle at either the L2-L3 or L3-L4 interspace. After observing spinal fluid, 3.2 mL 0.5% bupivacaine in an 8.5% dextrose solution was administered into intrathecal space and patients were placed in supine position. Establishment of spinal level of block (which usually occurred between T-6 and T-10), was tested for a loss of pin-prick sensation. Five minutes later, patients were placed into lateral position and were allowed to keep their arms at ease by placing a pillow between them. Oxygen at $5L.min^{-1}$ via venti-mask was administered during the surgery. At the start of the surgery, midazolam 1.5mg i.v and ondansetron 4mg was administered intravenously.

During surgery, any bradycardia (HR<50 per minutes) or hypotension (MBP<60 mmHg) were managed with atropine 0.5 mg and mephenteramine 5 mg intravenous respectively. At the end of surgery, the patient was turned from lateral position to supine, hemodynamic stability was confirmed and the patient was transferred to the PACU. In group GA, when patients were awake and had no pain, nausea, vomiting, or hemodynamic instability, they were shifted out from PACU. In group SA, when patients had no pain, nausea, vomiting, and at least two segment regression of spinal block, they were shifted out.

Outcome Assessment

Throughout the administration of anesthetics, changes in maximum heart rate and mean arterial blood pressure as compared to the baseline were recorded. Blood loss was monitored and recorded by calculating the volume of blood suctioned from the surgical field and sponge count. Blood loss >400mL was considered as major blood loss for spine surgery.

The operating surgeon was asked to record 'surgeon satisfaction' as a dichotomized factor immediately after the procedure while he was removing the gloves. He was asked to mentally compare the present surgery with his past experience with respect to but not limited to factors like oozing in the surgical field, being motionless, muscular relaxation and overall impression and comment if he was satisfied in 'Yes' or 'No'. Total time in the Operating Room (OR) (the time from the entry of patient into the OR till the patient is shifted out of operating room), the time taken for induction, positioning (turning into lateral position), pre-op preparation (scrubbing, painting and draping), duration of surgery (incision to skin closure), and exit time (end of surgery to leaving the OR) were recorded. In both the groups, patients were observed for 30 minutes in the recovery room. Anaesthesia time excluding the surgical time was also noted.

Sedation score was measured in all patients, as soon as they enter the recovery room, using a 4-point sedation score [16],

Grade 0- Awake

Grade1-Drowsy

Grade2-Sleeping but arousable on verbal commands

Grade 3-sleeping but arousable on tactile stimulation

Over the next 24 hrs, severity of pain was assessed using VAS score [17] at 2, 6, 12, 18 and 24 hrs in both groups. If the VAS score was more than 4, tramadol 100mg was given intravenously and, and the total ampoules of tramadol consumed in 24 hrs was recorded. In addition, the incidence of nausea was recorded. Intravenous metoclopramide at 0.1 $mg.kg^{-1}$ IV was administered to patients with vomiting and for nausea if lasted for more than 10 minutes.

Any case with failure of anesthesia or inability to adhere to the study protocol was excluded from the study.

Statistical Analysis

Continuous data were presented as mean±SD and categorical data were presented as percentage within the group. The mean values of two groups in the former variables were compared using Student t-test and latter by Pearson Chi-square test

and Fisher's exact test when needed. P-value < 0.05 was considered statistically significant. All statistical analyses were done using SPSS version 16.

Results

A total of 79 patients were randomized. There were 40 patients in GA group (Group I) and 39 in SA group (Group II). Two patients from SA group were later converted to general anesthesia and hence were dropped from the analysis (Fig 1. Consort Diagram). Demographic characteristics like age, sex, weight and ASA status are tabulated and were found to be comparable between the two groups (Table 1).

Baseline mean HR was comparable in both the groups, mean HR and MBP were lower in SA group during surgery as compared to GA group, which is statistically significant throughout the surgery. (Table 2).

VAS Score (Table 3) was higher in GA group at 2 hrs (5.2±0.6) and 12 hrs (5.6±0.67)and in SA group at 6 hrs(4.84±0.89) which were statistically significant (p<0.001). Overall the mean number of doses or ampoules of Inj. tramadol consumption(100 mg/ ampoule) was higher in GA group (3.12±0.33) as compared to SA group (2.19±0.40) (p<0.001)

Time in the OR was compared between the 2 groups (Table 4). Most of the time recordings were higher in GA group as compared to SA group with statistically significant difference. Overall 25 min was less in SA group as compared to GA group.

Both the groups were observed for 30 min in the recovery room, and we found that overall sedation score was higher in GA group (1.18±0.38) compared to SA group (0.06±0.002) with p<0.001.

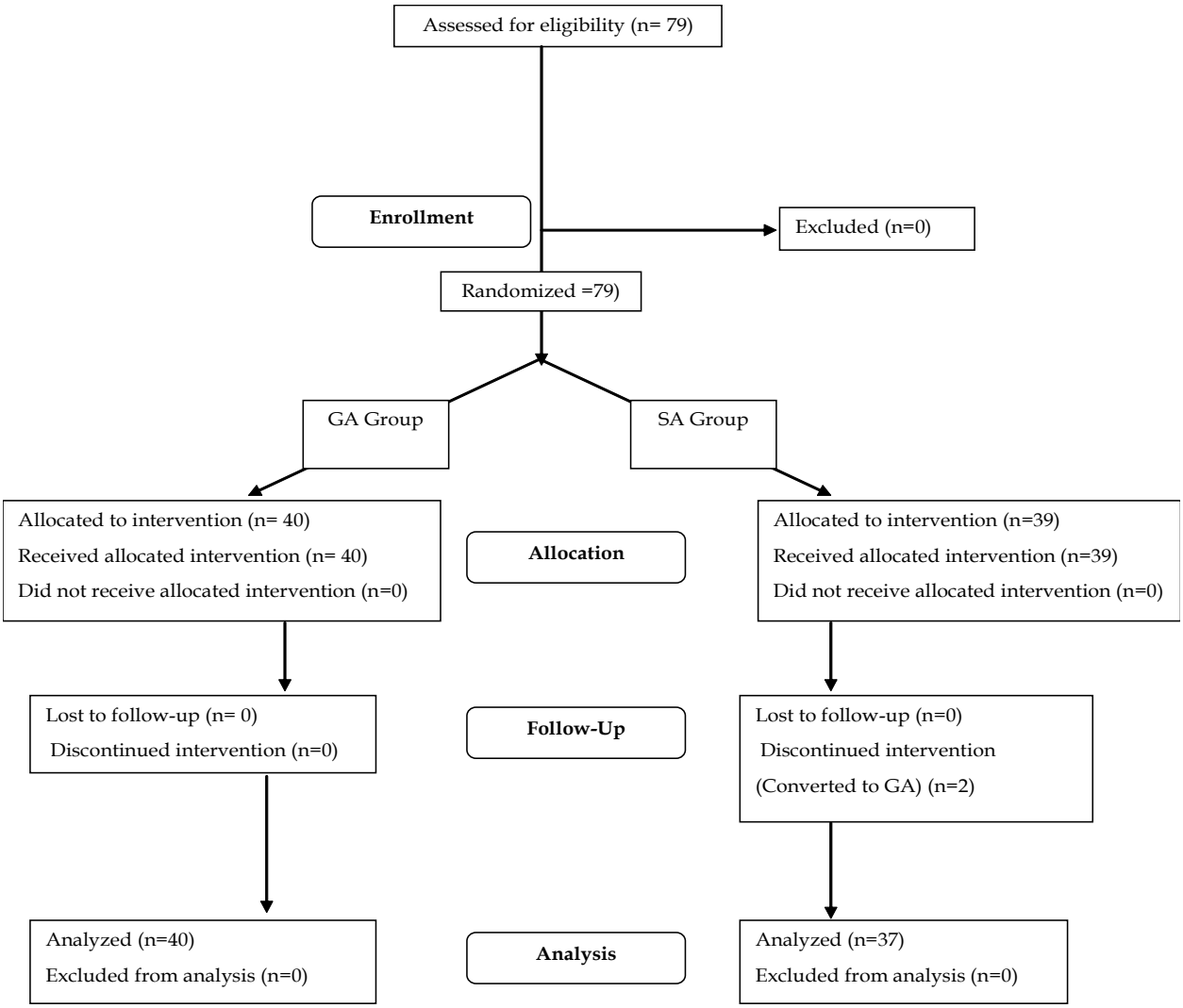

Fig. 1: Consort Diagram

Table 1: Demographic characteristics

Demographic Characteristics		GA	SA
AGE (years) (Mean ± SD)		49.50±8,73	50.95±10.11
SEX n (%)	M	24 (60%)	22 (59.5%)
	F	16 (40%)	15 (40.5%)
WEIGHT (Kg) (Mean ± SD)		63.70±6.32	66.24±8
ASA (number of patients)	I	28	21
	II	12	16

Table 2: Haemodynamic variations(Data are presented as mean ± SD)

Minutes		0	15	30	45	60	75	90
HR (BPM)	GA	87±4.17	92.70±3.1	87.50±50	85.10±3.6	85.40±6.2	90.1±6.2	91.3±4.4
	SA	87.9±4.4	84.9±6.1	81.86±7	79.95±5.7	78.65±5.4	75.68±5.17	76.4±4.8
	p-value	0.35	0.000	0.000	0.000	0.000	0.000	0.000
MBP (mm Hg)	GA	67.8±3.9	70.2±3.8	73.9±2.3	72.8±3.8	74.5±8.7	74.4±4	75.3±5.3
	SA	70.2±3.8	68 ±4.2	66.41±4.6	65.2±2.5	63.9±2.9	64.32±2.4	63.73±2
	p-value	0.008	0.000	0.000	0.000	0.000	0.000	0.000

Table 3: VAS Score (Data are presented as mean±SD)

	VAS-2 hours	VAS-6 hours	VAS-12 hours	VAS-18 hours	VAS-24 hours
GA	5.2±0.60	2.50±0.50	4±1.60	2.40±0.54	2.70±0.648
SA	2.38±0.49	4.84±0.89	2.65±0.48	2.38±0.54	2.49±0.50
p-value	<0.001	<0.001	<0.001	0.862	0.114

Table 4: Duration in the OR (in minutes) (Data are presented as mean±SD)

Duration (min)	Induction	Positioning	Pre-op prep	Surgery	Exit	Total Time	Anaesthesia Time
GA	11.70±0.68	4.60±0.49	5.40±0.49	50±2.9	15.7±0.79	119.2±6	89.20±6
SA	8.68±0.68	3.38±0.63	5.41±0.49	44.30±4.30	4.65±0.58	94.24±4.9	65.32±6.6
p	0.000	0.000	0.962	0.000	0.000	0.000	0.000

Surgeon satisfaction in SA group was 78.4% compared to GA group in which surgeon was satisfied in only 30% of the cases. (p<0.001). Blood loss> 400mL was seen in 67.5% in GA group which was higher compared to SA group where blood loss >400mL was seen in 18.9% of cases (p<0.001).

Nausea and vomiting occurred in 28 (70%) patients in GA group compared to only 2 (5.4%) patients in SA group. Three patients in SA group had episodes of hypotension and 1 patient in SA group had bradycardia. Three patients in SA group and 3 patients in GA group had urinary retention post-operatively. None of the patients in our study had episodes of desaturation and all patients maintained oxygen saturation > 95% throughout the surgery till shifting out from the recovery room

In SA group, two patients had discomfort after 15 minutes of spinal puncture and were promptly converted to GA with ETT. They were not included in the study. No other patient of SA complained of pain, anxiety or discomfort during the procedure.

Discussion

The study on many counts showed that, SA is actually better than GA for lower lumbar spine surgeries operated in lateral position. Intraoperative and postoperative hemodynamics were more stable in SA group compared to GA group. GA group showed episodes of hypertension and tachycardia. They were mainly due to laryngoscopy-intubation response, during extubation and immediate post-operative pain. Similar phenomenon were noted by Attari et al [9] and Jellish et al [18] studying regional and general anesthesia in spine surgeries.

Although there are studies [4, 8-12] which support that SA is more acceptable for lower lumbar spine surgeries, other authors contradict [15,19] the same. With respect to spine surgery in particular, the safety of SA was questioned by Hebl et al [19] who felt that pre-existing spinal canal pathology have higher incidence of neurological complications after neuraxial blockade than that previously reported

for patients without such underlying pathology. However, Reynolds et al [20] in his study concluded that patients with spine pathology who were operated under epidural anaesthesia, neurological deficits improved at the same rate as those operated on by the same surgeon under general anaesthesia.

Blood loss was found to be less in the SA group. Serkan [21] and Incikara [4] had similar findings, although the latter did not find statistical significance in the difference. It is generally thought to be due to two mechanisms. Sympathetic blockade by SA causes vasodilation leading to hypotension. Hence the bleeding is less vigorous and easily controllable. Secondly GA increases intrathoracic pressure due to assisted breathing. The paravertebral vessels thus get engorged leading to increased bleeding. It has also been explained by Reynolds et al [20] , in epidural anaesthesia for spine surgeries. We also feel that increased fluctuations of blood pressure noted in GA group also contributed to an increased bleeding in that group. Less bleeding also contributed to lower surgical time observed in SA group as it would facilitate dissection and removal of disc and result in less time needed to effect hemostasis prior to surgical closure.

In addition to a reduction in surgical time, SA group also showed significantly less time for induction, positioning, surgical time and exit as compared to GA. Around 25 minutes could be saved in SA group as compared to GA group. This is essentially a difference in the conduct of the two types of anesthesia. The same was also the finding by Helene Singeisen et al [22], who compared spine surgeries under both the anesthesias. Time factor becomes important in improving the efficiency of the operating room and the hospital. Agarwal et al[23] studied the cost analysis in GA and SA for spine surgeries and concluded that SA is less costly when used in patients undergoing lumbar discectomy and laminectomy. Singeisen et al [22] also found that reduction of time in OR also resulted in marked reduction in hospital costs.

Perhaps owing mainly to these reasons, overall surgeon satisfaction was greater in SA group as compared to GA in our study. Although Attari et al [8] and Incikara et al [4] also found similar result in their study in prone position, Sadroldadat et al [15] found it otherwise.

GA group with higher sedation, needed to be given oxygen through ventimask post-operatively and SA group patients were awake and did not require post-operative oxygen. The higher sedation scores in GA group could be attributed to the GA drugs and inhalational anaesthetics. This was also observed in study conducted by Attari et al [9] which showed, reduction in the duration of recovery stay.

Though not specific about patient position, McLain et al [10] reported that regional and general anaesthesia have similar effectiveness for performing elective lumbar surgeries and also regional anaesthesia showed some advantages over GA, including improved perioperative hemodynamic stability, decreased analgesic requirement, and decreased occurrence of postoperative nausea. The same co-related with our study. Hassi et al [14] also had similar results, but he said SA cannot be recommended in all cases, particularly in patients, where the surgical time may get prolonged since in his paper, patients were operated in prone position.

Lower postoperative VAS scores at 2 hours in SA group may be explained by the fact that SA group patients had preemptive analgesia by preventing afferent nociceptive sensitization pathway. They might also have had some residual sensory block. This also led to a lower analgesic consumption in 24 hrs which was also seen in Mehrebanian et al [23] and incikara et al [4] and Serkan et al [21].

In our study, overall nausea and vomiting was found to be higher in GA group compared to SA group. This could be attributed to the general anaesthetic drugs used, nitrous oxide, narcotic analgesics and post-operative pain as seen by Papadopoulos et al [1].

Other authors have experienced urinary retention to be associated with SA more than GA. In our study, we found no such difference between the groups. This may be due to the fact that we did not use subarachnoid opiods intrathecally. No neurological deficits were seen in SA group contrary to that observed by Hebl et al [19].

None of our patients had position related injuries in either group. Nevertheless, it is our observation that, since patients were allowed to position themselves comfortably under SA, position related injuries could be avoided more effectively as compared to GA group as noted by Susan Black et al [25] and Inci kara et al [4].

Two patients in SA group, had signs of inadequate block, and required conversion to GA with ETT intra-operatively. Since the patients were being operated in lateral position, endotracheal intubation could be done without difficulty unlike in prone position. This ease of converting to GA allows even bolder use of SA in lateral position.

Performing spine surgeries in lateral position has several more advantages other than anesthetic and

surgeon factors discussed. Chang SH et al [26] studied the incidence of perioperative ischemic optic neuropathy(POION) in spine surgeries and concluded that POION is a rare but potentially devastating and untreatable complication of spine surgery, particularly that performed with patients in prone position. This catastrophe is averted by avoiding a prone position.

Papadopoulos et al [1], Reynolds e al [19] and Lakkam et al [27] concluded that epidural anaesthesia is a better alternative to GA for lumbar laminectomies. However on the downside, immediate postoperative assessment of the patient's neurological status to detect spinal cord injury or evolving cord compression is not possible with SA [28]. Although applicable only to lower lumbar surgeries, the study fairly conclusively demonstrates advantages of SA over GA in lateral positions. However, validation of the inference of the study is limited to some extent by a lack of blinding and also varying spine characteristics and difficulty level that can never be standardized!

Conclusion

Spinal anaesthesia is a suitable and perhaps better alternative to general anaesthesia for lower lumbar spine surgeries when being operated in lateral position, leading to better hemodynamic stability, low incidence of nausea and vomiting, reduced time in the operating room and better post-operative analgesia.

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Evaluation of Addition of 50 μg of Dexmedetomidine to 10ML of 2% Lignocaine with Adrenaline and 10ML 0.5% Bupivacaine on Block Characteristics in Ultrasound Guided Supraclavicular Brachial Plexus Block

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Abstract

Introduction: Ultrasound has gained popularity in the last few years for peripheral nerve blocks which provides real time visualization of the nerves to be blocked and also reduces the volume of drug to be injected. *Aims and Objectives:* To study the effect of 50μg of Dexmedetomidine added to the local anaesthetics for ultrasound guided supraclavicular block in respect to onset, duration of sensory and motor block along with haemodynamic variables. *Materials and Methods*: This prospective randomized and double blind study was conducted in 60 ASA I and II patients scheduled for elective upperlimb surgeries under ultrasound guided Supraclavicular brachial plexus block were randomized into two groups. Group I patients received 0.5% bupivacaine (10ml) + 2% lignocaine with adrenaline (10ml) + dexmedetomidine (0.5ml-50mcg) and Group II patients received 0.5% bupivacaine (15ml) + 2% lignocaine with adrenaline (15ml) + normal saline (0.5ml) Onset and duration of Motor and sensory block block were recorded. *Results*: Though sensory block was achieved earlier in group I, it was not statistically significant but motor block onset times was statistically significant in group I as compared to group II ($p<0.05$). Sensory and motor blockade duration were longer in group I than in group II ($p<0.05$). Intra-operative hemodynamics was significantly lower in group I ($P < 0.05$) without any appreciable side-effects. *Conclusion:* We conclude that dexmedetomidine added to bupivacaine- lignocaine with adrenaline in ultrasound guided supraclavicular brachial plexus block is extremely effective in reducing the time of onset and prolonging the duration of both sensory & motor blockade.

Keywords: Dexmedetomidine; Ultrasound; Supraclavicular Brachial Plexus Block.

Introduction

Among the various approaches of brachial plexus block, supraclavicular approach is considered easier and most effective for upper limb surgeries.

Kulenkamff performed the first supraclavicular brachial plexus block in 1912 [1].

Conventional peripheral nerve block techniques are highly dependent on surface anatomical landmarks for localization of the target nerve. It is therefore not surprising that regional anaesthetic techniques are associated with a reported failure rate of up to 20% presumably because of incorrect needle and/or local anesthetic spread. Ultrasound for regional anaesthesia has gained popularity over the last few years. Ultrasound provides real time imaging guidance of nerves and spread of the drug during a nerve block which allows low volumes of drug keeping the toxicity levels in check.

Dexmedetomidine, an potent alpha-2 agonist provide sedation, analgesia, muscle relaxation & anxiolysis [2]. Pharmacologically Dexmedetomidine is an active s-enantiomer of medetomidine. The specificity of Dexmedetomidine for the alpha-2 receptor is 8 times that of clonidine, with an alpha-2 / alpha-1 binding affinity ratio of 1620:1 and hence, considered as the full agonist at alpha-2 receptors [3,4]. Various studies have shown that Dexmedetomidine prolongs the duration of sensory

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and motor block when used as an adjuvant to local anaesthetics for nerve blocks [5,6,7,8]. Our study was conducted to evaluate the efficacy of Dexmedetomidine as adjuvant to when added to 0.5% bupivacaine and 2% lignocaine with adrenaline.

Materials and Methods

After obtaining permission from institutional ethics Committee and written informed consent, 60 patients of American Society of Anesthesiologists (ASA) physical status I and II, aged between 18 - 60 years of both sexes undergoing elective orthopaedic surgeries of elbow, forearm and hand under ultrasound guided supraclavicular brachial plexus block were enrolled in the study.

Group I: Patients received 0.5% bupivacaine (10ml)+ 2% lignocaine with adrenaline (10ml) + Dexmedetomidine(0.5ml).

Group II: Patients received 0.5% bupivacaine (10ml)+ 2% lignocaine with adrenaline (10ml) + normal saline(0.5ml).

Exclusion criteria includes patient refusal, known hypersensitivity to local anaesthetics, pregnancy, hepatic, renal or cardiopulmonary abnormality, alcoholism, bleeding diathesis, local skin site infections were excluded from the study. Patients having a history of significant neurological, psychiatric, or neuromuscular disorders were also excluded. All the patients were kept nil per oral as per the fasting guidelines. On the day of surgery,in the operation theatre standard intra-operative monitors like ECG, pulse oximeter, non-invasive blood pressure were attached and baseline parameters were recorded. Intravenous (i.v) infusion of Ringers' lactate started and oxygen given at 3 L/min through a face mask. All patients received injection midazolam 0.05 mg/kg before procedure.

This procedure was done by using sonosite ultrasound machine with 13-6 MHz transducer by in-plane approach using 22G, 100mm needle. Under strict aseptic precautions Block was performed after real time visualization of the vessels, nerve & bone. The brachial plexus is seen as a cluster of hypoechoic nodules, lateral to the round pulsating hypoechoic subclavian artery lying on top of the hyperechoic first rib. Once brachial plexus is located Group I received 0.5% bupivacaine (10ml)+ 2% lignocaine with adrenaline (10ml) + Dexmedetomidine (0.5ml). Group II received 0.5% bupivacaine (10ml)+ 2% lignocaine with adrenaline (10ml) + normal saline (0.5ml) inplane approach. During the procedure & thereafter, the patient was observed for any complications of the block & for the toxicity of the drugs injected.

Onset of Sensory and motor blockade were assessed every 3 minutes till loss of sensation and movements. Heart rate, blood pressure were recorded every 5min intraoperatively & then at an interval of every 30mins postoperatively.The duration of sensory block was defined as the time interval between the onset of sensory block and the first post-operative pain. The duration of motor block was defined as the time interval between the onset of motor block and complete recovery of motor functions. Onset of sensory block was assessed by spirit swab method. Assessment of motor block was done using the *Bromage* three point score:

0 Normal motor function with full flexion and extension of elbow, wrist and fingers,

1 Decreased motor strength with ability to move fingers and/or wrist only

2 Complete motor blockade with inability to move fingers].

Statistical Analysis

All recorded data were entered using MS Excel software and analysed using SPSS 20 version software for determining the statistical significance. Results were expressed as mean±standard deviation. Proportions were compared using Chi-square test. The student't' test was used to determine whether there was a statistical difference between the study groups. "P" value of > 0.05 was considered not to be statistically significant, <0.05 was considered to be statistically significant, a value of <0.01 was highly statistically significant & a "P" value of <0.001 was considered as extremely statistically significant.

Results

Patients in both the groups were comparable in age, sex and weight (Table 1). Though the mean onset time of sensory blockade was faster in group I (3.54±0.74) compared to that in group II (3.86±0.88). This difference was not statistically significant (p 0.111) (Table 2) (Figure 1). The onset of motor blockade was faster in Group I (5.4±1.12 min) than Group II (6.34±1.14) and the difference was statistically very significant with p value of

<0.001 (p<0.05) (Table 2). (Figure 2). The duration of sensory blockade was longer in Group 1 (616.23±62.05 min) than Group 2 (574.71±61.14) and the difference was statistically significant with p value of 0.006 (p<0.05)(Table 2)(Figure 3). The duration of motor blockade was longer in Group 1 (635.86±57.82 min) than Group 2 (562.80±66.79) and the difference was statistically significant with p value of <0.001 (Table 2) (Figure 4). Group 1 (Dexmedetomidine) had lower heart rate compared to the group 2. The difference was statistically significant (<0.05) at 360, 420, 480, 540 and 600 min, but the fall in heart rate required no treatment. (Figure 5). Group 1 (Dexmedetomidine) had lower mean arterial pressure than baseline compared to the group 2. The difference was statistically significant (<0.05) at 60, 75, 90, 120, 150, 180, 210, 240, 300, 360, 420, 480, 540 minutes. But this fall in blood pressure required no treatment (Figure 6). Bradycardia was observed in 2 patients in group I whereas hypotension i.e. fall more than 30% of baseline was seen in 4 patients in group I and 2 patients in group II. No sedation was observed in both the groups.

Table 1: Demographic profile

		Group I	Group II	P value
Age		33.7±13.57	31.5± 13.76	0.53
Sex	Males	24	25	0.73
	Females	6	5	
Weight		65.9±8.1	64±7.16	0.33

Table 2:

	Group I	Group II	t value	P value
Onset of Sensory	3.54±0.74	3.86±0.88	1.62	0.111
Onset of Motor	5.40±1.12	6.34±1.14	3.50	0.001
Duration of Sensory	616.23±62.05	574.71±61.14	2.82	0.006
Duration of Motor	635.86±57.82	562.80±66.79	4.89	0.001
Side Effects				
Hypotension	2(6%)	0		
Bradycardia	4(13%)	2(6%)		0.355

Fig. 1:

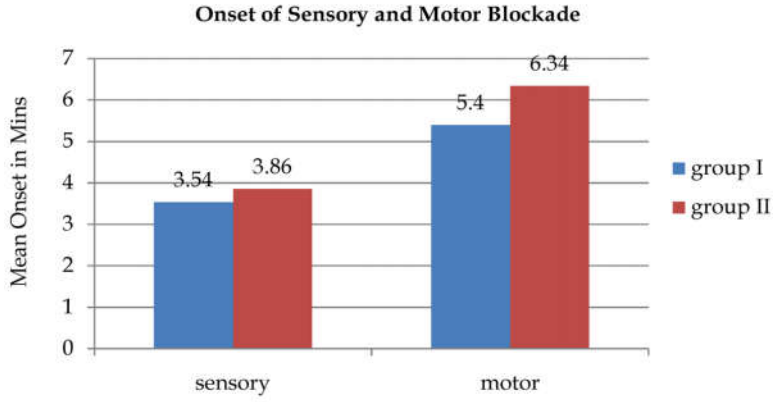
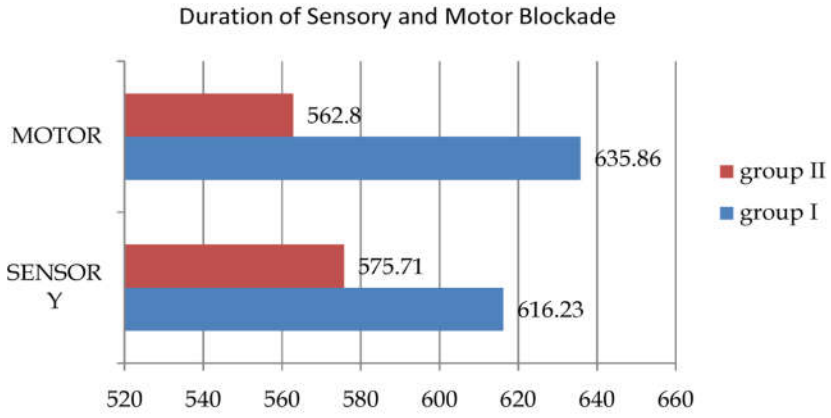


Fig. 2:



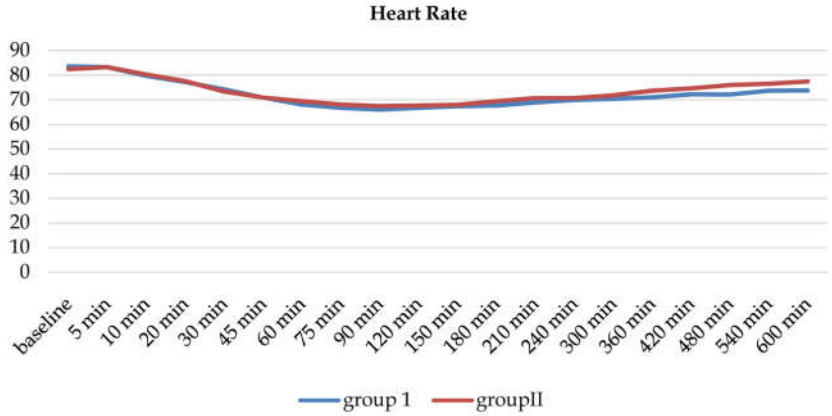


Fig. 3:

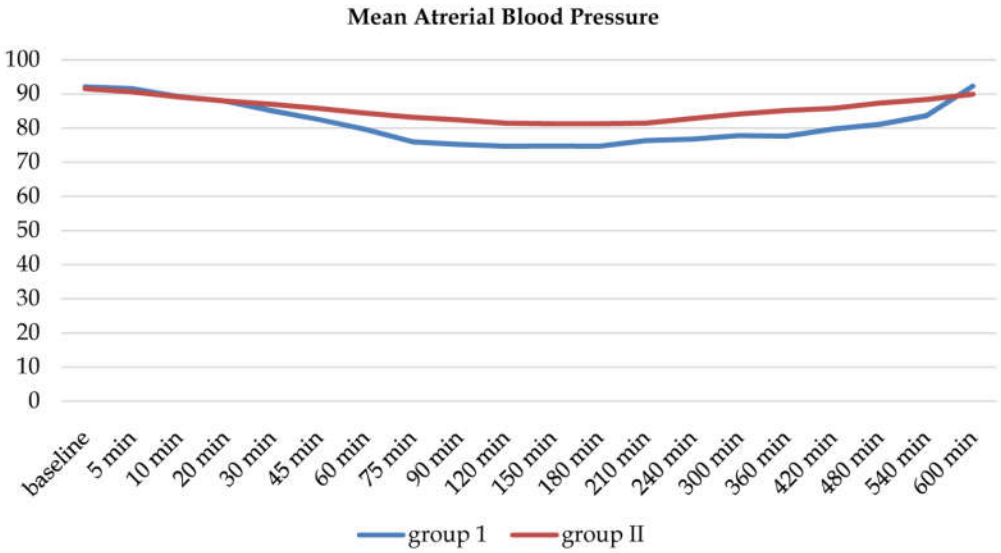


Fig. 4:

Discussion

Ultrasound has made its presence felt in regional anaesthesia practise particularly for peripheral nerve blocks as it allows real time visualisation of nerve plexus and deposition of the drugs around the nerve plexus reducing the margin of error for failures [9]. The volume of local anaesthetic required in such cases is lower than the one normally used in a blind or in an Electrical Nerve Stimulation (ENS) technique [10,11].

Local anesthetics alone for supraclavicular brachial plexus block provide good operative conditions but have a shorter duration of posto-perative analgesia. Hence various drugs such as opioids [12], α-2 agonists [13], neostigmine, dexamethasone [14], midazolam [15], magnesium [16] etc., were used as adjuvants to local anesthetics in brachial plexus block to achieve quick, dense and prolonged block.

In our study, we added Dexmedetomidine which is a potent α2 selective agonist to 0.5% bupivacaine and 2% lignocaine with adrenaline to evaluate onset and duration of sensory and motor block characteristics.

Rachana Gandhi, Alka Shah and Ila Patel [17] conducted a prospective double blind study to compare the postoperative analgesic efficacy and safety of dexmedetomidine (30µg) for brachial plexus blockade along with bupivacaine (0.25%). It was observed that in control group onset of motor and sensory blockade was faster, whereas, dexmedetomidine group have better hemodynamic stability and greater postoperative analgesia.

F.W. Abdallah & R. Brull [18] Conducted a study to study the whether perineural dexmedetomidine as a local anaesthetic (LA) adjuvant for neuraxial and peripheral nerve blocks can prolong the duration of analgesia compared with LA alone. Sensory block duration was prolonged by 150 min [P<0.00001] with intrathecal dexmedetomidine.

Perineural dexmedetomidine used in BP block may prolong the mean duration of sensory block by 284 min (P=0.05), but this difference did not reach statistical significance. Motor block duration and time to first analgesic request were prolonged for both intrathecal and BP block.

A Study by Rajesh Meena [19] showed the efficacy of Dexmedetomidine as an Adjuvant to Bupivacaine in Supraclavicular Brachial Plexus Block. Dexmedetomidine is good adjuvant to local anesthestic agents, as its addition to bupivacaine was associated with prolonged sensory and motor blockade, mild sedation and prolonged analgesia. Satisfactory hemodynamic stability without observed immediate post-operative side effects are other significant qualities related to it.

In our study the onset of sensory blockade was faster in Dexmedetomidine Group 1 (3.54±0.74 min) than clonidine Group 2 (3.86±88) but the difference was not statistically significant, p value of 0.111(>0.05).

The onset of motor blockade was faster in Group 1 (5.4±1.12 min) than Group 2 (6.34±1.14) and the difference was statistically significant with p value of <0.001. The duration of sensory blockade was longer in Group1 (616.23±62.05 min) than Group II (574.71±61.14) and the duration of motor blockade was longer in Group 1 (635.86±57.82 min) than Group 2 (562.80±66.79) and the differences were statistically significant with p value of <0.006 and <0.001 respectively.

Conclusion

We conclude that addition of 50µg of Dexmedetomidine to local anaesthetics for ultrasound guided supra clavicular block hastens the onset of sensory and motor block and also prolongs the duration of sensory and motor block significantly without significant side effects.

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Original Research Article

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An Observational Study to Compare Etomidate and Thiopentone as Inducing Agents in General Anaesthesia for Patients Posted under General and ENT Surgeries

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Abstract

Background and Objective: The clinical study was undertaken to evaluate the efficacy of Thiopentone & Etomidate with reference to time to loss of eyelash reflex, hemodynamic parameters, pain on injection, myoclonus & other side effects if any. *Material and Method:* Study was conducted on 60 patients (according to Solvin's formula) of either gender, ASA I & II, 20- 60 years old, posted for elective surgeries for general surgery and Ear Nose and Throat surgery. All the patients were premedicated with inj. Fentanyl 2 mcg/kg iv slowly along with other pre medicating drugs and divided into 2 groups. Group E induced with inj. Etomidate 0.3 mg/kg iv and the group T induced with inj. Thiopentone 5 mg/kg iv. The induction time was calculated from the start of injection to the loss of eyelash reflex. The patient's hemodynamic changes during baseline, at the time of induction and 1 min, 2 mins, 5 mins & 10 mins after the induction were recorded. Pain on injectionand myoclonus were recorded during induction and other side effects were noted. *Results:* Induction time was faster in Group E (23.23±5.2 seconds) when compared with group T (32.60±4.5 seconds) (p value<0.05). Hemodynamic changes were more stable in group E and Pain on injection and Myoclonus were observed only in group E (8 & 10 patients respectively). *Conclusion:* Etomidate causes good hemodynamic stability with rapid induction than Thiopentone.

Keywords: General Anaesthesia; Thiopentone; Etomidate; Fentanyl; Haemodynamics.

Introduction

An ideal intravenous induction agent should be rapid in onset with rapid recovery & haemodynamic stability with minimal side effects [4,5,6]. Thiopentone is the earliestultra- short acting barbiturate, producing rapid intravenous induction [7].

Recently Etomidate- a rapid acting non-barbiturate hypnotic agent was introduced into clinical practice in India. Its properties include hemodynamic stability, minimal respiratory depression, cerebral protection and rapid recovery after a single dose [8].

This study allows evaluation of Etomidate in comparison with Thiopentone as an induction agent and aims to compare hemodynamic changes and other untoward effects of both the drugs.

Material and Methodology

After permission and clearance from the ethical committee, this observational study was conducted in Department of Anesthesiology. We studied 60 patients of age 20–60 years, both the genders belonging to Grade-I and II of American Society of Anesthesiologist's (ASA) classification who were admitted for elective surgeries under general anaesthesia in general and ENT surgeries. All the patients participating in the study were explained clearly about the purpose and nature of the study

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in the language they understood. They were included in the study only after obtaining a written informed consent.

Whereas patients who refused for the study, belonging to American society of anesthesiology grade III and above, allergic to anydrug, having primaryand secondarysteroid deficiencyor onsteroid medication, severe respiratory & cardiac compromised or the patients who underwent any surgery under General Anaesthesia in past 1 week or emergency surgical intervention were excluded from this study.

A cross sectional analysis was made at the time of presentation. We collected the data for 1.5 years from Nov 2015 to May 2017 and analyze the data statistically.

60 Patients were randomized by simple random sampling method into two groups as follows:

- Group T (30 patients): induced with Thiopentone 5 mg/Kg iv.
- Group E (30 patients): induced with Etomidate 0.3 mg/ kg iv.

Keeping the power of study as 80% and confidence limit at 95%, to detect mean haemodynamic change between the two groups, the minimum sample size required was 20 in each group. For a better validation of results we included 30 patients in each group.

A routine pre-operative examination of all the patients was done as per routine protocols on the previous day of surgery. A night prior to surgery Tab. Alprazolam 0.5 mg per orally & Tab. Ranitidine 150 mg per orally were given to all the patients. And then they were kept nil by mouth at least eight hours before the operation.

On the day of surgery, patient was brought to the operation theatre. Intravenous line was secured with 18G cannula and the patients were given I.V. Fluids according to the requirement. Multipara monitors were attached and base line pulse rate, respiratory rate, non-invasive blood pressure, SPO_2 and ECG were recorded.

All the patients were premedicated with inj. Glycopyrrolate 0.004 mg/kg iv, inj. Ondensatron 0.1 mg/kg iv. Intravenous inj. Fentanyl 2 mcg/kg was given 5 minute before induction.After pre-oxygenation, Induction of anaesthesia was done either with etomidate 0.3 mg/kg iv or thiopentone 5 mg /kg iv. Loss of eye lash reflexes and lack of response to verbal commands was considered to be as end point of induction. Followed by this, inj. Succinylcholine 2mg/kg iv was given to facilitate tracheal intubation. Anaesthesia was maintained with 50% oxygen, 50% nitrous oxide along with inhalation agent and intravenous inj. Atracurium.

Time to loss of eye lash reflex, haemodynamic Parameters (HR, SBP, DBP)- Baseline, at the time of induction, one minute after induction, two minutes after induction, five minutes after induction and ten minutes after induction were monitored. Pain on injection and Myoclonus were observedduring induction. Side effects/ Complications if any were also observed.

Pain on Injection was Graded as follows

0: no pain,

1: grimace,

2: withdrawal of the arm,

3: both verbal complain and withdrawal of the arm

Severity of myoclonus was graded as follows:

0= No myoclonus;

1= Minormyoclonus; (short movement of a body segment e.g., a finger or a wrist)

2= Moderatemyoclonus; (mild movement of two different muscle groups e.g., face and arm)

3= Severe myoclonus. (intense myoclonic movement in two or more muscle groups, fast adduction of a limb).

Intraoperative fluid was calculated and replaced according to the patient weight and NBM status.

Patient was extubated as per routine protocols.

Observation and Results

The various observations were summarized as follows:-

Demographic data in two groups is comparable and no statistical difference found (p= 0.85).

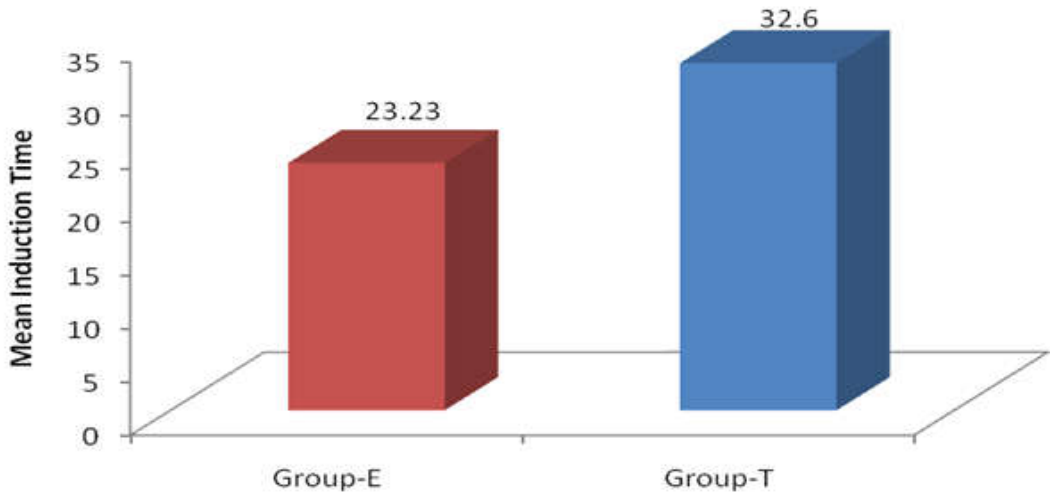
Mean induction time in Group E and Group T were 23.23±5.25 seconds and 32.60±4.59 seconds respectively. Time for induction in Group-E wasshorter compared to Group-T which was statistically significant. (p< 0.005) (Graph 1).

Graph 2 shows that there was an increase in HR in both the groups just prior to induction. However in Group E, it touches the pre induction value at 1 minute after induction and remained below baseline upto 10 minutes, whereas in Group T there was

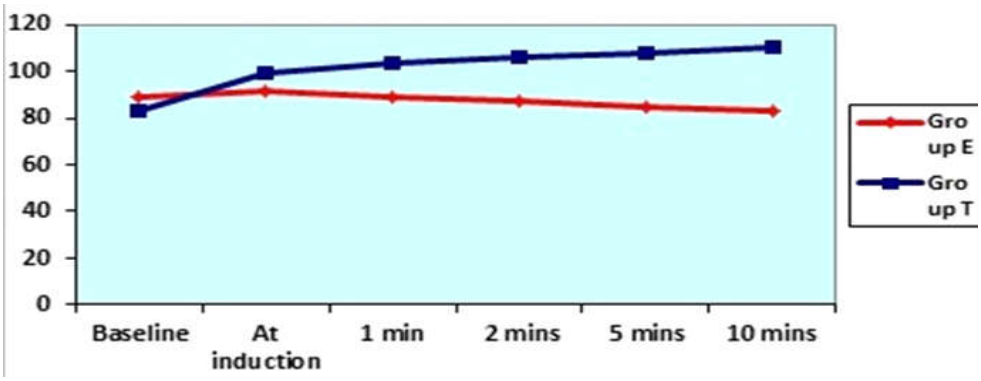
persistent increase even upto 10 mins which was statistically significant (p<0.05); Graph 3 & 4 shows SBP and DBP in Group T at induction, 1, 2, 5 &10 mins decreased in group-T> 20% which was statistically highly significant (P <0.001), whereas In Group E, it remained stable.

Pain on injection in the Group-E was observed in 26.66% patients, but none in Group-T. Which was statistically significant (p<0.05) (Graph 5).

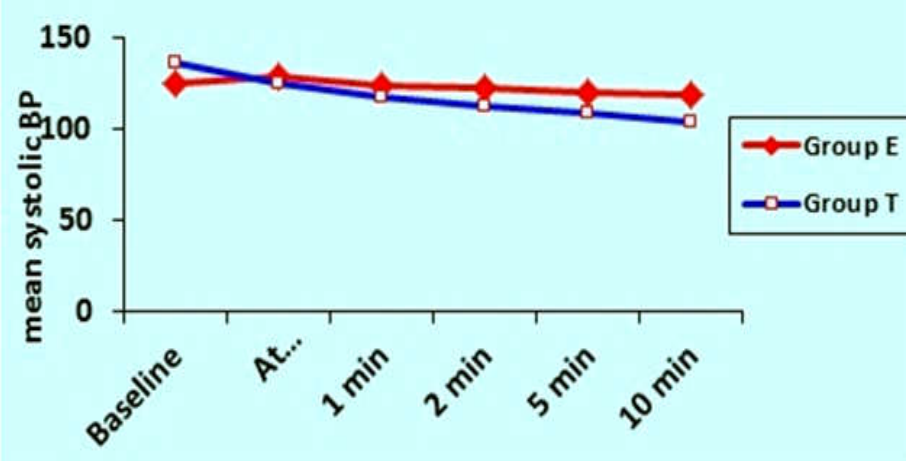
Incidence of side effect like myoclonus occurred in Group-E was 33.33% patients and in Group-T 0% which was statistically significant. (Graph 6).



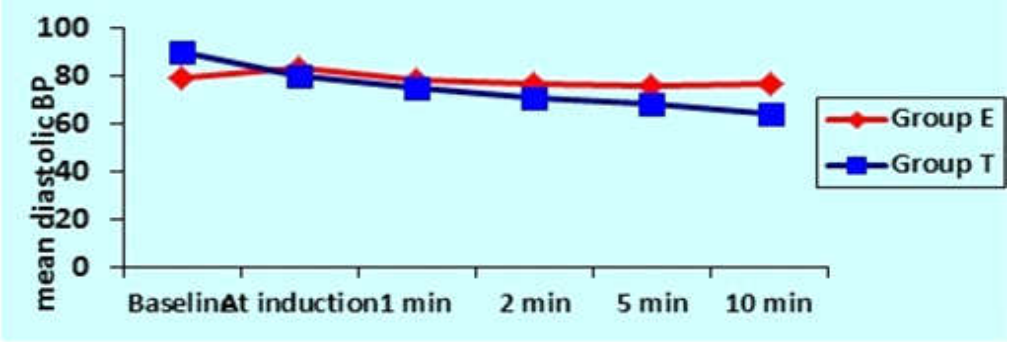
Graph 1: Induction time in both the groups



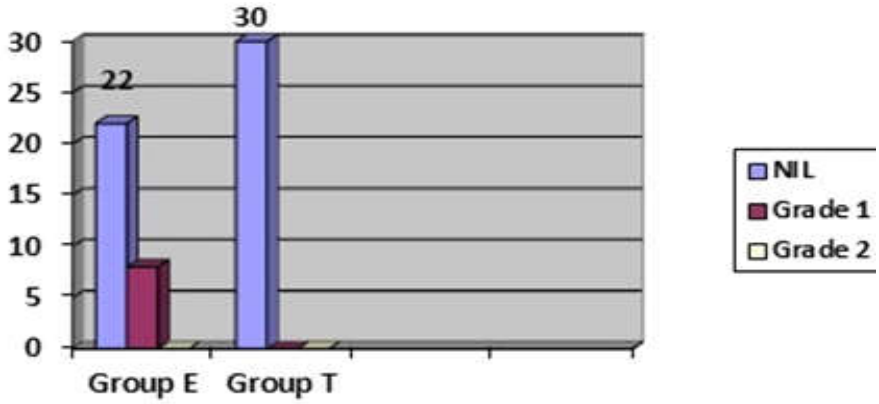
Graph 2: Heart Rate at different time intervals



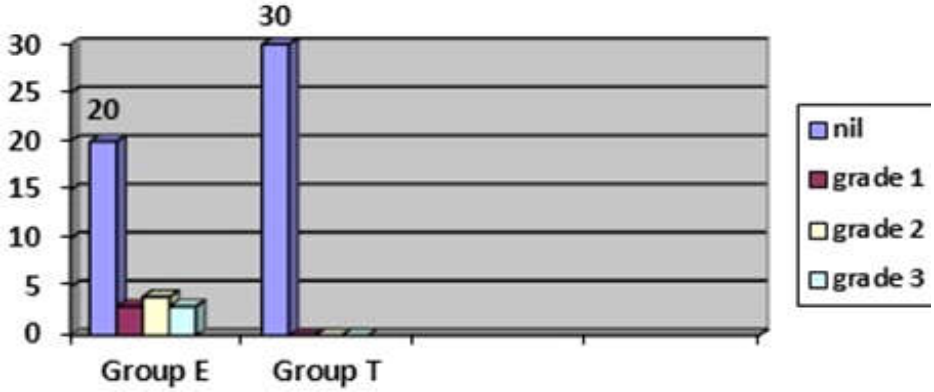
Graph 3: Mean systolic blood pressure at different intervals in both the groups



Graph 4: Mean diastolic blood pressure at different time intervals in both the groups



Graph 5: Pain on injection in both group



Graph 6: Myoclonus in both the groups

Discussion

In appropriate dosage, intravenous anaesthetic induction agents cause loss of consciousness. As discussed earlier, an ideal iv induction agent should have minimal disturbance to cardiovascular and respiratory functions, they should induce sleep in one arm brain circulation time, should be chemically stable, non -inflammable, non- toxic & easy to administer. However, in the choice of the induction agent, apart from desirable characters like rapid onset and recovery, analgesia as well as lack of excitatory phenomenon, cumulation, interaction with relaxants, post op vomiting, delirium etc, one of the main considerations will centre on cardiovascular stability that the drug possesses [4,5,6]. Etomidate is a unique drug used for induction of general anesthesia and sedation. The first report on etomidate was published in 1965 and introduced into clinical practice in 1972. Etomidate is known as propofol of 70s and 80s because of its reputation for non-cumulative and cardiostable properties, rapid onset with no stimulation of epileptiform properties. Etomidate causes

depression of reticular activating system and mimics inhibitoryeffectsof GABA. It appears to bind to a subunit of GABA type Areceptor, thus increasing its affinity for GABA. It also has disinhibitory effects on parts of nervous system that control extrapyramidal motor activity [8,10].

Etomidate has cardiovascular stability and produce minimal respiratory depression. These properties suggest that it is a useful alternative to thiopentone [8].

Since 1934, after the introduction of Thiopentone in to clinical practice by John Lundy, it has been the gold standard for induction. It is a safe, reliable and relatively inexpensive drug [7].

Thiopentone has some absolute contraindication for its use like:- Barbiturate sensitivity, hereditary intetermittent porphyria, status asthmaticus, severe anemia.

Because of cardio respiratory depressive effects of Thiopentone, it is not the drug of choice in patients with shock or patients with associated cardio respiratory disease.

The recommended induction dose is 3-6mg/kg for thiopentone and 0.2-0.5 mg/kgfor etomidate. Taking into account there levant literature and clinical experience wehave used etomidate 0.3 mg/kg and thiopentone 5mg/kg to do a randomized observational study.

All the patients in our study were similar in terms of Demographic data.

According to our study the mean time of induction (time to loss of eyelash reflex) with Inj. Etomidate was statistical significantly shorter when compared with Inj. Thiopentone ($P<0.05$).

The similar study was done by S. C Shah, et al (1980) showed Etomidate in the dose 0.3 mg/kg used achieved a fast and smooth induction of anesthesia. The average time from induction to loss of consciousness was 20 seconds. These results were consistent with our study the mean induction time with Etomidate was shorter than the mean induction time with Thiopentone (p value< 0.05).

Also similar to Shilpashri AM et al (2015) conducted a study of 60 ASA I & II patients. Induction was done with inj. Thiopentone 5 mg/kg in Group T and Group E- with inj. Etomidate 0.3 mg/kg. Induction time was faster in Etomidate group than Thiopentone group. SBP & mean HR were significantly increased in Group T, whereas in Group E there was minimal change. (p value< 0.05)

However, Batra, R.K et al (1984) showed no difference in the mean induction time between Thiopentone and Etomidate.

In the present study, both Group T and Group E were premedicated with inj. Glycopyrollate, inj. Ondensetron, inj. Midazolam & inj. Fentanyl. Hence the hemodynamic parameters were comparable post premedication.

In our study, herat rate in Group E increased at the time of induction, but then gradually decreased and remained below the baseline valueupto 10 minutes.

However heart rate in Group T increased at the time of induction as compared to baseline value and remained above the baseline value upto 10 minutes.

Our study was comparable to the study conducted byPrys Roberts et al (1971) (p value< 0.05). Whereas RP Kaushal et al (2015) observed significant increase in heart rate after administration of etomidate.

In etomidate group SBP gradually decreased at 1 minute after inductionand was well maintained near baseline values upto 10 mins.

In thiopentone group baseline SBP continuously decreased > 20% of the baseline value. There was significant fall in BP noted after 10 mins of induction. (This fall in Blood Pressure is may be beacause of the vasodilatory effect of Thiopentone)

Similar to our study, Batra et al (1984) reported arterial pressure remained steady throughout the anesthesia in Etomidate group, a fall in BP 80% patients with Thiopentone.

Similarly, Mousumi Das et al (2015) conducted a study in 90 ASA I & II patients using either Etomidate 0.3 mg/kg or Thiopentone 5 mg/kg as induction agent. There was no significant change in, Systolic blood pressure, in post induction and after intubation in etomidate group when compared to thiopentone group [9].

In this study the incidence of pain at the time of injection was higher with Etomidate i.e. In 8 patients out of 30 patients (26.66%) and none in Thiopentone group.

This correlates with the report by Batraet al (1984) observed that pain at the site of injection was noted in more number of cases of Etomidate (36%).

Myoclonus is induced by Etomidate in a dose dependent manner during induction of GA is undesirable. The consequence of this side effect can be serious in non-fasted emergency patients, patients with open eye injuries or with limited

cardiovascular reserve. Pretreatment with fentanyl and benzodizapine has shown to reduce the incidence to some extent.

Hence we premedicated all patients with inj. Midazolam and inj. Fentanyl 5 mins before induction.

One of the mechanisms proposed for Myoclonus, it is reported that it resulted from subcortical disinhibition similar to irritable leg syndrome.

In our study the incidence of myoclonus occurred in 30% of patients in Etomidate group and 0% in Thiopentone group, may be because we used 2 mcg/kg dose of fentanyl in premedication.

This is similar to reports by Batraet al (1984) Incidence of myoclonus is 28% of patients of Etomidate group and none in Thiopentone group.

No side effects were observed in any patient in both the groups.

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Comparitive Evaluation of Propofol with Ketamine versus Propofol with Fentanyl in Total Intravenous Anaesthesia for Day Care Surgeries

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Abstract

Aim of the Study The aim of the study is to compare the recovery times when Propofol with Fentanyl or Propofol with Ketamine are used for maintenance of anaesthesia in day case surgery and also to determine which agent combination is suitable to make the patient home fit at the earliest.

Keywords: Propofol; Ketamine; Fentanyl; Day Care Surgeries.

Introduction

An ideal general anaesthetic should provide quick and pleasant induction, predictable loss of consciousness, stable operating conditions, minimal adverse effects, rapid and smooth recovery of protective reflexes and psychomotor functions. The current practice is to use a balanced anaesthesia technique with depth of anaesthesia, analgesia and relaxation produced by different drugs in combination.

This study was conducted to evaluate and compare two drug combinations of Total Intravenous Anaesthesia using Propofol with Ketamine and Prop ofol with Fentanyl and to study the analgesic characteristics and recovery characteristics following anesthesia with these techniques. The development of anesthesia since its introduction has been erratic, long periods of stagnation being occasionally broken by improvement and advances. General anesthesia has undergone a vast number of improvements and modifications and even its recently modified form total intravenous anesthesia (TIVA; induction as well as maintenance of anesthesia with intravenous agents only) has undergone many improvements ever since its introduction into clinical practice.

TIVA has many advantages over inhalational anesthesia such as

- No operating room pollution
- Minimal cardiac depression
- Lesser neurohumoral response
- Decreased oxygen consumption
- Avoids distension of air -filled spaces within the patient's body, thus producing optimum operating conditions for the surgeon
- Avoids postoperative diffusion hypoxemia
- Decreases the incidence of postoperative nausea and vomiting (PONV)
- In day care surgery for rapid recovery.

Moreover, TIVA can be used not only in well - equipped hospital setting but at remote location also with only oxygen and ventilation facilities.

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Various drugs have been tried from time to time in TIVA. Since no single drug can provide all the characteristics of an ideal intravenous agent, several drugs are used in different combinations to provide balanced anesthesia in TIVA, that is, amnesia, hypnosis and analgesia.

Aim of the Study

The aim of the study is to compare the recovery times when Propofol with Fentanyl or Propofol with Ketamine are used for maintenance of anaesthesia in day case surgery and also to determine which agent combination is suitable to make the patient home fit at the earliest.

Materials and Methods

This study was carried out in the General Surgery theatre, Sree Balaji Medical college hospital, Chennai after obtaining institutional approval.

The aim of the study was to compare the Phase I and Phase II recovery times when Propofol with Fentanyl or Propofol with Ketamine are used for the maintenance of anaesthesia in day case procedures and also to determine which agent is suitable to make the patient home fit at the earliest.

Study Design

The study was a randomized prospective study.

Selection of Cases

Forty patients undergoing Day Case surgeries were selected for the study. Their age ranged from 18 to 50years. All the patients were assessed and those with normal clinical, biochemical radiological and hematological parameters were selected. Informed written consent was obtained from all the patients. Each patient was ran domly allocated to either the Fentanyl or the Ketamine group bylots. The groups were named 'F' for Fentanyl and 'K' for Ketamine

Inclusion Criteria

- Age group between 18 to 50 years
- Normal biochemical and hematological parameters
- ASA class I, II
- No known hypersensitivity to eggs or sulpha drugs
- Airway MPC 1, 2 and 3
- Minor Surgical and Obstetric procedures
- Surgery lasting less than 90 minutes duration
- Patients normally able to ambulate well
- Educated attender who can understand and carryout instructions

Exclusion Criteria

- Patient not willing
- ASA class III and above
- Known hypersensitivity to eggs or sulpha allergy
- Patient with known psychiatric disorder

Major surgeries requiring overnight hospital stay

- Surgeries near or involving the airway
- Patient having difficulty in walking
- No attender or attender not educated enough to carry out instruction

Materials

1. Boyles machine
2. Syringe infusion pump
3. Appropriate drugs in preloaded syringes
4. Appropriate sized Laryngeal Mask Airways
5. Functioning Laryngoscope with appropriate size blades
6. Appropriate sized Endotracheal tubes
7. Equipment and drugs for resuscitation
8. Suxamethonium for emergency use in airway control

Methods

Pre-Operative Preparation

Patients were assessed pre-operatively, procedure was explained to the patient and informed consent obtained. They were assessed with particular attention for any contraindications. The tests for recovery and the importance of strictly following instructions were emphasized.

Premedication

All the patients received Glycopyrrolate 5µg/Kg premedication fifteen minutes before induction.

Conduct of Anesthesia

On arrival of the patient in the operating room, monitors like pulseoximetry, Non invasive BP and ECG were connected and baseline values of HR, BP and SpO2 were recorded. An intravenous access was obtained in the nondominant arm.

Patients were randomly allotted by lots to Group F or Group K. Patients allocated to group F were induced with Propofol 2mg/Kg I.V. and Fentanyl 2ìg/Kg. An appropriate sized Laryngeal Mask Airway was introduced and its correct position confirmed. No muscle relaxants were used. In case of any movement by the patient, an additional bolus of Propofol 0.5mg/Kg was given.

Patients in group K were indu ced with Propofol 2mg/Kg I.V. and Ketamine 0.5mg/Kg. An appropriate sized Laryngeal Mask Airway was introduced and its correct position confirmed. No muscle relaxants were used. In case of any movement by the patient, an additional bolus of Propofol 0.5mg/Kg was given.

Fentanyl Group

Immediate post induction, this group of patients received a continuous infusion of Propofol from a syringe pump.(B Braun Melsungen 'S' series) according to the following scheme: -

- 12 mg/kg/h ´ 10 min (200 mcg/kg/min)
- 10 mg/kg/h ´ 20 min (167 mcg/kg/min)
- 8 mg/kg/h ´ 1 h (133 mcg/kg/min)
- 6 mg/kg/h maintenance (100 mcg/kg/min)

In addition, they were connected to the Bain breathing circuit with 66% Nitrous oxide and 33% Oxygen. The patient spontaneously ventilated througho ut the procedure. Any spontaneous movement was tackled with a 20mg bolus of Propofol. Supplementary Fentanyl 1µg/Kg bolus was given intraoperatively if the procedure extended beyond 1 hour.

Ketamine Group

Immediate post induction, this group of patients received a continuous infusion of Propofol from a syringe pump.(B Braun Melsungen 'S' series) according to the following scheme: -

- 12 mg/kg/h ´ 10 min (200 mcg/kg/min)
- 10 mg/kg/h ´ 20 min (167 mcg/kg/min)
- 8 mg/kg/h ´ 1 h (133 mcg/kg/min)
- 6 mg/kg/h maintenance (100 mcg/kg/min)

In addition, they were connected to the Bain breathing circuit with 66% Nitrous oxide and 33% Oxygen. The patient spontaneously ventilated throughout the procedure. Any spontaneous movement was tackled with a 20mg bolus of Propofol. Supplementary Ketamine 0.5mg/kg bolus was given every 20 minutes intraoperatively.

Parameters Studied

Time to Phase I Recovery: This is the time taken to the discontinuation of Propofol Aldrete time when the score is ≥ 9

Time to Phase II Recovery: This is the time taken from discontinuation of Propofol to the time when the PADSS score is ≥ 9. It is also taken as the time to Home readiness.

Patients in both the groups did not differ significantly with respect to the demographic data as well as duration of surgery and anaesthesia

The mean pulse rate was 75±4 for Group K and 77±8 for Group F at base line level and was statistically insignificant. There was slight increase in pulse rate after induction in both the groups which was statistically insignificant

The mean systolic blood pressure was 117±6 for Group K and 120±5 for Group F which was statistically insignificant. However there was statistically significant fall in systolic blood pressure in the Group F (P value 0.0001)

Table 1: Demographic data

Variables	Group (K) N=20	Group (P) N=20	P Value
Age (Years)	35±13	38±15	0.80
Weight (Kgs)	53±11	53±13	0.52
Sex (m/f)	14/16	11/19	0.54
Time of Surgery (mins)	49±6	51±4	0.051
Time of Anaesthesia (mins)	58±7	59±5	0.38

Table 2: Mean pulse rate

Time	Group (K) n=20	Group (F) n=20	p Value
Pre OP	7 5±4	77±8	0.181
After	82±4	84±5	0.068
Induction			
5 mins	80±5	83±7	0.061
10 mins	80±6	80±7	0.931
15 mins	80±6	77±6	0.093
20 mins	81±7	79±6	0.063
25 mins	81±5	79±5	0.069
30 mins	79±5	77±6	0.128
40 mins	79±6	78±5	0.327
50 mins	78±6	76±5	0.211
60 mins	79±5	78±4	0.243

Table 3: Mean systolic blood pressure

Time	Group (K) N=20	Group (F) N=20	p Value
Pre OP	1 17 ±6	120±5	0.15
After Induction	116±14	107±9	0.0001
5 mins	117±8	115±11	0.470
10 mins	117±7	115±12	0.273
15 mins	116±7	118±17	0.630
20 mins	116±6	117±16	0.634
25 mins	117±7	120±18	0.218
30 mins	117±6	114±12	0.152
40 mins	116±7	112±10	0.019
50 mins	116±6	114±12	0.230
60 mins	117±7	113±10	0.075

Table 4: Mean diastolic blood pressure

Time	Group (K) N=20	Group (F) N=20	p Value
Pre OP	77±7	75±6	0.17
After	74±5	73±6	0.54
Induction			
5 mins	77±4	76±6	0.10
10 mins	77±7	75±5	0.07
15 mins	77±6	74±6	0.08
20 mins	78±6	76±7	0.07
25 mins	77±6	75±7	0.30
30 mins	77±6	76±7	0.65
40 mins	76±7	75±7	0.44
50 mins	77±6	75±6	0.25
60 mins	76±5	74±6	0.12

Table 5: PONV

Nausea/Vomiting	Group (K) N=20	Group (F) N=20	p Value
Yes	2/20	3/20	0.74
No	18/20	17/20	

Table 6: Phase I Recovery

Duration of Phase I	Group (K) n=20	Group (F) n=20	p Value
Recovery Time	12±2	13±3	0.492

Table 7: Phase II Recovery

Duration of Phase II	Group (K) n=20	Group (F) n=20	p Value
Recovery Time	29±4	47±8	0.046

The mean diastolic blood pressure for the Group K was 77±7 and 75±6 for Group F at baseline level which was statistically insignificant. After induction there were statistically no significant changes in both the groups.

Post operative nausea and vomiting was noted in 2 patients in Group K and 3 patients in Group F which was statistically insignificant.

The mean time for Phase I recovery in Group K was 12±2 and Group F was 13±3 which was statistically not significant.

The mean time for the Phase II recovery in Group K was 29±4 and Group F was 47±8. There was a statistically significant difference in the time up to Home readinesses and was significantly shorter with Propofol with Ketamine group than with Propofol with Fentanyl Group (P value – 0.046).

Discussion

The growing importance of ambulatory surgery during the past decade has led to the development of efficient anaesthetic techniques in terms of quality and safety of anesthesia and recovery. In these challenging objectives, intravenous techniques have played an important role, as they provide safe, efficient, and cost-effective anaesthesia in the ambulatory setting. Among the numerous intravenous drugs, propofol, with its fast a nd smooth onset of action, short duration of action, and low incidence of postoperative side effects appears to be the anaesthetic of choice in this situation.

In last few decades, many new sedative -hypnotic drugs with improved induction, maintenance and recovery profiles have been introduced into clinical practice. Kay B Rolly. Anesthesiol Belgca concluded that Propofol is a substituted phenol anaesthetic, and is associated with smooth induction, good maintenance and rapid recovery.

Greifenstein FE, De Vault M: A study of a 1 -aryl cyclohexyl amino for anesthesia identified that Ketamine, a powerful analgesic has a high margin of safety. John Stone M, Evans V, Baigel S: Sernyl in their study Dissociative anesthesia further pharmacological studies and fi rst clinical experience with phencyclidine derivative found out that ketamine produces no negative influence on ventilation or circulation. Corssen G, Domino EF quoted that the main disadvantage of ketamine is emergence delirium.

Susan M. Steele, Karen C. Nielsen, Stephen M on their study on Ambulatory Anesthesia and Perioperative Analgesia identified that fentanyl, a phenylpeperidine derivative has analgesic potency 50 -100 times that of morphine. But it is associated with respiratory depression and post operative nausea and vomiting.

Joshi, Girish P., Inagaki, Yoshimi, et al; Molloy, Mary E, Buggy, Donal J, Scanlon, Patrick in their study on using the Laryngeal Mask Airway concluded that it is ideal for Daycase anaesthesia.

Figueredo Eduardo, Vivar-Diago, Miguel, Mu no z-Blanco, Francisco, found that post operative throat discomfort following anaesthesia using laryngeal mask depends on the type of ventilation. Spontaneous ventilation causes less discomfort than controlled ventilation. McCrory, Connail R., McShane, Alan J., in a study comparing non premedicated and premedicated patients in ambulatory surgery, concluded that reflux of gastric contents occurs only in non premedicated patients. With adequate premedication, reflux or micro aspiration did not occur. The use of Laryngeal mask airway for our study was based on the above studies

Patients in both the groups did not differ significantly with respect to the demographic data as well as duration of surgery and anesthesia which are consistent with those of Guit j.b. et al in their study used propofol 2 mg/kg for induction, maintenance with propofol 12 mg/kg/hr for first 30 minutes, 9 mg/kg/hr for next 30 minutes and then 6 mg/kg/hr thereafter. Ketamine was used as 0.5 mg/kg for induction followed by maintenance dose of 0.5 mg/kg every hour. It was compared with fentanyl 2 μg/kg bolus and 1μg/kg every hour for maintenance. Propofol-ketamine combination resulted in hemodynamically stable anesthesia without the need for additional analgesics as cited by Guit JB, Koning HM in their study Ketamine as analgesic for total intravenous anesthesia with Propofol. We followed a similar protocol in our study.

There was gradual increase in mean pulse rate in propofol-ketamine group and in propofol -fentanyl group which returned to baseline after 30 and 15

minutes respectively. Guit jb et al have also reported that heart rate was stable except for an increase in mean h eart rate by 24% after induction in propofol -ketamine group. heart rate does not change significantly after an induction dose of propofol. Propofol either resets or inhibits baro-reflector reflex. There is reduction in the techycardic response to hypotension which coincides with the study Effects of Propofol anesthesia on baroreceptor activity in humans by Cullen PM, Turtle M, Prys Roberts C Sigmoid EK, Kothary SP et al found out that ketamine causes release of nor epinephrine which can be b lo ck ed by benzodiazepine in their study Diazepam for prevention of the rise in plasma catecholamine caused by ketamine. Fentanyl causes dose dependent decrease in heart rate. Carotid sinus baro receptor reflex control of heart rate is markedly depressed by fentanyl. These findings are also consistent with those of Badrinath.S, Michail N. Avramov, M Shadrick, Thomas R. Witt, and Anthony D. Ivankovich who in their study concluded that, ketamine induced tachycardia and hypertension was not evident in hemodynamic response of patients treated with the propofol-ketamine combination.

Hui TW et al also concluded that heart rate and peripheral vascular resistance are increased due to ketamine.

Heart rate is frequently slowed with more significant vagotonic effects of large doses of propofol. The effect of individual drugs on heart rate and blood pressure counterpart each other when used in combination.

There was fall in systolic blood pressure in propofol fentanyl group after induction as compared to propofol - ketamine group. Guit jb et al have also reported similar trend though both groups were haemodynamically stable.

The hemodynamic stability of propofol -ketamine combination makes it suitable for use during outpatient anesthesia. Which was evident from Schuttler J, Schuttler M et al study Optimal dosage strategies in TIVA using Propofol-Ketamine, Anesthesia

In our study both groups did not differ significantly in relation to the time to Phase I recovery but there was a statistically significant difference in the time up to 'Home readiness' between the two groups. The time up to Phase II recovery was significantly shorter with Propofol with Ketamine than with Propofol with Fentanyl.

Propofol seems to be effective in eliminating the side effects of subanaesthetic dose of ketamine in humans. Which was similar to the study The effects of small dose ketamine on Propofol sedation: Respiration post operative mood perception, cognition and p ain by Mortero RF, Clark LD., Tolan MM, Metz RJ, Tsueda K Hypotension (<20% of basal blood pressure) was reported in 5 patients of propofol-fentanyl group which was corrected by fluid infusion. There was no difference in surgery and recovery time, incid ence of PONV requiring treatment in either of the groups.

We therefore conclude that with Propofol with Ketamine is more efficacious in view of the time taken for the recovery compared to the Propofol with Fentanyl combination in elective day care surgi cal cases.

Conclusion

On comparing the recovery time and home readiness in Ambulatory Anaesthesia using Total Intravenous Venous Anaesthesia using agents Propofol with Fentanyl and Propofol with Ketamine, it was found that: -

- Propofol and Ketamine combination had a quicker recover
- Phase I recovery of both the groups were comparable
- Phase II recovery with Propofol and Ketamine was much shorter than Propofol and Fentanyl combination.
- The earlier Home Readiness in using Propofol with Ketamine combination makes it more advantageous than Propofol with Fentanyl in TIVA in day care surgeries.

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Original Research Article

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Evaluation of Spinal Anaesthesia in Paediatric Patient undergoing Lower Abdominal and Lower Limb Surgeries

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Abstract

Purpose: Spinal anaesthesia is a useful technique for infraumbilical and lower limb surgeries. The misconceptions regarding its overall safety, feasibility and reliability can be better known with greater use, its applications and research. We have designed this study to analyze the success rate, complications, and hemodynamic stability related to spinal anaesthesia in paediatric patients aged 5 years to 12 years.

Methods: Total 60 patients were included in this study. Spinal anaesthesia was given with injection hyperbaric bupivacaine (0.5%) in a dose of 0.3 mg/kg. Demographic data, vital parameters, number of attempts for lumbar puncture, sensory-motor block characteristics and complications were noted.

Results: Lumbar puncture was successful in 1st attempt in 46 (76.66%) patients and 2nd attempt was required in 14 (23.34%) patients. Vital parameters were not altered. Mean peak sensory level achieved was $T_{7.1 \pm 1.67}$ ($T_{4\text{-}12}$) and mean time for two segment regression was 45.33±4.71 minutes. Modified Bromage score was 3 in all patients. Sensory and motor block recovery was complete in all patients. Mean duration of surgery was 77.2 ± 11.88 minutes. The incidence of complications was minimal with hypotension and bradycardia.

Conclusion: Our study concludes that spinal anaesthesia in paediatric patients is feasible owing to its safety, higher success rate, and very low complications. Due to its early motor recovery, batter postoperative analgesia with minimal physiological alteration, no risk of respiratory depression and pulmonary aspiration, it reduces overall morbidity and mortality. Hence it is a preferred technique for daycare lower abdominal and lower limb surgeries.

Keywords: Spinal Anaesthesia; Lower Limb Surgery; Lower Abdominal Surgery; Pediatric Spinal Anaesthesia; Bupivacaine.

Introduction

Spinal anaesthesia is the technique of regional anaesthesia whereby anaesthesia is obtained by blocking the spinal nerves in subarachnoid space. The anaesthetic agent is deposited in the subarachnoid space and act on spinal nerve roots and not on the substance of the cord. Spinal anaesthesia is a useful technique in infraumbilical and lower limb surgeries [1]. Infants and children are at more risk for General Anaesthesia (GA) related complications [2-5]. Thus, spinal anaesthesia could also be indicated as a substitute to GA, principally in circumstances such as potentially difficult airway, malignant hyperthermia, and chronic respiratory disease [6-11]. Spinal anaesthesia in children has been associated with decreased incidence of hypoxia, bradycardia, postoperative apnoea and hypotension as compared to GA [12-16] thus, providing a high degree of cardiovascular and respiratory stability.

Spinal anaesthesia, however, gaining popularity in children, the misconceptions regarding its overall

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safety, feasibility, complications, and reliability can only be better known with its greater use, its applications and research. There is no scientific research that shows results of spinal anaesthesia in children regarding its success rate, safety, tolerability and complications in the Indian scenario. This inspired us to design this study in which we have prospectively analyzed the success rate, complications, and hemodynamic stability related to spinal anaesthesia in paediatric patients aged 5 years to 12 years.

Material and Methodology

After obtaining Institutional Ethical Committee approval we have conducted this study. Informed consent was obtained from parents of each patient for participation in the study. 60 paediatric patients aged 05 to 12 years of age group, having American Society of Anaesthesiology (ASA) physical status I – II of either sex, weighing 15 – 35 kg, were given spinal anaesthesia for infraumbilical or lower extremity surgery. Parents not willing to participate their children in the study, patients with infection at the local site, coagulopathy disorder, cardiovascular and neurological abnormalities, history of psychiatric illness, and congenital abnormalities were excluded from the study.

All patients were evaluated for pre-anaesthetic check up and not allowed to take solid food for 6 hours and clear fluid for 2 hours before anaesthesia. No overnight premedication was given. After the establishment of intravenous access, all patients were preloaded with a crystalloid solution (Ringer's lactate) 10 ml/kg. Heart rate, respiratory rate, blood pressure, and oxygen saturation were measured and noted as baseline values. All patients were premedicated with injection Ondansetron 0.08 mg/kg i.v.injection Glycopyrrolate 0.004mg/kg i.v. and injection Midazolam 0.04 mg/kg i.v.

All children except those who were co-operative and calm were sedated on the operating table before subarachnoid block using ketamine 1 mg/kg i.v. to provide an immobile patient for lumbar puncture.

All patients received spinal anaesthesia via midline approach with patients in lateral position under aseptic and antiseptic precautions. Lumbar puncture was performed in L_{4-5} interspace using standard 25G or 27G quincke spinal needles (9 cm). After getting free flow of cerebrospinal fluid (CSF), hyperbaric bupivacaine (0.5%) in a dose of 0.3 mg/kg was injected in the subarachnoid space over 10 seconds.

Patients were positioned supine immediately after the administration of intrathecal agent. Fluid therapy was maintained with lactated Ringer's solution and other appropriate intravenous fluids. The end of injection was taken as time 'zero' for further data recording. Above mentioned technique is the usual spinal anaesthetic technique being followed in children in our institute for children. Data were recorded for this observational study. The sensory level was assessed by loss of pinprick sensation by 23-gauge hypodermic needle bilaterally along the midclavicular line and facial expression, (lack of response to firm pinprick to that dermatome level) [17]. We used T_2- as baseline point for normal sensation. The test was performed every 5 seconds till the onset of sensory block at shin of tibia, then every 1 minute till it reached T_{10} dermatome, thereafter every 10 minutes till its full recovery. The onset of sensory block was taken as the time interval between the completion of local anaesthetic solution injection to the achievement of complete loss of sensation at shin of tibia (L_4). Time taken to achieve complete sensory blockade at T_{10} level were, maximum sensory level and two segment regression times were noted. The total duration of sensory block was taken from the onset of sensory block to return of pinprick sensation at the heel of feet (S_1).

Similarly, Modified Bromage score [18] (0: Free movement of leg and feet with the ability to raise extended leg, 1: Inability to raise extended leg and decreased knee flexion decreased, 2: Inability to raise or flex knees; flexion of ankle and feet present, 3: Inability to raise leg, flex knee or ankle, able to move toes) was assessed and noted. After 10 min of the subarachnoid block if the peak sensory level achieved was at least T_{10} and Modified Bromage score 3 (complete motor block), surgery was allowed to start. If there was no response to surgical stimuli, it was considered as a successful spinal block. If the peak sensory level was below T_{10} and modified Bromage score <3, the case was classified as a failed spinal block and was given GA with intubation and was excluded from the study. Demographic data, vital parameters, number of attempts for lumbar puncture, sensory-motor block characteristics and complication related to anaesthesia such as vomiting, shivering, post-dural puncture headache, and any manifestation suggestive of neurological injury were also recorded. The patients were monitored until full recovery.

The data were recorded in the patient's case record form and analyzed using MS Excel 2007 and SPSS version (Statistical Package for the Social Sciences).

Result

Demographic Data

The mean age group of the patients was 8.83±2.44 years in our study. The mean weight in the patients was 23.67±5.37 kg in our study. There were 43 male patients and 17 female patients. Spinal anaesthesia provided was for a variety of surgeries [Table 1]. Mean duration of surgery was 77.2±11.88 minutes.

In our study, mean time of onset of the sensory blockade at shin of the tibia was 173.47±23.81 Seconds, mean time to reach T_{10} Dermatome was 6.45±1.08 minutes, mean of peak sensory level achieved $T_{7.1 \pm 1.67}$ ($T_{4\text{-}12}$) and mean time to two segment regression was 45.33±4.71 minutes. The total duration of sensory blockade was 104.80±11.57 minutes. The mean time to achieve the modified Bromage score 3 was 8.27±1.35 minutes. The mean time to return of Modified Bromage score 0 was 95.08±10.17 minutes. Sensory and motor block recovery was complete in all the patients [Table 2].

Vital Parameters

There was no significant change in the mean value of systolic blood pressure, diastolic blood pressure, respiratory rate, and oxygen saturation after subarachnoid block at all time periods (Figure 1)

The total duration of postoperative analgesia in our study was 111.33±8.11 minutes as shown in Figure 2.

Table 1: Type of surgery

Type of Surgery	No. of Patients
Herniotomy	5
Appendicectomy	4
Urogenital surgeries (circumcision,hydrocele)	10
Orthopaedic (nailing, debridement, biopsy, tendon repair)	41

Table 2: Block characteristics

Block characteristics	
Sensory Block	
Onset (Shin of Tibia – L4)	173.47 ± 23.81 (Seconds)
Time to reach T10 Dermatome	6.45 ± 1.08 (Minutes)
Peak sensory level achieved	T7.1 ± 1.67 (T4-T12)
Two segment Regression Time	45.33 ± 4.71 (Minutes)
Total duration of Blockage	104.80 ± 11.57 (Minutes)
Motor Block	
Time to achieve Bromage score 3	8.27 ± 1.35 (Minutes)
Time to return Bromage score 0	95.08 ± 10.17 (Minutes)

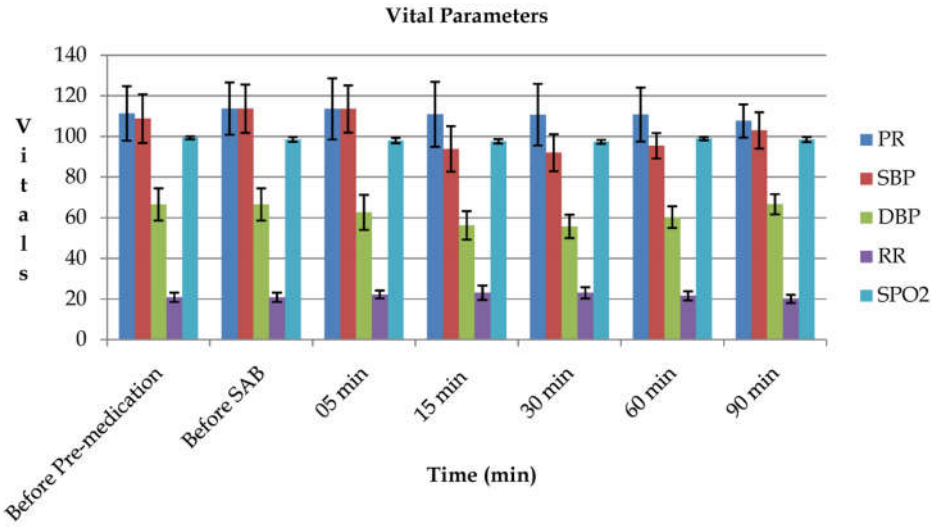

Fig. 1: Vital parameters

Table 3: Complication

Complication	No of patients
Bradycardia	1
Shivering	0
Hypotension	1
Nausea	0
Respiratory depression	0

Discussion

This study was undertaken to evaluate the safety and efficacy of spinal anaesthesia in the paediatric population aged 5 to 12 years. Spinal anaesthesia in paediatrics is a safe and cost-effective technique ideal for daycare surgeries. It provides intense and uniformly distributed sensory block with better muscle relaxation. The stress response to surgery is decreased and recovery is faster following spinal anaesthesia [19, 21].

The line joining the two superior iliac crests (inter-cristal line) crosses at L_5 S_1interspaces at birth, at L_5 vertebra in young children and at L_{3-4}inter spaces in adults. Because of this reason, the lumbar puncture is done at a level below which the cord ends; safest being at or below the inter-cristal line [19]. In our study, lumbar puncture was successful in 1st attempt in 46 (76.66%) patients and 2nd attempt was required in 14 (23.34%) patients. None of the patients required more than two attempts for lumbar puncture, which shows the ease and feasibility of lumbar puncture technique in the paediatric population.

Sensory and Motor Blockade

In our study, the mean time for onset of sensory block at shin of tibia was 173.47±23.81 seconds and motor block was 322.5±61.33 seconds. These results are consistent with the findings of H. Kokki and H. Hendolin [20].

The mean peak sensory level achieved was $T_{7.1 \pm 1.67}$ (T_{4-12}). The mean time of two segments regression was 45.33±4.71 minutes since the level of surgery was below T_{10} in all the patients, adequate dermatome level was present till the end of surgery. Thus, none of the patients required supplemental anaesthesia during surgery in our study. This finding is similar to Verma et al [21].

Ahmed et al [22] conducted a study on 78 children aged between 2 and 6 years undergoing different types of surgery in the lower part of the body and reported that sensory block showed widevariation of height from T_1 to T_7, which is consistent with our study. In our study, the mean time to achieve T_{10} sensory blockade was 6.45±1.08 minutes. With regard to the highest sensory level 10% patients attained T_4 level, 36.66% achieved T_6 level, 35% achievedT_8 level, 11.66% achieved T_{10} levels and 6.66% achieved T_{12} levels.

Jean P. Racleetal [23] observed in their study that time for two-segment regression (min) were 108±7min in group I (bupivacaine + normal saline) and 126±12min in group II (bupivacaine + epinephrine) and 171±12 min in group III (Bupivacaine + Clonidine.) In our study, the time for 2 segment regression was 45.33±4.71 minute. This difference in results might be attributable to the difference in age groups of patients selected. This can be explained by the fact that the drug uptake is faster in the subarachnoid space in infants owing to proportionally greater blood flow to the spinal cord as compared to adults [24]. With faster drug distribution and elimination, an infant's motor level regression is approximately 5 times faster than in adults. This causes a decreased duration of the block. Spinal anaesthesia, alone, for this reason, is generally restricted to 1 hour duration surgeries only. Duration, however, can be prolonged with the addition of opioids and clonidine [19].

Time for Complete Sensory and Motor Recovery

Duration of sensory block was 104.80 minutes which was less in our study compared to adults. Motor effect faded away earlier than sensory. Duration of motor effect in our study was 95.08 minutes. The results are consistent with the findings of Veronique Mahey and Claude Ecoffey [25] where they also noted shorter duration of motor block in children as compared to an adult. C.I. Junkin [26] in his study also noted the same findings as Verma et al. [21] and concluded that spinal anaesthesia in children is only meant for surgeries of shorter duration.

This can be explained on the basis that children have more CSF volume (4ml/kg) than adults (2ml/kg) and hence drug is diluted more. Also, there can be age-related differences in the diameter and surface area of spinal cord and nerve roots and rate

of absorption of local anaesthetic from subarachnoid space [27]. These authors further pointed out the difficulty in locating the subarachnoid space and injecting the drug while giving spinal anaesthesia. This may be due to fear of complication like trauma to cord or cauda equina which could cause neurological deficit. In present, study no difficulty was faced in locating subarachnoid space as we have taken due care in selecting space (L_{4-5}) and used small gauge needle. Cardiovascular changes related to spinal anaesthesia are less common in children than in adults. Children younger than 8 years of age have immature sympathetic nervous system and relatively small intravascular volume in the lower extremities and splanchnic system, which limits the venous pooling in this group [21,28].

It has been recommended that SpO_2 should remain more than 94% in children [29]. In present study, the SpO_2 level was more than 97% throughout the study. Respiratory rate was also not altered after spinal anaesthesia. Mean duration of analgesia is about 111.33min. C.I. Junkin [26] in his studies noted that duration of spinal anaesthesia is short in children but provides post operative analgesia satisfactorily in children.

Intraoperative hypotension (>20% fall in systolic blood pressure) was seen only in 1 (1.66%) patient which was treated with fluid and 3 mg mephentermine i.v.. Bradycardia was observed in 1 patient who was treated by injection Atropine 0.01mg/kg i.v. which are similar findings with the previous study [22]. No other complications like nausea, vomiting, respiratory depression or post-dural puncture headache was noted [Table 3].

Conclusion

Our study concludes that spinal anaesthesia in paediatric patient is feasible owing to its safety, higher success rate, and very low complications. Due to its early motor recovery, batter postoperative analgesia with minimal physiological alteration, no risk of respiratory depression and pulmonary aspiration, it reduces overall morbidity and mortality. Hence it is a preferred technique for daycare lower abdominal and lower limb surgeries.

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Comparison of Proseal Laryngeal Mask Airway Versus Endotracheal Tube in Anaesthetized Adult Patients

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Abstract

Endotracheal tube (ETT) is always considered as a standard device to keep an airway patent during surgery. Airway management of patients has also progressed form endotracheal tube to lesser invasive laryngeal mask airway. The proseal laryngeal mask airway (PLMA) is a recently introduced supraglottic airway device. It provides higher seal pressure and offer a better protection against regurgitation and gastric insufflation.

*Aims and Objective***:** To compare the efficacy of PLMA and ETT in terms of pulmonary ventilation, ease and no of attempts of placement and hemodynamic parameters.

*Material and Method***:** A prospective, simple randomized and comparative study was carried out after ethical committee approval in 60 patients, aged 20-50 years, with ASA grade I and II of either gender undergoing elective surgery under general anaesthesia at tertiary care centre in india during 2015 and 2016 to compare the efficacy of PLMA and ETT in terms of pulmonary ventilation, ease and no of attempts of placement and hemodynamic parameters.

Result: Both the groups were comparable regarding age, gender, height and baseline vitals. Patients intubated with PLMA showed no or minimal change in heart rate and mean arterial pressure as compared to ETT. The intubation time was comparable in both groups. The two groups were comparable with respect to number of attempts required for insertion of both the devices, (P> 0.05).

Conculsion: The comparative study showed PLMA has a good hemodynamic stability. It is concluded from our study that placement of PLMA is relatively easy and simple. The performance of PLMA is as good as the conventional ETT in providing general anaesthesia.

Keywords: Proseal Laryngeal Mask Airway; Regurgitation; Insufflation and Hemodynamic.

Introduction

The general anesthesia with cuffed ETT effectively maintains ventilation and protects the respiratory tract against regurgitation and aspiration [1]. The exaggerated hemodynamic responses [2], situations of failed intubation and damage to oropharyngeal structure at insertion are the serious concerns with endotracheal intubation [3].

Laryngeal Airway Mark (LMA) is a supraglotic device developed by British anesthetist Archie Brain and has been in use since 1988. LMA has more recently come into use in the emergency setting as an important accessory device for management of the difficult airway [4]. The drawbacks of LMA classic has a low pressure cuff which is inadequate for controlled ventilation and to protect the lungs against aspiration [5].

Brain [6] in 2000 developed a new modification of LMA called PLMA with improved ventilatory characteristics. It offers protection against regurgitation and gastric insufflations [5]. Proseal

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LMA has double cuff, reinforced airway tube and an oesophageal drainage tube. It provides better seal around the glottis and permits high airway pressure without leak. This study therefore was undertaken to compare the efficacy of PLMA and ETT in terms of pulmonary ventilation, ease of placement and hemodynamic parameters.

Aims and Objectives

The primary objectives of our study are:

1. Comparison of intubation response
2. Comparison of intubating conditions in terms of ease and number of attempts.

Method and Material

A prospective, simple randomized and comparative study was carried out after ethical committee approval in 60 patients, aged 20-50 years, with ASA grade I and II of either gender undergoing elective surgery under general anaesthesia at tertiary care centre in india during 2015 and 2016.

Patients were divided randomly by computer generated numbers to one of the following groups.

Group A (n=30) - Patients were intubated with PLMA

Group B (n=30) - Patients were intubated with ETT

Patients with hypertension, ischemic heart disease, cerebrovascular disease, mallampati grade III and IV, ASA grade III and IV, heart block, heart failure and body mass index ≥ 30 kg/m^2 previous difficult intubation, severe respiratory distress, patients on beta blockers and vasodilators and patients undergoing ENT surgery were excluded from study.

Software NCAA PASS 2000 was used to calculate sample size. To achieve power of 80% and α error of 0.05, 60 patients were required with 30 patients in each group.

Pre anaesthetic check up was done one day prior to surgery along with airway examination. Mallampati grading was done. Written informed consent was obtained from all the patients. Tab alprazolam 0.5mg was given night before surgery. Tab ranitidine 150 mg was given an hour before surgery with a sip of water. In preoperative room, baseline parameters were recorded. Intravenous line was secured with 20 gauge cannula. Midazolam 2 mg was given 30 minutes prior to surgery.

Anaesthesia Technique

After shifting the patient to operation theatre, monitors were attached and baseline parameters (BP, Pulse rate and ECG) were recorded using Philips intellivue mx700 monitor. Pre oxygenation was done with 100% oxygen for 3 minutes before induction. Patients were induced with thiopentone 5mg/kg, nalbufine 0.1-0.2 mg/kg, vecuronium bromide 0.08-0.1 mg/kg body weight, Oxygen, N_2O (50:50) and halothane 2%. IPPV was done for 3 minutes. Intubation was performed by senior anaesthesiologist who has atleast five years experience of working in anaesthesia

In group A, an appropriate size PLMA was selected based on weight criteria. The Cuff of the PLMA was fully deflated prior to insertion. Its posterior surface was lubricated with 2% lignocaine jelly. PLMA was inserted through the oral cavity using index finger technique, index finger was kept anteriorly at the the base of the bowl. After placement the PLMA cuff was inflated. Chest movements were checked visually as well as with ascultation on manual ventilation. All these factors indicated that PLMA was properly positioned.

In group B the patients were intubated with appropriate size ETT using Macintosh laryngoscopic blade. Anaesthesia was maintained by controlled ventilation with O_2:N_2O, (50:50), isoflurane 0.5% and vecronium as per requirement.

After Insertion of Device following Parameters were Recorded

No of attempts: successful insertion at first attempt was considered as easy insertion where as insertion at 2^{nd} or 3^{rd} attempt was considered as difficult insertion.

Mean time of placement: time taken from removal of face mask till successful placement of the airway

Haemodynamic responses like heart rate, mean arterial blood pressure were recorded before induction and also after insertion of devices at 1, 3 and 5 minutes.

Signs of correct PLMA placement are correct position of bite block, bilateral equal chest expansion, capnograph tracing and easy passage of orogastric tube.

Results

Both the groups were comparable regarding age, weight, gender, ASA grading and mallampatti

grading. Mean time of PLMA placement was lower as compared to ETT (Table 1).

In group A, the insertion of PLMA in first attempt was seen in 24 (80.0%) patients as compared to 23 (76.7%) patients in group B. In group A, the insertion in second attempt was seen in 6 (20.0%) patients as compared to 7 (23.3%) in group B. The two groups were comparable with respect to number of attempts required for insertion of both the devices. The difference was statistically not significant (p> 0.05) (Table 2).

There was significant difference seen in mean heart rate in both the groups at 1 and 3 minute after airway device placement. Similarly significant difference was seen in mean blood pressure at 3 minute in both the groups (Table 3 and 4).

Table 1:

Demographic Data	Group A PLMA	Group B ETT
AGE	45.12± 10.03	44.74±9.45
Gender M/F	12/18	14/16
Weight	66.23±8.51	66.76±7.98
ASA Physical Status I / II	26/4	25/5
Mallampatti Grading Grade I / Grade II	22/8	23/7
Mean time of placement	15 ± 3	18± 4

Table 2: Distribution of Patients according to no. of attempts required for insertion of device

No. of Attempts	Group A (PLMA)	Group B (ETT)	p value	Significance
1 attempt	24 (80.0%)	23 (76.7%)	P= 0.754	NS
2 attempt	6 (20.0%)	7 (23.3%)		
Total	30 (100.0%)	30 (100.0%)		

Table 3: Changes in Heart rate (HR) in two groups at different time intervals

Heart Rate	PLMA	ETT	T-Test	P- Value	Significance
Pre-induction	67.37±10.91	72.73±13.13	-1.085	0.090	NS
After insertion at 1 min	69.53±11.04	77.2±11.78	-2.6	0.012	Significant
3 min	67.00±7.52	93.50±10.46	11.268	<0.001	Highly Significant
5min	69.67±9.07	69.97±10.88	-0.129	0.898	NS

Table 4: Change in Mean Arterial pressure (MAP) in two groups at different intervals

MAP	PLMA	ETT	t- test	p-value	Significance
Pre-induction	92.63±7.41	88.77±10.77	1.620	0.111	NS
After induction 1min	92.87± 5.8	92.10±6.78	2.926	0.225	NS
3 min	90.77± 4.28	101.1±7.21	-6.751	<0.001	Highly significant
5min	94.17±6.48	94.03±7.15	0.076	0.94	NS

Discussion

Cuffed ETT ensures a patent airway and adequate ventilation. It also provides safe glottic seal especially for laparoscopic procedures under general anesthesia. The pressure response to tracheal intubation may be harmful to patients with ischemic heart disease or hypertensive patients. Attempts have been made to attenuate this response over a period of time. A variety of new airway devices have been added. A relatively new device, the PLMA is an improved version of a classic LMA and offers some added safety features over the classic LMA such as providing a better glottic at low mucossal pressure and a drain tube to vent out air and regurgitation material from the stomach. (Cook TM. Nolam) [12].

In our study patients in both the groups were significantly comparable regarding ease of placement and number of attempts. Two third of the patients in both the groups could be intubated in the first attempt. There was no third attempt or failed insertion in either group. Similar study done by Saraswat N et-al [8] and Maltby R et-al [9] in patients undergoing laproscopic surgeries found PLMA as effective alternative to ETT. In their studies they found higher success rate with PLMA than ETT. Mean time of placement of PLMA was less as compared to ETT. Furthermore the technique of placement of PLMA using introducer or stellete

could reduce the insertion time. When both the groups were compared after insertion of device there was significant increase in mean heart rate at 1 minute and 3 minute. At 5 minute the mean heart rate in both groups were the same. This increase in heart rate could be due to sympathetic stimulation associated with laryngoscopy and intubation for ETT placement. Similarly significant increase in MAP after insertion of device was found at 1 and 3 minutes in ETT group. When finding of MAP were compared in the two groups, highly significant difference was seen at 3 minute. These findings were comparable with the study of Y. Lim [10] and Saraswat N[8]. These are due to sympathetic stimulation with laryngoscopy and intubation with ETT where as PLMA being a supraglottic device does not requires laryngoscopy.

There was no incident of regurgitation, vomiting at the time of removal of device in any patient. The double cough arrangement of the PLMA is effectively prevents the chances of aspiration. Nasogastric tube was inserted in all cases via drain tube after confirming that there was no evidence of leak. Oxygen saturation and End tidal carbon dioxide were within normal limit throughout the procedure.

Conclusion

It is concluded from our study that the placement of PLMA is easy, effective and performance is as good as the conventional ETT in respect of providing effective patent airway during the controlled ventilation. This comparative study also shows that PLMA provides good haemodynamic stability.

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A Prospective Randomized Comparative Study of Epidural Block and General Anesthesia for Percutaneous Nephrolithotomy for Hemodynamic Stability and Postoperative Analgesia

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Abstract

Percutaneous nephrolithotomy (PCNL) is a minimally invasive procedure for removal of calculi in pelvicalyceal system which is usually performed under general anaesthesia. We conducted a prospective, randomized, comparative study to compare epidural block and general anesthesia with respect to hemodynamic stability and postoperative analgesia in patients undergoing PCNL. *Methods:* 80 urological patients of ASA I and II grade,posted for percutaneous nephrolithotomy were included in our study. They were divided into two groups of 40 each. In patients belonging to Group G, surgery was performed under General Anaesthesia and in Group E, surgery was performed under Epidural Anaesthesia using 1.5mg/kg of 0.5% bupivacaine and 1mcg/kg of Fentanyl to a maximum of 50mcg. Intraoperative hemodynamics, postoperative analgesia, amount of rescue analgesic required and patient satisfaction were compared between the two groups. Complications, if any were also compared. *Results:* In our study, we found that the Heart rate, Mean arterial pressure were increased in the initial 5 minutes after giving General Anaesthesia in patients belonging to Group G when compared to Group E. Time duration of post-operative analgesia was more in Group E with less amount of analgesic requirement than in patients belonging to Group G. Post-operative complications were also less in Group E than in Group G. With the results obtained in our study, we concluded that Epidural anaesthesia is better than General anaesthesia in patients undergoing PCNL.

Keywords: Epidural block; General anesthesia; Percutaneous-nephrolithotomy.

Introduction

Percutaneous nephrolithomy (PCNL) is a minimally invasive procedure for removal of renal calculi > 20 mm in size, multiple stones, staghorn stone in pelvicalycealsystem. This procedure was first described by Fernstorm and Johansson in 1976 [1].

Percutaneous nephrolithotomy can be done under general anesthesia, regional anesthesia, local anesthesia and under interpleural block [2-9]. It is usually done under general anesthesia with endotracheal intubation in most of the centers. Few disadvantages of general anesthesia are polypharmacy, airway complications like endotracheal tube displacement in prone position, aspiration of gastric contents, pulmonary atelectasis and neurological complications.

Peterson GN et al in 1985 first described the technique of regional anaesthesia for performing PCNL [10]. Since then many authors have used regional anaesthesia techniques like Spinal, Combined Spinal Epidural, sole Epidural for the procedure and have found out that regional anaesthesia is a better choice in patients undergoing PCNL [2-9,11].

Since most of them have used single drug like 0.5% bupivacaine, 0.75% ropivacaine, 0.5% ropivacaine in different doses for performing Epidural anaesthesia for PCNL, we have used 0.5% bupivacaine and fentanyl combination to find out the suprimacy and advantage in these patients.

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Materials and Methods

This prospective, randomized, comparative study was planned at Rajarajeswari Medical College and Hospital after taking approval from institutional ethical committee. 80 Patients aged between 18 to 60 years belonging to ASA I and ASA II grade between 30 to 60 years admitted for elective percutaneous nephrolithotomy were included in the study. Patients with uncontrolled medical illness, severe cardiac disease, severe respiratory disease, hypersensitivity for the drugs which were used for the study, patients with contraindication for regional anesthesia like neuromuscular disease, patients refusing to participate in the study, skin infection at the proposed sight of injection and with coagulation abnormalities were excluded from the study. They were randomly divided into two groups of 40 each by computer generated randomization. Group G received General anaesthesia with endotracheal intubation, whereas Group E received 1.5 mg/kg of Inj.Bupivacaine 0.5% + Inj. Fentanyl 1 mcg/kg through epidural catheter inserted at T10-T11 level or T11-T12 level.

Thorough preoperative evaluation was done. Routine and specific investigations required were carried out. Informed and written consent was taken from those patients who were willing to participate in the study. Participants were briefed about the study and were kept nil per oral 6 hours for solids. All the participants were given Tablet Alprazolam 0.25 mg on the previous night.

On the day of surgery, an 18 G intravenous line was secured in preoperative holding area and 500ml of Ringers lactate was started. Standard monitoring like ECG, Noninvasive blood pressure, Pulse oximeter, were monitored.

Group G patients received general anaesthesia. They were given Inj. Ranitidine 1 mg/ kg, Inj. Ondansetron 0.08 mg/kgintravenously. Pre-medicated with Inj.Glycopyrolate 0.2 mg. and Inj. Midazolam 0.02mg/kg. Pre-oxygenated for three minutes. Induced with Inj. Propofol 2 mg/kg, Inj.Fentanyl 2mcg/kg. Neuromuscular blockade was obtained with Inj.Vecuronium 0.1 mg/kg and intubated using appropriate size flexometallic endotracheal tube. Anaesthesia was maintained with intermittent doses of Vecuronium 1 mg each, Oxygen and Nitrous oxide and inhalation agent Isoflurane 1MAC throughout the procedure. At the end of the surgery 1gm paracetamol I.V. and local infiltration with 0.25% bupivacaine was given and reversed with Inj.Neostigmine 0.06 mg/kgand Inj. Glycoprolate 0.008 mg/kg. Extubation was done when they were fully awake and obeyed verbal commands and had good muscle power. All the vital parameters were recorded and shifted to post anaesthesia care unit for observation for another 2 hours.

Group E Patients were placed in sitting position. Under aseptic precautions, skin over T10-T 11/ T11-T12 interspace was infiltrated with 2% lidocaine. Epidural space was located using 18g Tuohy needle by loss of resistance technique to air. Epidural catheter was threaded with 20 G catheter and 5 cm of catheter was left in epidural space and fixed. Epidural test dose was given with 3cc of 2% lidocaine with adrenaline. If uneventful, 1.2mg/kg of 0.5% bupivacaine and 1mcg/kg of fentanyl to a maximum of 50mcg was given through epidural catheter. Level of analgesia was checked with pinprick test and level of sensory block was achieved till T6. Then patients were placed in lithotomy position.

Surgical procedure consisted of Cystoscopy and D J stenting in lithotomy position. Then patients were turned prone followed by percutaneous renal access using fluoroscopy. Stones were removed by fragmenting them. All the precautions were taken to protect the pressure points and neck. Vital parameters were monitored throughout surgery.

Perioperative hemodynamic parameters like Heart rate, Systolic blood pressure, mean arterial pressure along with arterial Oxygen saturation (SpO_2) were recorded every five minutes for the first thirty minutes and later every fifteen minutes till the end of the surgery. Any Hypotension (>25% fall in systolic blood pressure), Hypertension (>25% rise in the systolic blood pressure) Bradycardia (Heart rate <50/ min) Tachycardia (Heart rate > 100/min) was noted. Total duration of surgery was noted. Side effects if any were noted and recorded. Time taken for complete analgesia (loss of sensation to cold swab), and the level of anaesthesia in Group Epatients was noted. Time duration from epidural bolus and patient's request for the first rescue analgesic was taken as total duration of analgesia in Group E patients. Patients were monitored in the post anesthesia care unit for 2 hours. Haemodynamics and visual analogue score (VAS) for pain intensity were recorded in the scale of 0 to 10.Group G patients received Inj. Paracetamol 15mg/kg as rescue analgesic if VAS score was >4. Group E patients received inj. bupivacaine 0.125% 6 ml with 25mcg fentanyl as post - operative rescue analgesic when the VAS score was >4. Amount of rescue analgesics requested in next 48 hours were

noted. After 48 hours epidural catheter was removed. Patient satisfaction during perioperative period was recorded with a score from 0 to 10, 0 being best score and 10 being worst score.

Statistical Methods

The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc. Descriptive and inferential statistical analysis has been carried out in the present study. Quantitative data was analyzed using unpaired t-test and qualitative data was analyzed using chi-square test.

Results

This study was performed in 80 urological patients of ASA I and ASA II grade undergoing elective percutaneous nephro-lithotomy to evaluate the efficacy of Epidural anaesthesia over General anaesthesia. They were randomly divided into two groups, Group G (40 number) and Group E (40 number).

There was no significant difference between the groups with respect to age (45.125±7.34 in Group G and 44.875±8.37 in Group E), weight (63.325±7.65 kg. in Group G and 64.15± 5.916 kg. in Group E), sex, ASA grading, duration of surgery (94.5±23.66 min. in Group G and 86.875±24.66 min. in Group E) Base line Heart rate (88.9±17.376 in Group G and 84.1±7.83 in GroupE) and mean arterial pressure (90.08±6.161 in Group G, 88.25±6.634 in Group E) (Table 1, 2 & 3)

No significant difference in the size of stone between the groups was noted (38.4±28.8 mm.in Group G and 36.8±24.6 mm. in Group E). Site of the stone in both the groups in percentage is shown in Table 2.

There was significant rise in heart rate (90.9±16.201), and MAP (96.266±6.232 mm. of Hg) in the initial 5 minutes after intubation in Group G, compared to epidural group (76.825±9.156/min. and 80.2±6.812 mm. of Hg). (Group G=90.9±16.201, Group E=76.825±9.156). Intraoperative heart rate was significantly less in the epidural group compared to general anesthesia group. (P value 0.008 at 30 minutes to 0.0001 at 120 minutes) (Table 2). Mean arterial pressure (MAP) was significantly lower in Group E 5 minutes after epidural bolus and remained significantly lower throughout the surgery (P value 0.0001) (Table 3).

Postoperative analgesia was assessed with VAS score. 97.5% of patients in Group E had VAS < 3 at 2nd hour postoperatively, while 27.5% patients in Group G had VAS<3 while 17 (42.5%) had VAS between 4 to 7. (Table 5) Total duration of analgesia was significantly prolonged in Group E patients (5.097±1.458 Hrs.) compared with Group G (1.487±0.524 Hrs). with a P value of 0.0001.

Table 1: Comparison of demographic characteristics

Demographic Characteristics	Group E	Group G	P Value
Age in Years.	44.875±8.379	45.125±7.34	0.8875
Weight in Kg	64.15±5.916	63.325±7.65	0.5912
Sex			
Male	23	22	chi square
Female	17	18	0.8217
ASA Grade.			
I	23	22	chi square
II	17	18	0.8217
Duration of Surgery in Minutes.	86.875±24.66	94.5±23.66	0.1623

Table 2: Comparison of stone size and position

	Group E	Group G
Stone Size(MM)	36.8±26.6	38.4±28.8
Stone Position Number of Patients		
Staghorn	4(10%)	6(15%)
Pelvic Stone	16(40%)	28(70%)
Pelvic and Calyceal	8(20%)	4(10%)
Upper Calcyeal	8(20%)	2(5%)
Lower Calcyeal	4(10%)	0
Multiple Stones	9(22.5%)	7(17.5%)

Table 3: Cardiac parameters

	Heart Rate			MAP		
	Group E	Group G	P Value	Group E	Group G	P Value
0MIN	84.1±7.83	88.9±17.376	0.791	88.25±6.634	90.08±6.161	0.223
5MIN	76.825±9.15644	94.9±16.201	0.0001	80.2±6.812	96.266±6.232	0.0001
15MIN	74.475±8.506	86.125±12.916	0.0001	76.175±7.104	82.133±6.381	0.02
30MIN	73.3±8.724	79.05±10.215	0.008	72.966±6.309	83.475±7.333	0.0001
60MIN	69.95±12.238	76.45±8.569	0.001	72.283±4.795	80.466±4.569	0.0001
90MIN	71.775±6.836	77.6±9.896	0.027	75.916±5.831	81.116±5.809	0.0001
120MIN	71.6±7.6524	81.75±13.511	0.0001	82.2±6.771	88.25±6.243	0.0001

Table 4: VAS score

	Group E			Group G		
	0 TO 3	4TO 7	8TO 10	0 TO 3	4TO 7	8 TO 10
2HRS	39 (97.5%)	1(2.5%)	NIL	11(27.5%)	17(42.5%)	12(30%)
4HRS	37 (92.5%)	3(7.5%)	NIL	16(40%)	22(55%)	2(5%)
12HRS	38(95%)	2 (5%)	NIL	30(75%)	10(25%)	NIL
24HRS	40 (100%)	0	NIL	36(90%)	4(10%)	NIL
48HRS	40(100%)	0	NIL	38(95%)	2(5%)	NIL

Table 5: Rescue analgesic required

No of Hours	Group G	Group E	Epidural Top Ups in Group E No of Epidural Top Ups	No of Patients
0	NIL	NIL	0	NIL
1	19	NIL	1	NIL
2	17	NIL	2	NIL
4	4	16	3	3
6	ALL 40	17	4	8
12	ALL 40	32	5	13
24	ALL 40	22	6	16
48	28	12		

	Group E	Group G	P value
Time of first Rescue Anagesia (Hours)	5.097±1.458	1.487±.524	0.0001

Table 6: Patient satisfaction score

	Group E			Group G	
0 TO 3	4TO 7	8TO 10	0 TO 3	4TO 7	8 TO 10
37(92.5%)	3(7.5%)	NIL	20(50%)	20(50%)	NIL

Table 7: Postoperative complications

	Adverse Effects Group E	Group G
Hypotension	3(7.5%)	2(5%)
Shivering	5(12.5%)	2(5%)
Nausea/ Vomiting	2(5%)	9(22.5%)
Itching	4(10%)	0

Length of Hospital stay was also less in Group E (2.7±0.516 days) than Group G (3.125±0.607 days) with a P value of 0.0012 which is statistically significant. 9 patients in Group G had postoperative nausea and 9 had hypotension while 2 patients in Group E complained of nausea/vomiting and only one had hypotension postoperatively. 4 patients in Group E complained of itching postoperatively. Patient satisfaction score were significantly better in Group E patients (Table 6).

Discussion

Though General anaesthesia has been used as a standard technique for PCNL. Many of the previous studies have concluded that general anaesthesia is likely to cause more morbidities like anaphylaxis due to polypharmacy, complications associated with endotracheal intubation, cardiovascular, pulmonary and neurological complications during prone positioning [2-9].

In our prospective, randomized comparative study on 80 patients (40 in each group) we have tried to establish the efficacy and safety of Thoracic epidural anaesthesia for PCNL against General anaesthesia.

Singh V et al in their comparative study epidural anaesthesia with general anaesthesia for PCNL have reported lower VAS score, less need for analgesics, shorter hospital stay [2]. Kimm SS et al have also found haemodynamic stability, better analgesia, better patient satisfaction, lower VAS score in patients undergoing PCNL under regional anaesthesia[11]. Other studies conducted by Kuzugunbay B et al [3], Karacalar S et al [4], Bajwa SJ et al [5], Virkar ND et al [6], Tangpaitoon T et al [7], Parkh DA et al [8] have concluded Epidural anaesthesia is better in terms of hamodynamic stability, lower VAS score, and lower postoperative complications which is in consistent with our study.

We have found that patients under epidural anaesthesia (Group E) have more stable hemodynamic parameters, prolonged analgesia, lower postoperative analgesic requirement, more patient satisfaction (Table 6), and lesser number of days in the hospital compared to patients undergoing PCNL under general anaesthesia (Group G) (2.7+/-0.516 days in Group E against 3.125+/-0.607 in Group G). Postoperative complications like nausea and vomiting was more in Group G (9 compared to 2 in Group E), while 10% of Group E patients had itching compared to no incidence of itching in Group G.

We have also found that blocking the spinal segments with epidural injection to T6-T12, gives good analgesia, anaesthesia, cardio stability with minimal postoperative complications. This may be due to lesser motor blockade in the lower limbs with more intense analgesia in the operative site (T10 to L2). Higher incidence of PONV in Group G may be due to nitrous oxide, opioids and inhalational agents used in the technique.

Conclusion

Most of the urologists prefer to do PCNL under general anaesthesia. In our study we have found that Thoracic Epidural anaesthesia using T10-T11 or T11-T12 space, gives as effective analgesia and anaesthesia as General anaesthesia with more haemodynamic stability, prolonged analgesia, less VAS score, lesser amount of postoperative analgesic requirement, more patient satisfaction and lesser incidences of postoperative complications. Patient co-operation due to long surgical time and prone position during surgery should be sought out by explaining to the patient preoperatively. Airway and Oxygen saturation should be monitored throughout the procedure. So Thoracic Epidural anaesthesia is an alternative and efficient technique for performing PCNL.

Limitations of the Study

We have conducted our study on a limited number of patients of ASA I/ASA II grade. More studies on increased number of patients with other co-morbidities like diabetes, hypertension may also be required to give it's feasibilities and safety in these patients.

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Neostigmine as an Adjuvant to Paediatric Caudal Analgesia

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Abstract

Caudal analgesia is one of the most popular method for intra and post-operative method for abdominal, perennial and lower limb surgeries for children's. For local anesthetic common drug used is Bupivacaine. In children caudal epidural block is one of the common anesthetics techniques in children. It is the general, simple and safe procedure for local anesthetics. It is administered as single shot technique. Several adjuncts such as opioids, ketamine, midazolam,clonidine and neostigmine have been used with bupivacaine to prolong its action & thus extend the duration of post-operative analgesia provided by the 'single shot' caudal technique.

Keywords: Caudal Analgesia; 'Single Shot' Caudal Technique; Post-Operative Analgesia and Bupivacaine.

Introduction

In neuraxial blocks alpha 2 agonist clonidine and peripheral nerve blocks are used for prolong use of bupivacaine. These two are commonly used additive for caudal analgesia in children. Clonidine is shown to be one of the safe procedure without any respiratory depressions after systemic, epidural or spinal administration. Although epidural clonidine may also cause hypotension, bradycardia and sedation in higher doses, serious adverse effects are uncommon in the dose range normally used in children (1-2 μg/kg) [2]. These are explained in three possible actions.

First methods include clonidine blocks in A and C fibers as a consequence of increased potassium conductance in isolated neurons thus intensifying local anesthetic block. Second method clonidine is used as local vasoconstriction thus it decreases the local spread and remove block around neural structures. This method shows little evidence in clinical doses. Third method uses combined clonidine with spinal local anesthetic of prolongs analgesia.

However in different studies it is shown that clonidine has improving and prolonged analgesia procedure for caudal bupivacaine. Also in post-operative analgesia mixtures of caudal clonidine varies. With this in mind, we conducted this study to assess the efficacy of clonidine in prolonging the action of bupivacaine when used for caudal epidural analgesia in childrenundergoing surgeries

Literature Review

A study was conducted in 100 patients, ASA status 1 and 2, age 1-3 years, undergoing sub-umbilical surgeries under general anaesthesia. They were randomised into two groups. Group A

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(control group) received 1 ml/kg of 0.25% bupivacaine in normal saline and Group B patients received 1 ml/kg of 0.25% bupivacaine with 1μg/kg of clonidine in normal saline. It was concluded that clonidine in a dose of 1 μg/kg added to 0.25% bupivacaine for caudal analgesia and administered as a 1 ml/kg mixture in children for sub-umbilical surgery significantly prolongs the duration of post operative analgesia when compared to 1 ml/kg of 0.25% bupivacaine alone without any side effects. In adoubleblined studies which was conducted in 46 childrens for 104 months under hypospadias repair were randamised into two groups ASA 1 or 2 aged the iv group received clonidine 2μg/kg i.v. and simultaneously the same volume of saline caudally. The caudal group received clonidine 2μg/kg caudally and a similar volume of saline i.v. It was concluded that the analgesic effect of clonidine 2μg/kg as an adjunct to caudal block with bupivacaine 0.25%, 0.5 ml/kg is similar whether administered i.v. or caudally.

A study of 60 ASA status 1 and 2 patients of age 6 months to 6 years who were undergone abdominal surgeries are randamised into three groups. Group A received bupivacaine 0.25%(1ml/kg) with dexmedetomidine 2μg/kg in 1 ml normal saline. Group B received bupivacaine 0.25%(1 ml/kg) with clonidine 2 μg/kg in 1 ml normal saline & Group C received bupivacaine 0.25%(1ml/kg) with 1 ml normal saline. It was concluded that the addition of 2μg/kg of dexmedetomidine or clonidine 2μg/kg to caudal bupivacaine 0.25%, 1 ml/kg significantly promoted analgesia after anaesthetic recovery in children aged 6 months to 6 year. Moreover, dexmedetomidine did not offer significant advantage over clonidine as regards to the analgesia duration.

Around a study of 60 boys aged 1 to 10 years undergone orchidopexy were recived three solutions of injections. Group A received 0.25% bupivacaine 1 ml/kg with adrenaline 5 μg/ml (1/200000), Group C received 0.25% bupivacaine 1 ml/kg with clonidine 2 μg/kg and Group K received 0.25% bupivacaine 1 ml/kg with ketamine 0.5 mg/kg. The median duration of caudal analgesia was 12.5 hrs in Group K compared with 5.8 hrs in Group C and 3.2 hrs in Group A. There were no differences between the groups in the incidence of motor block, urinary retention or post operative sedation

In a randomized surgery of upper abdomen surgery two groups of CB and MB are taken. which CB Group received clonidine 2 μg /kg in 1.25 ml/kg of bupivacaine 0.2%. Group MB received morphine 30 μg/kg in 1.25 ml/kg of bupivacaine 0.2%(total bupivacaine did not exceed 2.5 mg/kg). The total volume of injectate was 1.25 ml/kg. It was concluded that the addition of clonidine 2 μg/kg to bupivacaine administered caudally provided an increase in sedation and duration of postoperative analgesia compared with the addition of morphine 30 μg/kg to bupivacaine.

For a group of 60 boys of age 2 to 10 years who undergonehypospadias repair surgery where admimistrated as Group 1 received a caudal injection of 0.25% bupivacaine 1 ml/kg. Group 2 received an identical local anesthetic dosage mixed with neostigmine 2 μg/kg. Group 3 received caudal neostigmine 2 μg/kg diluted in 0.9 Naclsolution to a total volume of 1 ml/kg. It was concluded that caudal neostigmine 2 μg/kg provide post-operative analgesia comparable to 1 ml/kg of caudal bupivacaine 0.25% in children undergoing hypospadias repair surgery. Co-administration of the two drugs is associated with extended duration of post-operative analgesia & reduced need for supplementary analgesics.

A randomised prospective, parallel group , double blinded study, 60 children were recruited and allocated into two groups: Group R(n=30) received 0.25% ropivacaine 1 ml/kg+0.5 ml normal saline and Group RD(n=30) received 0.25% ropivacaine 1 ml/kg with dexmedetomidine 2 μg/kg, making the volume to 0.5 ml. It was concluded that caudal dexmedetomidine (2μg/kg) with 0.25% ropivacaine(1 ml/kg) for paediatric lower abdominal surgeries achieved significant post operative pain relief that resulted in a better quality of sleep and prolonged duration of arousable sedation and produced less incidence of emergence agitation following sevofluraneanaesthesia.

A randomised double blind study was conducted in a total of 44 ASA-1 pediatric patients between the ages of 1-9 years, scheduled for elective hernia surgery. They were randomised into two groups and caudal block was given: Group 1 received 0.25% ropivacaine and Group 2 received 0.25% ropivacaine and clonidine 2 μg/kg after induction of general anaesthesia. It was concluded that the duration of analgesia was significantly prolonged in Group 2. It was concluded that caudal block with 0.25% ropivacaine isobaric combined with 2 μg/kg of clonidine provides efficient analgesia intra-operatively and prolonged duration of analgesia post-operatively.

A randomised, prospective double blind study was conducted in a total of 90 children of ASA 1-2 aged 3-8 years scheduled for infraumbilical surgical

procedures. They were randomised into two groups: Group 1 received 0.25% ropivacaine 1 ml/kg + clonidine 2 μg/kg and Group 2 received 0.25% ropivacaine 1ml/kg + fentanyl 1 μg/kg. It was concluded that the analgesic properties of clonidine and fentanyl as additives to ropivacaine in single shot caudal epidural in children are comparable but clonidine offers a more favourable side effect profile and increased patient comfort.

A randomised prospective parallel group open level study was conducted on 50 children aged 2-8 years undergoing infra-umbilical surgery. Group B received 0.25% bupivacaine 0.75 ml/kg and Group BM received a combination of 0.25% bupivacaine 0.75 ml/kg and morphine 0.03 mg/kg. It was concluded that 0.25% bupivacaine along with low dose morphine (0.03 mg/kg) provided effective and longer duration of analgesia in comparison to 0.25% bupivacaine alone.

Objectives of Study

This study is clinical profile of an alpha 2 agonist clonidine with bupivacaine administered caudually. The parameters are

1. To compare the onset of analgesia.
2. To compare the ability to provide smooth intraoperative and post operative analgesia.
3. To compare the duration of analgesia provided.
4. To compare the side effects
5. To compare sedation.

Materials & Methods

In double blined controlled study of 60 patients of ASA 1 and ASA2 status agrd between 1 to 12 years who were undergone elective surgery satisfy all criteria.

Group A (n=30) Patients receiving 1 ml/kg 0.25% bupivacaine in normal saline. Group B (n=30) Patients receiving 1 ml/kg of 0.25% bupivacaine with 1 μg/kg of clonidine in normal saline.

Inclusion Criteria

1. ASA Grade 1 and 2 status.
2. 1 to 12 years of age.
3. Parents giving informed written consent.
4. Patients scheduled to undergo elective sub-umbilical, perineal and lower limb surgeries.

Exclusion Criteria

1. ASA 3 or greater.
2. Age more than 12 years.
3. Any contraindications to epidural anaesthesia like sacral spine abnormalities, local site infection & coagulation abnormalities.
4. Patients with haematological diseases, neurologic, psychiatric disease, severe renal and hepatic derangement.
5. Patients on anticoagulants, anti psychotic drugs, tricyclic antidepressants, alpha 2 adrenergic agonists and beta blockers.

Method of Study

The solution used for study will be prepared by anaesthesiologist who were not involved in patient care. The patients are blinded by the study solution. In the pre anesthetic evaluation in patients the test were conducted a day before surgery. The patient with inclusive criteria were taken and written in a valid consent in following groups.

1. *Group A:* (n=30) Patients receiving 1 ml/kg of 0.25% bupivacaine in normal saline.
2. *Group B:* (n=30) Patients receiving 1 ml/kg of 0.25% bupivacaine with 1 μg/kg of clonidine in normal saline.

In the operation theatre peripheral intravenous access is secured bu using 22 G or 24 G cannula depending on patient age. For non-invasive blood pressure baseline, pulse rate, oximetry will be removed. About 20 minutes before surgery all patients were made to receive 0.5-0.75 mg/kg orally (standard formulation mixed with sweet fruit syrup) or rectally (standard formulation).

As a preloading solution berilyte–p or ringer lactate is given before surgery that to depend on age group. The intravenous fluids is given depending upon the body weight and operative loss requirements.

The airway management is lifted to discretion to all patients with facemask, laryngeal mask or endotracheal tube with or without relaxants for children's maintaining with 70 percentage nitrous oxide in oxygen and 0.5 to 2.5 percentage halothane. Patients are put in lateral positions and single shot is given under aseptic precaution using23G hypodermic needle.

Patients in Group A will receive 0.25% isobaric bupivacaine 1 ml/kg in normal saline and Group B will receive 1 ml/kg of 0.25% bupivacaine with 1

μg/kg clonidine in normal saline. One millilitre of clonidine contains 150 μg/ml which is diluted with 9 ml saline in a 10 ml syringe. For each child two syringes are prepared : one syringe contained the diluted clonidine(15 μg/ml) to give a dose of 1 μg/kg (a total volume of 0.07 ml/kg), and the other contained the same volume of normal saline.

Parameters Observed

Baseline pulse rate, respiratory rate, non invasive blood pressure will be recorded. Cardio-respiratory parameters will be monitored continuously and recordings will be made every 5 minutes until 30 minutes and at 10 minute interval, there after up-to 60 minute and then at 15 minute interval until the completion of the surgery. Intraoperatively and post operatively, incidence of bradycardia(Heart rate less than 80 beats/minute) will be treated with atropine (0.02 mg/kg) and hypotension (SBP less than 70 mm/Hg) or systolic BP falling more than 20% will be treated with Injection mephentermine bolus(0.3 mg/kg). Post operatively the heart rate and blood pressure will be measured at 15, 30, 45, 60, 90 and 120 minutes. The following parameters will be assessed at 15, 30, 45, 60, 90, 120 mins, 4hrs, 6hrs, 12hrs and 24hrs postoperatively.

1. Pain severity
2. Sedation

- Pain severity will be assessed using FLACC scale where in FLACC includes Face, Leg, Activity, Cry and Consolability.

0: No Pain

1-3: Mild Pain

4-7: Moderate Pain

-10: Severe Pain

Each of the five categories is scored from 0-2, resulting in total range of 0-10, FLACC=Face, Leg, Activity, Cry, Consolability.

Table 1: FLACC Scale for Pain Assessment

Category	Scoring		
	0	1	2
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent too constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid and jerking
Cry	No cry(Awake or asleep)	Moans or whimpers; occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to; distractable	Difficult to console

- Sedation &Post operative nausea and vomiting will be assessed using sedation score and Post operative nausea and vomiting score(PONV score) respectively.

Sedation Score

0 : Alert and Aware

1 : Asleep, Arousable by verbal contact

2 : Asleep, Arousable by physical contact

3 : Asleep, not arousable and it was noted whether the child was in normal sleep,recorded as X.

Duration of analgesia will be recorded as the time interval from the completion of anaesthesia to the time when the patient complains of pain.In the post anaesthesia care unit, the necessity for rescue medicine was decided by the pain score. Rescue medication was administered when the FLACC score was greater than or equal to 4. Rescue analgesia will be provided by paracetamol suppository with a loading dose of 40 mg/kg followed by 20 mg/kg every 6 hrs.

The number of doses of rescue medication required and the time to first administration of rescue medication will be also noted. In the post-operative period, patients will be also monitored for adverse effects, including respiratory depression, vomiting, hypotension and bradycardia.

During surgical procedure adverse effects like vomiting, hypotension(defined as systolic BP less than 70 mm/Hg), bradycardia(heart rate less than 80 beats/minute) and respiratory depression (defined as O_2 saturation less than 93%, requiring oxygen via face mask) will be recorded.

Statistical Analgesia

Appropriate statistical analysis of data will be done using the following tests.

1. Student t test for parametric data
2. Chi-square test for non-parametric data

$P<0.05$ will be considered as statistically significant.

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Femoral Nerve Block Versus Intravenous Fentanyl for Positioning During Central Neuraxial Block: A Comparitive Study

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Abstract

Background: Fracture of the femur is a common orthopaedic problem following trauma in patients of all ages. This study was undertaken to compare the effectiveness of intravenous (IV) fentanyl with femoral nerve block (FNB) in positioning the patients for combined spinal epidural anesthesia (CSE).

Methods: 100 patients between the ages 25 to 75 years, of ASA grade I, II and III, scheduled for elective surgeries of femur fracture were evaluated in 2 groups. Group-1 (n=50) received femoral nerve block with 15ml of 1.5% lignocaine and Group-2 (n=50) patients received one dose of IV fentanyl 1μg/kg. Assessment of pain was carried out using visual analog scale (VAS). This was rated before, during and after the procedure of positioning for spinal/combined spinal epidural anesthesia (CSE). Vital parameters were tabulated.

Results: VAS scores were noted at 0, 2, 5,10,15 minutes and at the time of positioning. The average VAS scores at 15 minutes in Group-1 was 1.47 and 3.82 in patients in Group-2. Time taken for CSE was significantly less in Group-1 (13.02 minutes) as compared to Group-2 (19.66 minutes). Patient satisfaction scores were significantly higher in Group-1 (45/50) 1.49 as compared to non Group-2 (10/50) 0.34. Quality of patient positioning was better in Group-1 (2.78) as compared to Group-2 (1.38).

Conclusions: This study concludes that FNB is highly effective in giving good pain relief for positioning for regional anaesthetic procedures improving performance time and offers higher acceptance among patients with femoral fractures as compared to IV fentanyl.

Keywords: Combined Spinal Epidural; Femoral Nerve Block; Fentanyl; Fracture Femur; Positioning.

Introduction

Femur fractures are are at a rise due to trauma in all age group patients. In elderly patients it leads to severe pain and considerable morbidity [1]. Patients with fracture of the femur present special problems to the anesthesiologist. The femoral shaft is subjected to major muscle forces that, especially in young patients, can deform the hip and/or thigh and angulate the bone fragments, and hence is challenging for the orthopaedic surgeon to attain reduction of the fracture [2]. Therefore, absolute muscle relaxation is required for the same. For this purpose, spinal or epidural anesthesia is routinely used in these patients. A proper positioning of the patient is required for a successful central neuraxial block. Inability of the patient to properly position the limb and extreme pain at the fracture site poses a challenge for the anaesthesiologist in terms of ideal positioning for CSE [3]. Also, any overriding of the fracture ends causes deformity and is extremely painful. Delay in positioning further aggravates pain. Administration of epidural requires relatively longer time hence positioning for patients becomes more problematic. Hence the procedure of patient

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positioning to perform a spinal block, in most cases, requires the administration of IV analgesics [4].

Several modalities like intravenous (IV) fentanyl, femoral nerve block (FNB) or fascia iliac block with local anaesthetic have been tried so as to reduce the pain and improve the positioning of these patients for CSE [4,5]. Few studies have demonstrated that a fascia iliac compartment (FIC) block provides effective analgesia for a fractured femur in terms of facilitating an adequate position for spinal anaesthesia or when administered either during pre-hospital management or in emergency departments [6-8].

Systemic analgesics, such as narcotics, are commonly used, but their morbid side effects including respiratory depression, cognitive impairment, vomiting, urinary retention etc limits their clinical utility, especially in injuries of the head, chest, or abdomen [9-11]. Various studies in the recent times have suggested that the use of femoral nerve block (FNB) using local anaesthetics. It was in fact found to be a safe and effective method [12,13].

Although femoral nerve block is one of the easiest peripheral nerve blocks to perform because the landmarks are easy to identify and the nerve is usually superficial yet the anaesthesiologist must be aware of possible risks and complications of the procedure if not done correctly. Possible complications included vascular puncture, hematoma, difficulty weight bearing/ mobilizing leading to falls and injuries [14,15]. We conducted this study to compare the analgesic effect provided by FNB with IV fentanyl prior to positioning for combined spinal epidural block in patients who are posted for the femur fracture surgery.

Materials & Methods

After the approval of institutional ethics committee and with the informed consent, a prospective randomized double blinded study was conducted from June 2017 to December 2017. 100 patients of both sexes who were posted for femur fracture surgery between the age group of 25 to 75 years, with ASA I, II and III were included in the study. Fracture types were graded by one senior orthopedic surgeon.

Type of fractures were as shown in Figure 1. Patients were randomised into 2 groups using computer generated random number. Each group comprised 50 patients each. In Group-1 patients were given FNB before positioning for combined spinal epidural block, while in Group-2 patients were given IV fentanyl 1μg/kg 5 minutes prior to combined spinal epidural block. Patients with multiple fractures, polytrauma, peripheral neuropathy, bleeding disorders, mental disorders, neurological deficits which might hinder proper assessment during block, any allergy to study drugs were excluded from study.

Patients were asked to stay nil orally for six hours. They received a premedication with tablet Ranitidine 150 mg and tablet Alprazolam 0.5 mg at bed time. On the morning of surgery all patients had peripheral IV access with 18-gauge cannula and received an infusion with ringer lactate at a rate of 15ml/kg. Standard multipara monitor connected and electrocardiography, pulse rate, SpO_2, respiratory rate and non-invasive blood pressure measurement recorded. All patients were supplied with oxygen (5L/min) via a face mask.

No premedication or sedation was given. Femoral nerve blocks were administered in the anaesthesia induction room, which was adequately equipped with resuscitation equipment. All the patients were explained about the FNB procedure and also about the scoring of VAS (visual analogue score).

The blocks were given by the blind technique by loss of resistance after confirming paraesthesia. The patient was positioned supine, the anterior superior iliac spine and the pubic symphysis were marked. The line joining these 2 landmarks represents the inguinal ligament. The landmark for the femoral nerve is the center of this line where the needle is placed. Then the femoral pulse was palpated and marked.

A 23-gauge needle was used in this study and was inserted directly lateral (1-1.5 cm) to the artery in the inguinal crease. At this location, the femoral nerve is wide and superficial, and easier to pass the needle as the muscle mass is less. The needle is directed upwards toward the center of the inguinal ligament, paraesthesias elicited and the drug was injected. 15 ml of lignocaine 1.5% was injected slowly after a negative aspiration keeping the needle steady at the point of eliciting paraesthesia in the thigh. In this study 2% lignocaine was used for FNB, which was diluted to make the drug concentration 1.5% of lignocaine.

The relief of pain following FNB was assessed quantitatively using visual analog scale (VAS) (0-no pain to 10-worst pain) and satisfaction score (Table 1) at interval of 2 minutes, 5 minutes, 10 minutes, and 15 minutes. Then, patients were shifted

to the operating room and combined spinal epidural performed in sitting position after 15 minutes of giving FNB while checking VAS during positioning. After confirming the appropriate interspace, 2% lignocaine (3 ml) was injected, followed by insertion of 18 gauge Tuohy's needle in the epidural space which was confirmed by the loss of resistance to air technique.

Test dose of 3 ml lignocaine with adrenaline was given through the epidural catheter while closely monitoring the heart rate. The subarachnoid block was then performed using 25 gauge Quincke's needle one level below the insertion of the epidural catheter and 3 ml of 0.5% bupivacaine was injected into the space after obtaining a clear flow of cerebrospinal fluid. Time to perform spinal anesthesia was noted. Intra operatively the time of onset, maximum level and duration of sensory block were recorded.

In patients, wherein IV fentanyl was used were directly shifted to the operation room for the central neuraxial block in sitting position. IV fentanyl was given 5 minutes prior to the neuraxial block. VAS score was noted during positioning for the central neuraxial block. Time to perform combined spinal epidural block was noted in both groups, starting from positioning for the spinal block till the patient is made supine after the combined block. Patients acceptance and satisfaction scores were noted.

Results

Demographic data in both the groups were comparable (Table 2). VAS values were checked regularly just before FNB/IV fentanyl (T0), then 2 minutes, 5 minutes, 10 minutes, 15 minutes after FNB (T2, T5, T10, T15) and during positioning of the patient.

Group I (FNB group) 1.473±0.1639 had lower VAS scores compared to Group II (IV fentanyl) 3.820±0.3615 and the difference was statistically significant ($P < 0.001$) as shown in Table 3. Satisfaction score was better in Group I when compared with Group II always (1.4952±0.033 versus 0.3460±0.1786).

Table 1: Satisfaction scores

Visual Analog scale (VAS)	Satisfaction score
0	Not Satisfactory
1	Satisfactory
2	Good
3	Optimal

Table 2: Demographic data of the patients in both groups

	Group-1	Group-2
No. of patients	50	50
Mean age (years)	58	57
Sex (M/F)	28/22	27/23
ASA (1/2/3)	9/22/19	10/28/12
	Site of fracture	
Neck of femur	28	30
Inter-trochanteric	10	12
Sub-trochanteric	3	1
Shaft of femur	9	7

Table 3: Summary of results of the procedure

	Group-1 (n=50)	Group-2 (n=50)	P-value
VAS at T0	7.202±0.3560	7.294±0.3793	0.214(NS)
VAS at T2	5.554±0.2358	6.280±0.3511	0.014*(HS)
VAS at T5	3.384±0.1920	5.66±0.3837	<0.001*(HS)
VAS at T10	1.736±0.1535	5.382±0.4154	<0.001*(HS)
VAS at T15	0.768±0.1491	3.820±0.4552	<0.001*(HS)
VAS during positioning	1.474±0.1639	5.250±0.3615	<0.001*(HS)
Quality of patient positioning (0-3)	2.782±0.1273	1.382±0.2413	<0.001*(HS)
Mean satisfaction scores (0-1.8)	1.4952±0.0333	0.3760+0.17867	<0.001*(HS)
Time for anesthesia (minute)	13.026±0.4628	19.660±0.3742	<0.001*(HS)

*Significance value is 0.000; HS=highly significant; NS=not significant.

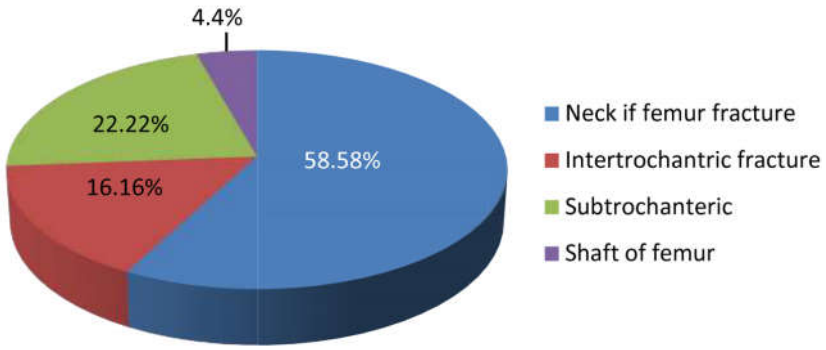

Fig. 1: Type of fractures in study groups

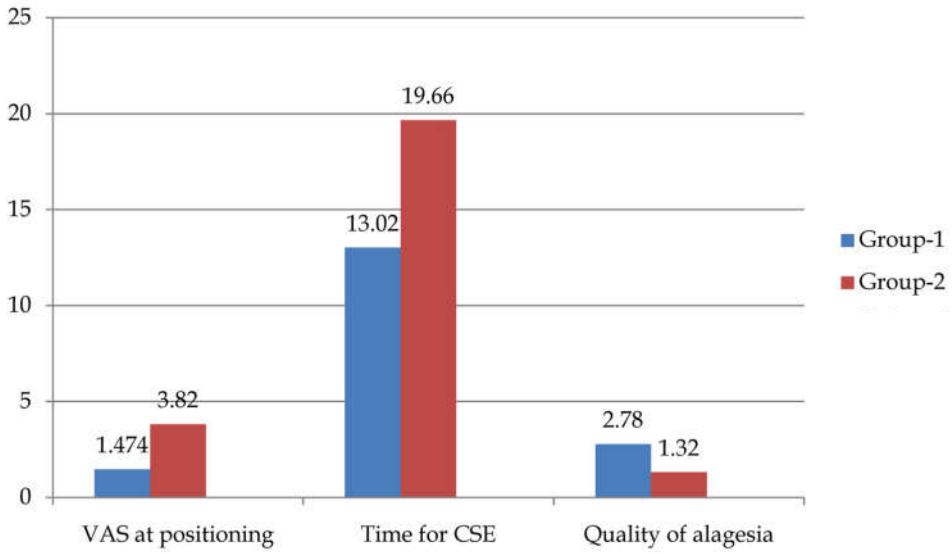

Fig. 2: Comparison of VAS at positioning (0-10), time for CSE (minute), quality of analgesia (0-3)

Time to perform spinal-epidural anesthesia was shorter in Group I versus Group II ($P < 0.001$) (13.026±0.4628 minutes versus 19.660±0.3742 minutes).

Quality of patient positioning for spinal anesthesia was higher in Group-1 (2.782±0.1273 as compared to Group-2 (1.382±0.2473) (Figure 2).

There was no significant difference in intra-operative hemodynamic parameters and post-operative complications between the two groups. No patients had signs of drug toxicity.

Discussion

Central neuraxial anaesthesia is the most accepted and preferred technique of anaesthesia for surgery of fracture femur [16]. They have several advantages, the biggest of which is that the patients can be mobilised early, because of which there is a very less chance of deep vein thrombosis and mortality [17,18].

The major drawback of the CSE block is the pain during positioning for the block in patients with femur fractures, which become even worser if the patients are obese. Previously FNB has been successful in providing analgesia in patients with femoral shaft fracture. We studied the analgesic effect of the FNB to ensure proper positioning for regional techniques of CSE in comparison with IV fentanyl.

Sandby Thomas et al reported that midazolam, ketamine, and propofol, fentanyl, remifentanil, morphine, nitrous oxide, and sevoflurane are commonly used drugs to help in positioning for central neuraxial block [16]. Previously nerve blocks were infrequently used to aid positioning in spinal-epidural block. There is sufficient data to show the

usefulness of FNB in terms of analgesia in caes of fracture of the femur, which has now prompted to use the same for positioning during central neuraxial blockade as well [3,4,12,19-22].

Femoral nerve block can be performed using peripheral nerve stimulator, ultrasound guided technique or by loss of resistance technique. Geier KO concluded that there were no significant differences regarding efficiency between loss of resistance and peripheral nerve stimulator methods [25]. In present study we used blind technique that is loss of resistance and by eliciting paresthesia as shown by Khoo [26].

Sia et al compared IV fentanyl with FNB using lidocaine [4]. VAS values during placement in the sitting position were lower in the FNB group (0.5±0.5 versus 3.3±1.4 for FNB and IV fentanyl, respectively). Mosaffa et al compared IV fentanyl with fascia iliaca block using lidocaine.5 VAS values during placement in the lateral decubitus position were lower in the fascia iliaca block group [0.5 (0–1) versus 4 (2–6) for fascia iliaca block and IV fentanyl, respectively].

The results of this prospective, randomized study demonstrate that FNB using 15 ml of 1.5% lignocaine provided better pain relief prior to positioning of patients with fractured femur for the combined spinal epidural block. The VAS score and patient satisfaction was better in patients with FNB Block than those with IV fentanyl while positioning for combined spinal epidural block. We also found that the time required for the epidural block was less in FNB group patients than IV fentanyl group patients.

Bhoslse, Durranni et al also found similar results in their studies [1,14]. Also, many authors while comparing FNB with other modalities for positioning for central neuraxial block found FNB to be superior to all other modalities [3,4,6,12,14]. The drug used for the block also has a significant difference on the duration and results as shown in study conducted by Iamaroon et al, did not find much advantage of FNB over other modalities as bupivacaine was used instead of lignocaine. The effect of lignocaine in FNB comes in 5 minutes.

However, onset of analgesic effect of bupivacaine is variable and may take 25-30 minutes for full effect [5,23,24]. In this study FNB was performed with 1.5% lignocaine and time to onset was 5 min with a peak at 12 minutes. It is due to the fact that as FNB produces relaxation of the quadriceps and hence provided adequate pain relief for positioning and hence a shorter time to perform central neuraxial block [7]. Similarly, A five minute interval between T0 and the performance of CSE was chosen to maximize the analgesic effect of fentanyl [27]. Also the dosage of fentanyl was chosen to obtain potent, short-lasting analgesia with minimal side effects [27].

Arissara Iamaroon et al, in their comparative study found no significant difference between IV fentanyl and FNB in positioning for CSE block [22]. They also advocated utility of a multimodal approach (FNB + IV fentanyl) as a possible option for pain relief during positioning. In another study by Sia et al, they found that patients who received FNB had a slight better analgesia than those who received IV fentany l.4 Several authors have used two doses of IV fentanyl at 0.5-1 μg/kg with a five-minute interval between doses. But they have encountered potential adverse effects due to the same. In our study we used only a single dose of 1 μg/kg of IV fentanyl and we did not encounter any adverse events due to the same [4,22].

The major limitation of the study was that the anaesthesiologist who performed the FNB or who administered IV fentanyl proceeded with CSE block and recorded the VAS scores. So they were not blinded and hence there can be observer bias which might have a slight affect on the final outcome of our results.

Conclusion

FNB before central neuraxial block reduces VAS score, improves satisfaction rates, lower duration for epidural bock and improves quality of patient positioning as compared to those who received IV fentanyl for positioning for central neuraxial block.

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Original Research Article

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Observational Study to Compare Dexmedetomidine and Dexamethasone as an Adjuvant to Ropivacaine 0.2% in Potentiation of Post Operative Analgesia in Caudal Block

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Abstract

Introduction: Caudal block is commonly performed in paediatric anaesthesia for post-operative analgesia using various adjuvants.

Aim of Study: To compare efficacy and safety of dexmedetomidine and dexamethasone in view of post-operative analgesia along with haemodynamic stability when used as adjuvant to local anaesthetic.

Material and Method: After the approval of ethical committee, an observational study of 60 pediatric patients calculated using website http://openepi.com (2-6 years old) of either gender and ASA I and II scheduled for infra-umbilical surgeries under general anesthesia allocated to 2 groups of which Group A received inj dexmedetomidine and group B received inj dexamethasone as an adjuvant to inj ropivacaine 0.2% (1 ml/kg) caudally after completion of surgery Haemodynamic parameters and pain score (FLACC) were recorded every 2 hourly upto 8 hours in post operative period. Rescue analgesia was given when score was ≥4. Total duration of analgesia was recorded.

Statistical Analysis: Numerical variables were presented as mean and standard deviation while categorical variables were presented as frequency and percent. For analysis, unpaired student – t test and chi – square test were used.

Results: The groups were comparable in demographics and haemodynamics. The mean duration of analgesia was similar in both the groups. The pain score in the two groups were comparable.

Conclusion: Both dexamethasone and dexmedetomidine prolonged the duration of analgesia with no significant difference between them. Dexamethasone can be used as an alternative to dexmedetomidine as an adjuvant in caudal block in paediatric patients.

Keywords: Dexmedetomidine; Dexamethasone; Ropivacaine; FLACC Score; Caudal Block.

Introduction

Paediatric patients react to pain with tachycardia, hypertension and intracranial pressure [17]. Caudal epidural block is is reliable, popular and relatively safe for post operative analgesia.

Caudal epidural block is popular and commonly performed but has shorter duration of action when only local anaesthetics are used.

Dexmedetomidine, a stereoisomer of medetomidine, is a highly selective α2-adrenergic receptor agonist [8]. Dexamethasone added to local anaesthetics was found to prolong the duration of the epidural block [18,12].

This study was undertaken to evaluate the efficacy of dexmedetomidine and dexamethasone as an adjuvant to ropivacaine in prolonging analgesia when used in paediatric patients undergoing infra-umbilical surgeries.

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Method

Sample size is calculated using website http://openepi.com results from openepi version 3,open source calculator-ssmean. For better validation of results the sample size is taken 30 in each group.

SSmean is taken from reference - Hossam A, El Shamaa , Mohamed Ibrahim A comparative study of the effect of caudal dexmedetomidine versus morphine added to bupivacaine in paediatric infra umbilical surgeries. Saudi J Anesth 2014; 8:155-60.

Setting: Dhiraj general hospital, Piparia.

Patients with ASA grade I and II of age between 2 and 6 years of either gender posted for infraumbilical surgeries were included in study. Whereas patients not giving consent for procedure, patients on adrenoreceptor agonist and antagonist therapy, known hypersensitivity to local anesthetics, infection at the site of block, patients with systemic diseases, patients with bleeding disorder and patients of ASA III and above were excluded from the study.

After approval of institutional ethical committee and obtaining written and informed consent, 60 patients fulfilling the inclusion criteria were considered for the study. A pre-anesthetic checkup was done for all patients which included a detailed history, general physical and systemic examination and investigations were carried out.

Patients were kept nil per oral for 6 hours and after shifting the patient to operation theatre, an intravenous (IV) access was secured. Patient were given Injection glycopyrrolate 0.004mg/kg, Injection ondansetron 0.1mg/kg and Injection midazolam 0.05mg/kg intravenously as a premedication prior to induction of anaesthesia. All the baseline parameters like pulse rate (PR), mean arterial pressure (MAP) and arterial oxygen saturation (SpO_2) were observed and recorded. Patient was pre-oxygenated with 100% oxygen for 5 minutes. Anesthetic induction was achieved by Injection thiopentone 5mg/kg and Injection succinylcholine 2mg/kg. Patient was intubated with appropriate size endotracheal tube. Anaesthesia was maintained with O_2, N_2O, sevoflurane and atracurium. Intra-operative haemodynamic monitoring was done at regular intervals. After the completion of surgery, the patient was turned to left lateral position for performing caudal block.

Under all aseptic and antiseptic precautions, caudal anaesthesia was given. Group A patients (n=30) received Inj. ropivacaine 0.2% (1 ml/kg) with Inj. dexmedetomidine (1 µg/kg) while group B patients (n=30) received Inj. ropivacaine 0.2% (1 ml/kg) with Inj. Dexamethasone (0.1mg/kg) and after performing caudal block patient was turned to supine position. The inhalational anaesthetic agents were turned off. Injection neostigmine (0.05mg/kg) with Injection glycopyrrolate (0.008mg/kg) was used as reversal agent for muscle relaxant after checking for spontaneous respiration. Patient was extubated after full recovery from general anesthesia.

The patient was then shifted to Post Anesthesia Care Unit (PACU) where vital parameters were observed such as heart rate, systolic and diastolic blood pressure every 2 hourly upto 8 hours.

The pain intensity of patient was observed using the paediatric observational face, legs, activity, cry, consolability (FLACC) pain score every 2 hourly till the FLACC score is 4 or more. When the FLACC pain score reaches 4, syrup paracetamol 15 mg/kg was given. The duration of analgesia (from the time of caudal injection to the time at which FLACC score ≥ 4) was recorded.

Results

There was no significant difference observed between the two groups with respect to demographic parameters such as mean age, weight, gender and ASA physical status.

There was no statistically significant difference observed between two groups with respect to haemodynamic parameters such as heart rate, systolic and diastolic blood pressure.

Time interval(hours)	FLACC Score ≥ 4	
	No. of Patients in Group A	No. of Patients in Group B
0	0	0
2	0	0
4	5(16.6%)	2(6.6%)
6	26(86%)	20(66.6%)
8	30(100%)	27(90%)

Changes in Pain Score

The Paediatric observational FLACC Pain Score was below 4 at the end of first 4 hours in both the groups and did not require any analgesia.

At the end of 6 hours, 26 patients (86%) in group A achieved a FLACC score of ≥4 and required the administration of analgesia while 20 patients (66.6%) achieved FLACC score of ≥4 and required analgesia in group B, the difference was not significant. At the end of 8 hours, all the patients in group A achieved FLACC score of ≥4 as against 27 patients (90%) achieved score ≥4 in group B.

Duration of Post Operative Analgesia

The duration of analgesia was comparable in both the groups with a p value 0.08.

Group	Mean duration of analgesia(minutes)	Standard deviation	p value	Statistical significance
A	360.2	17.84	0.08	NS
B	370.6	27.4		

Discussion

Post-operative analgesia not only offers pain relief but also inhibits trauma- induced nociceptive impulses so as to blunt autonomic response. It allows the patients to breathe freely and ambulate early to enhance early restoration of function [7].

Anand V et al [1] in 2011 used dexmedetomidine 2μg/kg with 0.25% ropivacaine in caudal block and observed that the patients had prolonged duration of sedation post operatively. Hence to prevent excessive sedation, we used dexmedetomidine in the dose of 1μg/kg. Kim et al [14] in 2014 used either 0.15% ropivacaine alone or in conjunction with 0.1mg/kg dexamethasone with no significant haemodynamic changes or side effects.

In the present study, both the groups were similar with respect to age, weight, gender and ASA status. There were no significant differences with respect to these parameters. There were no females in the study. This could be due to the fact that common paediatric infra-umbilical surgeries are circumcision, herniotomy and orchidopexy which are male-specific surgeries or more common in males. Our study was similar to a study conducted by Cook et al [3] and kamal M et al [11].

In present study, the baseline heart rate, systolic blood pressure and diastolic blood pressure at the time of giving caudal block as well as during study period were comparable and no significant differences were observed between these two groups. Our findings were similar to study conducted by Elham et al [5] .

In group A, percentage of patients who reached higher pain scores in a shorter duration was more as compared to group B. Our study had similar results when compared to study done by Santosh chaudhary et al [2] and M solanki Nilesh [15].

The mean total duration of analgesia in both the groups was comparable (p 0.08).

Similar observation was made by Raghvendra S et al [6] and Elham M et al [5] .

Dexmedetomidine, an imidazole compound, is the pharmacologically active dextroisomer of medetomidine that displays specific and selective α_2-adrenoceptor agonism. The mechanism of action is unique and differs from those of currently used sedative agents. Activation of the receptors in the brain and spinal cord inhibits neuronal firing, causing analgesia [13].

The mechanisms by which dexamethasone increased the duration of nerve blockade and analgesic effect are not fully understood, though it is commonly attributed to anti-inflammatory and immunosuppressive actions. This is supported by the finding that the block length is increased by glucocorticoid potency and is completely reversed by administration of a specific glucocorticoid receptor antagonist [9,11].

The effect of dexamethasone on the spinal cord is due to the presence of transcription factor nuclear factor-kappa B (NF-κB), present throughout the nervous system [4]. Dexamethasone by regulating NF-κB inhibits central sensitisation after surgery and potentiates analgesia of the caudal block.

No side effects or any complications were observed in our study. Results were similar to study done by Kamal M et al [11] .

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Evaluation of Low Dose Bupivacaine with Clonidine for Unilateral Spinal Anesthesia in Lower Limb Surgeries

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Abstract

Introduction: Unilateral spinal anaesthesia has been extensively studied for short duration elective lower limb surgeries with favorable results i.e when block is desired on operative side only with absence of block on non-operative side. Unilateral block minimizes cardiovascular effects, avoids motor block of nonoperative limb thereby early ambulation and early discharge.

Aim: The aim of this study was to determine the sensory and motor block characteristics and haemodynamic variables (HR, MAP, RR) by comparing 7.5 mg of 0.5% hyperbaric bupivacaine used alone and along with 30μg clonidine.

Methods: It was a prospective, double blind , hospital based study undertaken at Department of Anaesthesiology, Gandhi Medical College, Bhopal after approval of the Institutional Ethics Committee. 60 patients of either sex aged 20-60years with ASA grade I and II scheduled for elective lower limb surgery with informed consent were randomly allocated into two groups. All patients received subarachnoid block with 7.5 mg of 0.5% hyperbaric bupivacaine. In group BC 30 μg of clonidine and in group BS 0.2 ml of Normal Saline was added to bupivacaine and the volume was kept similar (1.7 ml) for each group.

Statistical Analysis Used: Chi-Square (c^2) test and Unpaired Student's *t*-test

Results: Although there was not much significant difference between the haemodynamic parameters in both the groups, the onset of sensory block (6.0±0.58 mins in group BS and 3.9±0.48 mins in group BC) and the onset of motor block (10.08±0.54 mins in group BS and 7.03±0.57 mins in group BC) was significantly earlier and the average duration of analgesia and motor block was significantly prolonged in patients receiving clonidine as an adjuvant along with bupivacaine. Likewise, the time for the first rescue analgesic request (258±20 & 331±23 mins respectively in groups BS & BC, $p<0.0001$) was delayed in patients receiving clonidine as an adjuvant.

Conclusion: From our study we conclude that 7.5mg of 0.5% hyperbaric bupivacaine used along with clonidine is superior than 7.5mg of 0.5% bupivacaine used alone in prolonging duration of analgesia and motor block while maintaining the unilaterality of spinal block and haemodynamic stability.

Keywords: Low Dose 0.5% Hyperbaric Bupivacaine with Clonidine; Unilateral Subarachnoid Block; Lower Limb Surgeries.

Introduction

An exclusively unilatearal block affects sensory, motor and sympathetic function on one side of body only and offers the advantage of subarachnoid block without typical side effects associated with conventional block. Conventionally used dose of bupivacaine is associated with hemodynamic instability, delayed recovery of motor functions, urinary retention and therefore require prolonged postoperative observation [1]. To overcome these consequences small dose of bupivacaine is gaining popularity for ambulatory anaesthesia.

Unilateral spinal block procedure is advantageous over conventional spinal anaesthesia in producing extreme longer lasting block in the

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operative limb reduced incidence of hypotension, faster recovery and increased patient satisfaction [2].

Various adjuncts to local anesthetics have been studied for improving the quality of subarachnoid block. Intrathecal administration of clonidine increases the duration of both sensory and motor block, as well as postoperative analgesia.

The purpose of this study was to compare the effectiveness of 7.5 mg of hyperbaric bupivacaine with or without clonidine (30 μg) in unilateral spinal anaesthesia for lower limb surgery.

Material and Methods

Institutional Ethics committee approval and informed consent from the patients were taken for the study. This study was conducted in 60 patients of either sex, aged 20-60years with ASA grade I and II scheduled for elective lower limb surgery. Patients with any contraindication for subarachnoid block were excluded from the study.

All these patients underwent a pre-anaesthetic check-up a day prior to surgery, and all the routine and specific investigations were noted. The patients were kept nil by mouth 6 hours prior to surgery. Before surgery a written and informed consent was taken from the patients. An intravenous line was secured, standard monitors like electrocardiogram, pulse oximeter and non-invasive blood pressure were applied. All patients were hydrated with 500ml of Ringer's lactate and subarachnoid block was performed under aseptic precautions in L3-L4 interspinous space using 25 G Quincke spinal needle in lateral decubitus position with the limb to be operated in the dependent position. All patients received 7.5 mg of 0.5% hyperbaric bupivacaine. In group BC 30 μg of clonidine and in group BS 0.2 ml of Normal Saline was added to bupivacaine and the total volume was kept similar (1.7 ml) for each group. The patients were maintained in the same position for 10 minutes before turning supine.

- Haemodynamic parameters (Heart rate, respiratory rate, MAP) were recorded immediately before spinal injection and every 5 minute after spinal injection for first 30 minutes and then every 15 minutes till completion of surgery. Hypotension was labeled as significant if fall was more than 30% from baseline and bradycardia if heart rate decreased below 50 bpm.
- The level of sensory and motor block was determined on both operated and nonoperated limbs. Assessments were done immediately after spinal injection and at 5 minutes interval for 20 minutes and every 15 minutes until end of surgery and regression of block to L2 level. Time of complete motor recovery was also recorded. Sensory testing was done by pricking 20 G hypodermic needle at the mid-clavicular line bilaterally after the end of block from caudal to cephalad and analgesic level was defined as the cephalad most dermatome at which the patient had decreased sharp sensation.
- The degree of motor block was assessed using the Modified Bromage scale(0-no block, 1-hip blocked, 2-hip and knee blocked, 3- hip, knee and ankle blocked).

Ramsay Sedation Score [3]

Was measured using the following scale at 15, 30 and 60 minutes after tracheal extubation:

1= anxious, agitated, or restless;

2= cooperative, oriented, and tranquil;

3= responsive to commands

4= asleep, but with brisk response to light, glabellar tap, or loud auditory stimulus

5= asleep, sluggish response to glabellar tap, or auditory stimulus

6= asleep, no response. Patients will also be asked for recalling of intra operative events or any sign of awareness.

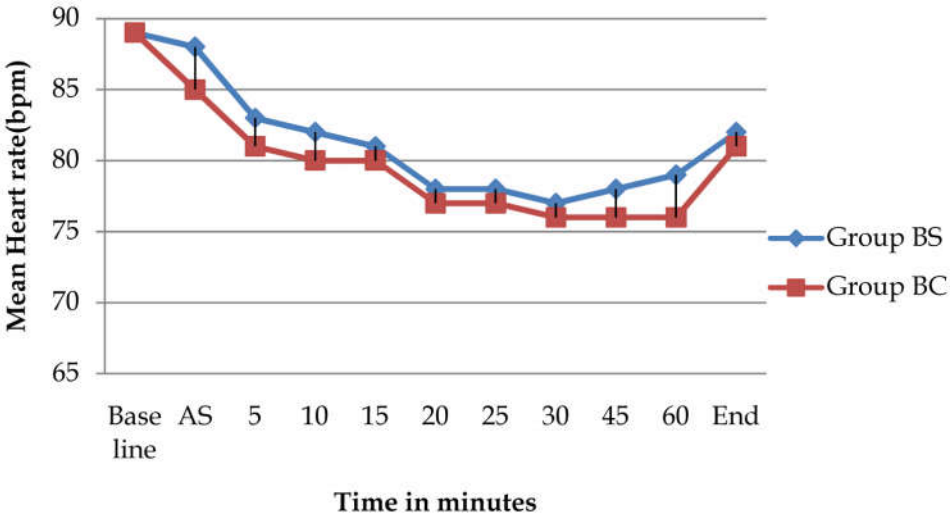
- Postoperatively all the patients were observed for 2 hours in recovery room before returning to the ward. Side effects like Nausea, vomiting, hypotension, bradycardia, & urinary retention if any were noted. HR,MAP, RR were recorded continuously.
- All the observations were recorded and the results were analysed. Statistical analysis was performed using SPSS version 20. The two-sample unpaired student 't' test was used to compare demographic data and times for readiness to surgery, block resolution. Ordinal data were analysed using the contingency table analysis with the Chi-square test. A p value < 0.05 was considered significant.

Results

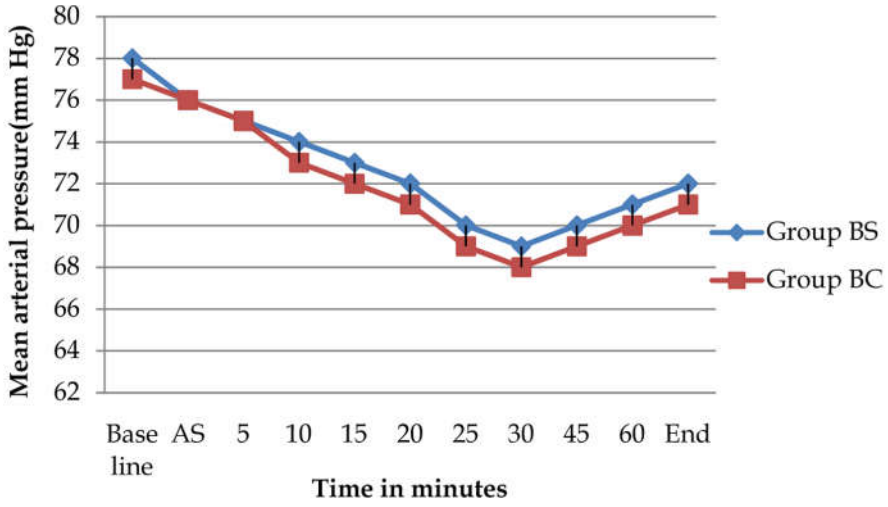
Mean age, weight, sex distribution, ASA status and duration of surgery in both groups were comparable and found to be statistically insignificant.

Table 1: Demographic data & Duration of surgery

Variables	Group BS	Group BC	p value
Age (years):	40.10± 9.57	38.10±9.46	0.419
Weight(kg)	54.57 ±3.26	53.77± 3.47	0.869
Sex ratio(M/F)	19:11	17:13	0.522
ASA status (I/II)	21/9	23/7	0.340
Duration of surgery (mins)	99±22	100±20	0.854



AS=immediately after subarachnoid block
Fig. 1: Mean Heart rate



AS=immediately after subarachnoid block
Fig. 2: Changes in Mean arterial pressure

Table 2: Sensory block characteristics

Variables	Group BS	Group BC	P value
Onset of sensory block (min)	6.033±0.586	3.933±0.487	<0.0001
Peak sensory level	T10	T10	
Operated limb	(T12 – T9)	(T12 – T8)	>0.05
Non-operated limb	L3(T12-S3)	L2(T12-S1)	>0.05
Time to reach peak(T10) level (min)	14.73±1.4	10.33±2.11	<0.0001
Time of regression of sensory block till L2(mins)	140±13.43	190±15.04	<0.0001

Haemodynamic Variables

Intraoperative and postoperative haemodynamic parameters(HR, MAP & RR) in both the groups were comparable and there was no significant difference. Cardiovascular parameters were stable throughout in both the groups[except for one case where intra-operative bradycardia was noted but it was not considered significant as the patient's baseline PR was 60bpm].

Table 2 shows that the onset of sensory block was faster and time of regression of sensory block till L2 in group BC was significantly prolonged than group BS.

Sensory level was significantly higher and motor block was more intense (Modified Bromage scale >2) in operative limb as compared to non-operative limb in both the groups (p>0.05).

Table 3 shows onset of motor block was earlier and time of complete recovery of motor block was significantly higher in group BC as compared to group BS.

Table 3: Motor block characteristics

	Group BS	Group BC	p value
Onset of motor block (mins)	10.083±0.543	7.033±0.571	<0.0001
Modified Bromage scale(0/1/2/3)			
Operated limb	0/2/2/26	0/1/1/28	-
Non operated limb	22/4/3/1	23/5/1/1	-
Time of complete recovery of motor in operated limb(mins)	191.9±9.90	262±20.87	<0.0001

Table 4: The time when the first rescue analgesic request was significantly higher in group BC as compared to group BS.

	Group BS	Group BC	p value
Time of first rescue analgesic required (in mins)	258.25±20.50	331±23.09	<0.0001

Table 5: Comparison of complications and side effects between the two groups

Side effects	Group BS	Group BC	Total
Hypotension	0	0	0
Bradycardia	0	1	0
Sedation	0	2	2
Nausea & vomiting	0	1	1
Urinary retention	0	0	0
PDPH	0	0	0

There were no significant adverse effects noted in either group.

Discussion

Unilateral spinal anaesthesia is used when block is desired only on operative side[4]. When surgery involves only one lower limb, such type of anaesthesia is advantageous and minimizes hemodynamic variations associated with conventional spinal anaesthesia. It also enables faster recovery, good cardiovascular stability and early discharge [5-7].

The technique to achieve unilateral distribution of spinal anaesthesia used in the present study has been discussed earlier in the studies done by Valanne et al [8].

Our results showed that the low dose of intrathecal clonidine co-administered with a low dose of bupivacaine reduced the time of onset of sensory and motor block and prolonged the duration of sensory block (from time of first request for supplemental analgesia). However, Clonidine also significantly prolonged the recovery of motor block. These results are similar to that of Singh TK et al [9].

There was significant difference in spread of anaesthesia between operative and contralateral limb. In operative limb sensory levels were much higher and motor block was denser in comparison to non-operative limb. Just after subarachnoid block, unilateral spinal anaesthesia was achieved in 88%

& 93% patients of Group BS & BC respectively. Unilateral block restricted to operative limb in more than 75% of patients with minimal changes in cardiovascular parameters has been reported by previous investigators using hyperbaric bupivacaine [10]. This is due to more anaesthetic concentration achieved near the nerve roots of operative limb.

Our study confirmed previous reports of prolongation of postoperative analgesia by addition of clonidine [11] to spinal local anaesthetic. Clonidine is a selective partial agonist for α-2 adrenergic receptors; the analgesic effect following its intrathecal administration is mediated spinally through the activation of postsynaptic α-2 receptors in substantia gelatinosa of the spinal cord [12].

In addition, there was some prolongation of motor block in patients receiving intrathecal clonidine. These findings concur with previous reports [11]. The mechanism of prolongation of motor block by clonidine remains speculative [11] and can be due to direct inhibition of impulse conduction in motor nerve fibres [13].

Relative hemodynamic stability was maintained in both the groups as observed in previous study[14] none of the patient had significant fall in BP ,this may be due to low dose of anaesthetic used and laterality of block [14]. Only one patient in group BC had bradycardia which was treated by i.v.Atropine and the same patient had complain of nausea and vomiting which was also treated. PDPH and urinary retention were not seen in any patient.

Only two patients in group BC had Rramsay sedation score of 4 at 15 minute postoperatively. But at 30 and 60 minutes postoperatively, there was no statistical significant difference in sedation score in between two groups.

Low dose of local anesthetic, slow speed of injection[14-15], lateral decubitus position [16] during and subsequently after subarachnoid block and duration of this position are main determinants of distribution of spinal block to one side. The optimum duration of lateral position is difficult to define as it is also related to dose of local anaesthetic. As we used intermediate dose of hyperbaric bupivacaine we positioned the patients in lateral position with operative side in dependent position and maintained this position for 10 minutes after subarachnoid block. Slow speed of injection minimizes mixing of local anaesthetic with CSF and thus facilitates unilateral block [16].

None of the patients had failed or inadequate block in both the groups. This may be due to high anaesthetic concentration achieved near nerve roots of operated limb which could account for slow regression of sensory block due to reduced surface available for absorption and elimination of local anaesthetic from subarachnoid space. The quality of subarachnoid block was improved by the addition of clonidine in group BC.

Conclusion

From our study we conclude that limiting the spread of subarachnoid block provides two benefits firstly better haemodynamics and secondly earlier patient mobilization however coadministration of clonidine along with 7.5mg of 0.5% hyperbaric bupivacaine is found to be superior than 7.5mg of 0.5% hyperbaric bupivacaine used alone in prolonging duration of sensory and motor block as well as postoperative analgesia in unilateral spinal anaesthesia of sufficient duration in majority of patients undergoing elective lower limb surgeries.

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Conflicts of Interest: None

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Haemodynamic Responses to Laryngoscopy and Intubation in Patients Undergoing Craniotomy: Comparison between Macintosh and Mccoy Laryngoscope Blades, with Monitoring of Entropy

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Abstract

Aim: To compare the haemodynamic responses, during laryngoscopy and intubation, using Macintosh and McCoy blades, in patients of ASA grades I and II, undergoing craniotomy for supratentorial lesions, under general anaesthesia, with monitoring of entropy, to ensure uniform depth of anaesthesia.

Methodology: A prospective, randomized, comparative study conducted at Nizam's Institute of Medical Sciences , between January 2013 and April 2013 . Total 60 patients were included in study with 30 patients in each group divided as Group A -- Macintosh laryngoscope was used & Group B -- McCoy laryngoscope was used. Patients included were undergoing elective supratentorial lesion surgery, aged between 18 to 60 years & belonged to ASA grade I & II. Depth of anaesthesia by monitoring entropy was kept uniform during laryngoscopy and intubation (Between 40 to 60). Airway assessment and difficult intubation scoring systems and also intubation related parameters were noted and compared between the 2 groups . Heart rate, Invasive blood pressure, which included systolic, diastolic and mean arterial pressure, RE and SE were recorded and compared at the following time points: preinduction (baseline Tb), before laryngoscopy (T0), during laryngoscopy (TL) , during intubation (In), post intubation at 1, 2, 3, 4 and 5 minutes (T1-T5) , between the 2 groups.

Results: Haemodynamic response consisting of an increase in HR, SBP, DBP and MAP were seen during laryngoscopy and intubation, using Macintosh and McCoy blades in this study. It was also observed that, the haemodynamic responses to laryngoscopy and intubation was slightly greater with Macintosh blade than with McCoy blade. This was due to better laryngeal visualization and shorter time of ETT insertion with the McCoy balde, than with the Macintosh and this was contributory to the lower haemodynamic responses seen with the McCoy blade. But these responses were statistically insignificant between the two blades ($p>0.05$), when depth of anaesthesia by monitoring entropy was kept uniform throughout the study (Between 40 to 60). The stress responses were also short lived in both groups, as uniform depth of anaesthesia using entropy monitoring, blunted the overall responses to laryngoscopy and intubation, and the awareness component, which could have occurred if not monitored.

Conclusion: We conclude that, although McCoy blade was superior in terms of better glottic visualization, ease of intubation and overall operability, the haemodynamic responses produced during laryngoscopy, intubation and post intubation were similar and comparable with the Macintosh blade and statistically insignificant ($p>0.05$), when depth of anaesthesia is uniform and adequate.

Keywords: Macintosh Blade; McCoy Blade; Laryngoscopy.

Introduction

Anaesthesia for neurosurgical cases presents special considerations. Majority of craniotomies are performed for space occupying lesions. The brain is enclosed in a rigid skull and is a highly vascular organ. Tolerance of brain to the interruption of substrate delivery is minimal [1]. About 85% of intracranial tumors are primary and among them, about 60% are supratentorial tumors [2,3].

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Anaesthesia for the surgical removal of intracranial tumors requires an understanding of the pathophysiology of localised and generalised rise in intracranial pressure (ICP), effects of anaesthesia on ICP, therapeutic options available for decreasing ICP perioperatively [4,5] and maintenance of intracerebral perfusion. ICP is sensitive, to the anaesthetic effects and any acute changes in ICP, is potentially devastating.

Laryngoscopy forms an important part of general anaesthesia and endotracheal intubation. The aim of laryngoscopy, is to obtain good visualization of vocal cords in order to facilitate smooth intubation. To ease the process of intubation, laryngoscopes of different shapes and sizes have been designed. The McCoy blade is a modification of the Macintosh blade, with its tip hinged [6]. Stress response to laryngoscopy and tracheal intubation, has a profound influence on the circulatory parameters and the ICP [7]. This response manifests as tachycardia, hypertension and can have deleterious effects on neurological and cardiovascular systems [8]. The principle mechanism of hypertension and tachycardia is sympathetic response, due to increase in catecholamine activity. Forces transmitted by the laryngoscope blade, on the base of the tongue, is assumed to be a major stimulus [7].

When planning anaesthesia induction, especially in the high risk population, like patients with coronary artery disease, aortic dissection, elevated ICP and cerebral aneurysm, tachycardia and hypertension must be blunted, as much as possible, as these transient haemodynamic responses can result in deleterious effects, like left ventricular failure, arrhythmias, myocardial ischemia, rupture of cerebral aneurysm, cerebral hemorrhage and herniation of cerebral contents [7]. In neurosurgical patients with space occupying lesions, effective haemodynamic control is required during laryngoscopy and intubation, as any increase in these parameters may increase the already raised ICP and thus jeopardize the brain function.

The Macintosh blade is the most successful and durable blade in the history of anaesthesia till date [9]. It is postulated that McCoy blade causes less mechanical stimulation of respiratory tract, than the Macintosh blade, by decreasing the amount of forces exerted during laryngoscopy and endotracheal intubation. When the McCoy blade is inserted into the valeculla, activation of the tip of McCoy, on the hyo-epiglottic ligament, lifts the epiglottis out of the view, to expose more of the glottis, while decreasing the overall laryngoscope movement [7]. Thus, only a modest increase in the reflex haemodynamic responses, is seen with McCoy blade, as compared with the Macintosh blade.

Depth of anaesthesia has a bearing on awareness and haemodynamic parameters. Clinical end points, in assessing depth of anaesthesia during induction include , loss of verbal responsiveness (LVR), loss of eyelash reflex, and loss of corneal reflex. Awareness during laryngoscopy and intubation, can exaggerate haemodynamic parameters and can have deleterious effect on the ICP and cerebral blood flow. Awareness during this period, may be monitored with traditional clinical signs, such as movement, tachycardia, hypertension, pupillary responses, lacrimation or by EEG based indices.

M-ENTROPY (GE Healthcare , Helsinki, Finland) is a EEG based, depth of anaesthesia index, based on calculation of Spectral Entropy (SpEn). In M-ENTROPY, the depth of anaesthesia is expressed using variables: state entropy (SE) and response entropy (RE). SE represents cortical EEG activity and reflects the hypnotic component of anaesthesia. RE includes both the EEG activity and the EMG activity of facial muscles (fEMG). RE ranges from 0 and 100, whereas SE varies between 0 and 91, low values indicating deep anaesthesia. RE-SE difference is considered to give information about the level of analgesia. For clinically meaningful anaesthesia and low probability of consciousness, entropy values between 40 and 60 are considered appropriate.

Little is known about the mechanisms of the cerebral responses to laryngoscopy and tracheal intubation. Although studies using entropy for laryngoscopy and intubation in general surgical patients are available, similar studies in neurosurgical patients are very few. Perhaps, there is no literature, about the haemodynamic responses during laryngoscopy and intubation, by maintaining uniform depth of anaesthesia. To address the above issue in neurosurgical patients, we carried out a prospective, randomized controlled trial, to observe the haemodynamic responses to laryngoscopy & intubation with Macintosh and McCoy laryngoscope blades, with monitoring of entropy, to ensure uniform depth of anaesthesia.

In the present study, M-Entropy module was used as a guide, to eliminate the risk of awareness during laryngoscopy and intubation, which may otherwise happen if traditional endpoints like loss of verbal response, loss of eyelash reflex are used. It is also used as a guide, to ensure uniform and adequate depth of anaesthesia, during and after

intubation, by keeping the entropy value, between 40 and 60 in all subjects.

Methodology

A prospective, randomized, comparative study was conducted, after institution ethics committee approval. The study was conducted at, Nizam's Institute of Medical Sciences, Panjagutta, Hyderabad. This study was conducted between January 2013 and April 2013. The study recruited adult patients, between the age of 18 to 60 years, who were ASA I and ASA II, of both sexes, presenting for elective craniotomy, for supra-tentorial lesions.

Sample size was estimated, from previous three studies [7,8,10] by taking the SBP at 1 min as a parameter. As dropout of cases were expected because of unanticipated difficulty in intubation , a sample size of 60 (30 in each group) had been selected for the study even though, the power analysis showed the sample size required was 54 with $\alpha = 0.05$, $(1- \beta) = 0.90$ and effect size(d) = 0.90. The patients were assigned to one of the following two groups using simple randomization, according to the computer-generated table of random numbers.

Group A: Macintosh laryngoscope was used.

Group B: McCoy laryngoscope was used.

Single blinding method was followed, where a skilled anaesthesiologist, having more than three years of experience in using laryngoscope and ETT, knew the type of blade used, according to randomization and the anaesthesiologist noting the haemodynamic values was blinded to the procedure.

Inclusion Criteria

Patients undergoing elective supratentorial lesion surgery, age between 18 to 60 years, ASA I and ASA II, willing to participate in the study, by giving written informed consent.

Exclusion Criteria

Morbid obesity, pregnant patients, H/o hypertension and coronary artery disease, H/o beta blocker therapy, antihypertensive therapy, Major renal, hepatic, cardiovascular, respiratory ailments & cerebral aneurysms, Allergy to any of the drugs used in the study, Anticipated difficult airway, Age <18 or >60 yrs.

Procedure

A day prior to the surgery, preoperative visit was made and a detailed history and clinical examination of the patient was done. Airway assessment using Modified Mallampati Score [11] was also done. All patients were kept nil per oral (NPO) for 8 hrs prior to the surgery. They were premedicated with tab. ranitidine 150mg on the night and morning of surgery.

In the operation theatre, after connecting the patient to standard monitoring consisting of ECG and SpO_2, intravenous access was secured using 2 large bore 16G iv cannulas. A 20 G arterial switch & 14/16 G cavafix for arterial and central venous pressure monitoring were secured respectively. Entropy leads were attached to forehead for monitoring depth of anaesthesia and connected to Entropy module (Datex Ohmeda, GE Healthcare, Helsinki, Finland). Premedication with glycopyrrolate 0.1 mg, and fentanyl 2ug/kg prior to induction was done. All patients were preoxygenated for 3 mins. Induction was done with intravenous thiopentone, 4mg/kg titrated to loss of eyelash reflex. After induction, patients were ventilated with (60:40) N_2O & O_2 mixture. Anaesthesia was maintained with isoflurane (1 MAC), followed by intravenous bolus dose of atracurium 0.6mg/kg for achieving adequate muscle relaxation for intubation. By altering isoflurane concentration, to attain adequate anaesthetic depth, as indicated by Entropy values between 40 and 60, orotracheal intubation was attempted, with Macintosh or McCoy blades according to simple randomization. Post intubation, uniform depth of anaesthesia (entropy between 40 and 60) was maintained with N_2O, O_2 (60:40) and isoflurane, for 5 minutes.

Endotracheal tubes of size 7/7.5mm for female and 8/8.5mm for male patients were used according to formula age/4+4. Size of laryngoscope blade, time taken for laryngoscopy and intubation were noted. Difficulty of intubation was graded I – IV according to the Cormack and Lehane criteria [12]. Patients requiring more than one attempt at laryngoscopy and intubation; bucking, coughing on intubation or requiring optimal external laryngeal manipulation (OELM), were planned to be excluded from the study. Surgery or any other manipulations were not allowed to commence, till the study was completed i.e. for five minutes after intubation.

Monitoring

Heart rate, Invasive blood pressure, which included systolic, diastolic and mean arterial

pressure, RE and SE were monitored throughout the study and recorded at the following time points: preinduction (baseline Tb), before laryngoscopy (T0), during laryngoscopy (TL) , during intubation (In), post intubation at 1, 2, 3, 4 and 5 minutes (T1-T5).

Oxygen saturation, $EtCO_2$ and ECG were also monitored throughout the study period. During laryngoscopy, intubation and post intubation, entropy was maintained between 40 and 60, by altering the concentration of isoflurane. Duration of laryngoscopy was defined as the time from start of laryngoscopy to start of ET tube insertion. Duration of intubation was defined as the time from the start of ET tube insertion, until cuff inflation.

Pre-operative Airway assessment was graded according to Modified Mallampatti Score & Difficulty of intubation was graded according to the Cormack and Lehane criteria.

Data Recording and Statistical Analysis

All the data was collected, tabulated and checked for correctness and consistency. There were no dropouts during the study. Statistical analysis was carried out using NCSS 2007 version 7.1.19 statistical software. Continuous data were represented as mean (SD), both categorical data and ordinal data as frequency and percentages.

The pre-requisite assumption for Independent two sample 't' test like normality of data for Gaussian distribution, was assessed graphically and by Anderson- Darling test. Equality of variance was also assessed, by modified-Levene Equal-Variance test, for all the parameters. Imbalance of baseline parameters, was assessed by Chi-square test and observing the mean values in the two groups.

Both the tests and graphical presentation, confirmed normality of data for gaussian distribution and the equal variances of the data. As all the assumptions of independent two sample student 't' test were accomplished, this test was used for the analysis of continuous data. The chi-square test and Mann-Whitney U test were performed for categorical data and ordinal data respectively.

P value < 0.05 was considered as statistically significant.

Results

A total of 60 patients, who underwent craniotomy for supratentorial lesions, had been studied. The data was collected, tabulated, analyzed and the following observations were made.

Demographic data was analyzed, by using two sample 't' test and gender of the patients by Chi-square test. The two groups were comparable in terms of demographic data as there were no significant differences in terms of age, weight, height and sex.

Table 1: Demographic parameters and Intubation related parameters [Mean(SD)]

Parameter	Group A(Macintosh) Mean(SD)	Group B (McCoy) Mean(SD)	P-value
Age (Years)	37.73 (13.12)	38.8 (12.82)	0.061
Weight (Kgs)	56.3 (9.95)	54.23 (10.48)	0.44
Height (cm)	160.03 (10.4)	157.36 (8.12)	0.19
Sex (M:F)	19:11	17:13	0.28
Blade Size	3.1(0.3)	3(0)	0.08
Laryngoscopy Time(Sec)	14.03(3.13)	12.66(2.6)	0.070
ET Tube Size (mm)	7.9 (0.62)	7.9 (0.53)	1.00
Intubation Time (sec)	10.1(2.82)	9.26(2.35)	0.22

Table 2: Types of supratentorial lesions

Brain tumor	Group A	Group B	Total	p value
Glioma	14	16	30(50%)	0.15
Meningioma	7	7	14 (23%)	1
Pitutary Adenoma	3	2	5(8%)	0.15
Craniopharyngioma	3	1	4 (7%)	0.15
Ventricular cyst	1	3	4 (7%)	0.15
Abscess	2	1	3 (5%)	0.15

Table 3: Airway assessment and difficult intubation scoring systems

Parameter	Group A (n=30) (Macintosh)	Group B (n=30) (McCoy)	p-Value
Modified Mallampati Score(n) (I/II/III/IV)	12/18/0/0	17/11/2/0	0.34
Cormark and Lehane's score(n) (I/II/III/IV)	8/8/11/3	11/9/7/3	0.21

Note: (n) = number of cases

The intubation related parameters like laryngoscope blade size, endotracheal tube size, laryngoscopy time and intubation time, were analyzed by using independent two sample 't' test and were found to be statistically insignificant (p >0.05) between the two groups. Macintosh blade of size 3 or 4 was used and McCoy blade of size 3 was used for laryngoscopy. It took longer time for ET tube insertion in Group A than in Group B, but this was statistically insignificant.

Type of Supra tentorial lesion was comparable between the two groups. 50% of patients underwent surgery for glioma, 23% for meningioma. Rest for pituitary adenoma, craniopharyngioma, ventricular cyst and abscess.

The airway assessment and difficulty of intubation scoring system parameters were analyzed using Mann-Whitney U Test and it was found to be statistically insignificant (p >0.05) between the two groups. Of the 30 patients in Group A, 8 (27%) were grade I, 8 (27%) grade II, 11 (36%) grade III, 3 (10%) were grade IV and in Group B, 11 (36%) were grade I, 9 (30%) grade II, 7 (24%) grade III, 3 (10%) were grade IV with regards to Cormack and Lehane score.

Haemodynamic Data

Heart rates in the two groups were comparable throughout the period of study and there was statistically insignificant (p >0.05) difference between the two groups. It took 4 minutes in Group A to return to pre-laryngoscopy values, whereas 3 minutes in Group B. After induction the heart rate increased by 15.22% & 10.03% in Group A & Group B respectively. Rise in HR during laryngoscopy & intubation from prelaryngoscopy values was 6.62% & 16.14% in Group A and 5.76% & 13.77% in Group B respectively. This rise persisted for 4 mins in Group A and 3 mins in Group B, till pre-laryngoscopy values were attained.

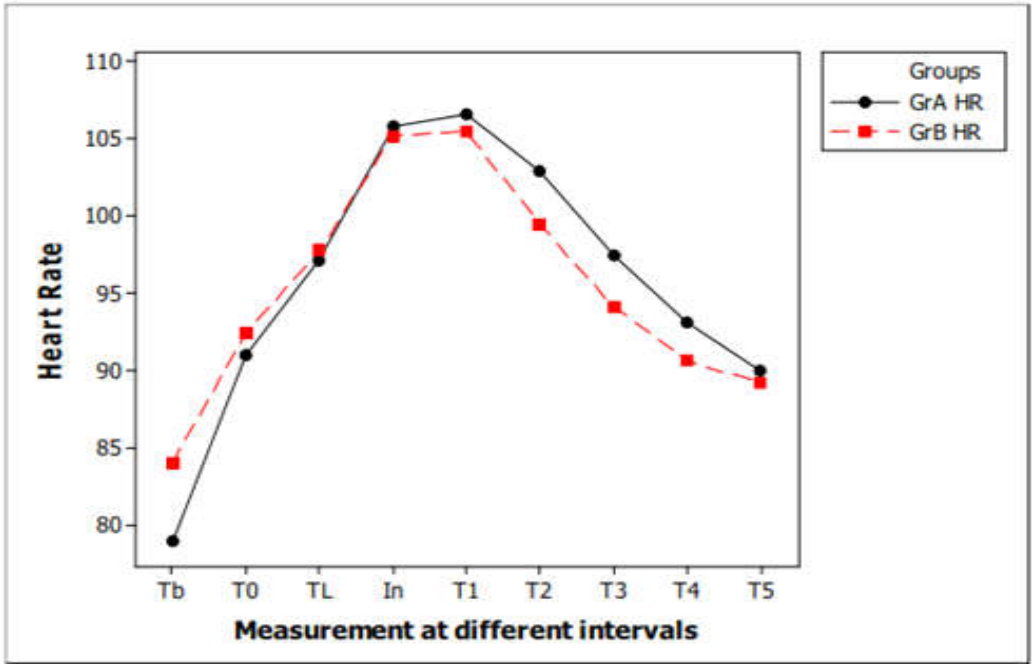

Fig. 1: Heart rate changes in Group A and Group B

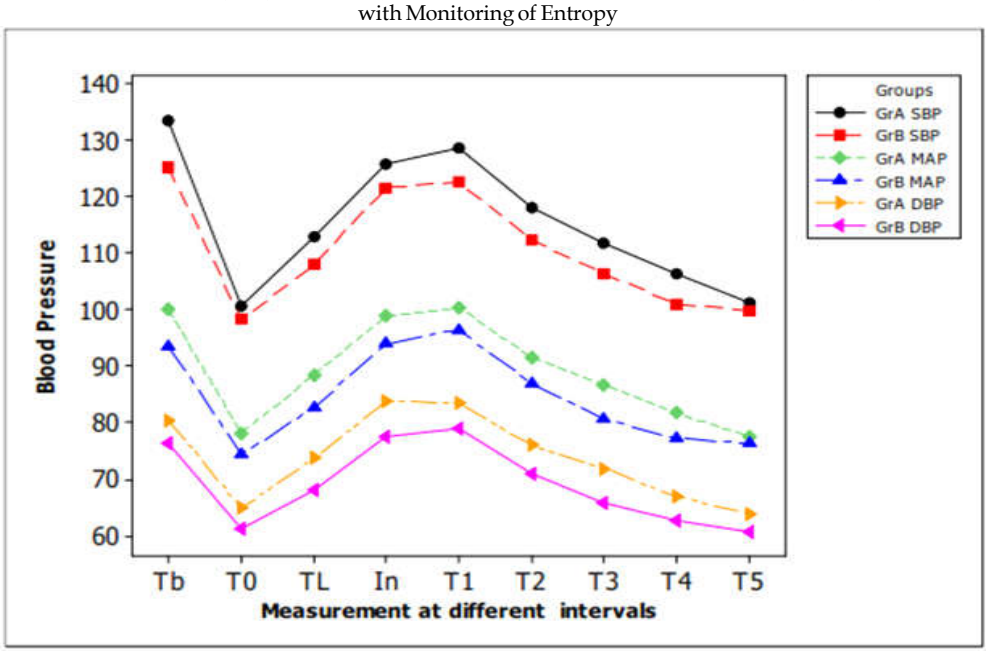

Fig. 2: Blood Pressure changes (SBP , MAP , DBP) in Group A and Group B

SBP, MAP and DBP in the two groups were comparable throughout the period of study, and there was statistically insignificant (p >0.05) difference between the two groups. It took beyond 5 minutes for SBP and 5 minutes for DBP in both Groups and 5 minutes in Group A & beyond 5 minutes in Group B for MAP to return to pre-laryngoscopy values.

After induction the SBP decreased by 24.42% & 21.46% in Group A & Group B respectively. Rise in SBP during laryngoscopy & intubation from pre-laryngoscopy values was 12.24% & 24.94% in Group A and 9.79% & 23.92% in Group B respectively. This rise persisted for more than 5 mins in both Groups, till pre- laryngoscopy values were attained. After induction the MAP decreased by 21.77% & 20.30% in Group A & Group B respectively. Rise in MAP during laryngoscopy & intubation from pre-laryngoscopy values was 13.07% & 26.42% in Group A and 11.14% & 26.37% in Group B respectively. This rise persisted for 5 mins in Group A and beyond 5 mins in Group B, till pre-laryngoscopy values were attained.

After induction the DBP decreased by 19.37% & 19.81% in Group A & Group B respectively. Rise in DBP during laryngoscopy & intubation from pre-laryngoscopy values was 13.75% & 29.21% in Group A and 11.21% & 26.83% in Group B respectively. This rise persisted for 5 mins in both Groups, till pre- laryngoscopy values were attained.

RE and SE in the two groups were comparable throughout the period of study, and there was statistically insignificant (p >0.05) difference between the two groups.

After induction the RE decreased by 50.98% & 51.81% in Group A & Group B respectively. Rise in RE during laryngoscopy & intubation from pre-laryngoscopy values was 2.55% & 8.78% respectively in Group A . But there was additional

Table 4: Response Entropy (RE) and State entropy (SE) [Mean(SD)]

	Response Entropy (Mean(SD)			State Entropy (Mean(SD)		
	Group A	Group B	P	Group A	Group B	P
Tb	95.96(2.34)	96.5 (1.85)	0.33	86.26(2.33)	86.4(2.35)	0.82
T0	47.03(8.38)	46.5(9.49)	0.81	45.4(8.62)	44(8.99)	0.54
TL	48.23(8.13)	44.75(10.53)	0.16	46.43(7.63)	42.63(10.23)	0.108
In	51.16(10.97)	45.43(12.04)	0.05	47.13(9.05)	42.7(12.11)	0.11
T1	47.86(8.67)	43.73(9.86)	0.09	46.23(8.85)	41.46(9.36)	0.052
T2	43.83(8.70)	44.76(9.20)	0.68	42.5(9.14)	42.0(9.09)	0.83
T3	42.53(7.25)	43.3 (8.92)	0.71	41.93(7.02)	41.43(8.84)	0.33
T4	43.1(8.05)	42.8(9.92)	0.89	41.76(7.90)	41.13(9.48)	0.77
T5	44.0(8.70)	43.56(10.58)	0.86	42.6(8.31)	41.63(10.37)	0.69

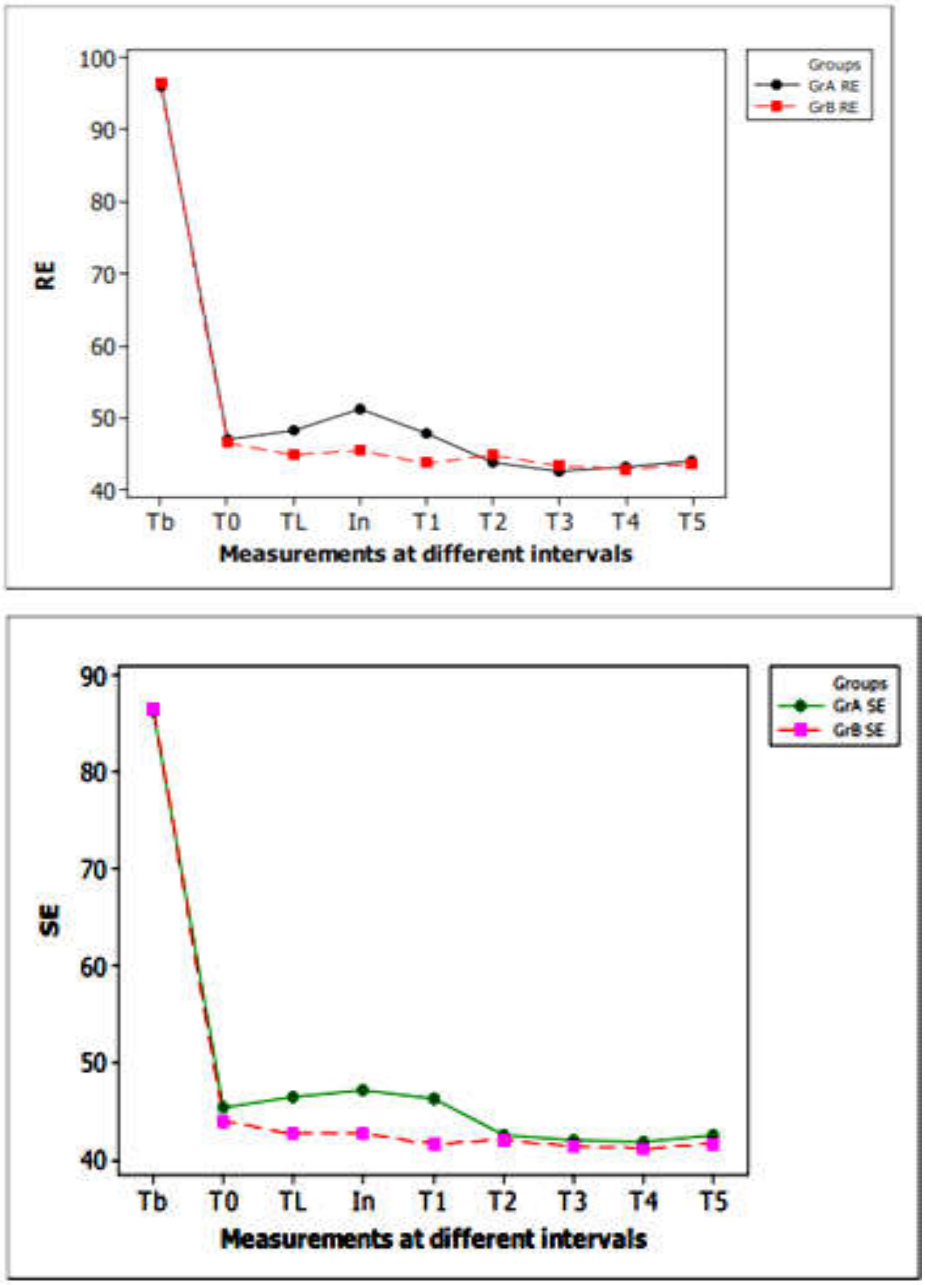

Fig. 3: Changes in Response Entropy (RE) and State entropy (SE)

decrease in RE by 3.76% & 2.30% in Group B during laryngoscopy & intubation respectively from pre-laryngoscopy values. The rise persisted for 1 min in Group A only, till pre-laryngoscopy values were attained. After induction the SE decreased by 47.36% & 49.07% in Group A & Group B respectively. Rise in SE during laryngoscopy and intubation, from pre-laryngoscopy values was 2.26% & 3.81% respectively in Group A . But there was additional decrease in SE by 3.11% & 2.95% in Group B during laryngoscopy & intubation respectively from pre-laryngoscopy values. The rise persisted for more than 1 min in Group A only, till pre-laryngoscopy values were attained.

RE-SE values increased in Group A by 10.42% and 147.23% during laryngoscopy and intubation, from the pre-laryngoscopy values. But this increase, was soon suppressed after intubation, by the end of first minute, by maintaining uniform depth of anaesthesia. RE-SE values decreased in Group B by 15.2% during laryngoscopy, but increased by 9.20% during intubation from the pre-laryngoscopy values. This increase was also suppressed by end of first minute.

Discussion

The stress response to laryngoscopy and intubation, is a well known centrally mediated, sympathetic reflex [13] associated with a cardiovascular response, of elevated blood pressure, heart rate and dysrhythmias, cough reflexes, increased ICP and increased intraocular pressure. If no specific measures are taken to prevent haemodynamic response, the HR can increase from 26%-66% depending on the method of induction [14] and SBP can increase from 36%-45% [15]. Hazards of acute arterial hypertension in a neurosurgical patient, with potentially decreased intracranial compliance, is very well recognized and this results in an increased ICP [16] especially, if cerebral vessels have decreased ability to autoregulate [4]. Hence anaesthesia for craniotomy, must be conducted with emphasis on haemodynamic stability, optimal cerebral perfusion pressure (CPP), and avoidance of procedures that increase the ICP.

Monitoring the adequacy of depth of anaesthesia is of vital importance, in neurosurgical patients so as to prevent arousal, awareness and exaggerated haemodynamic responses during induction, laryngoscopy and intubation. Many anaesthesia providers rely on monitoring of patient's haemodynamic responses as a method of awareness assessment, as haemodynamic responses are thought to be indirect indicators of awareness and brain perfusion. Studies have shown relation between neuronal activity and regional blood flow, and this is confirmed by single photon emission computed tomography, positron emission tomography and transcranial Doppler sonography techniques [17].

Klingelhofer et al [17] reported that simple sensory stimulation and mental tasks, changed blood flow velocities in the basal intracranial arteries. Electroencephalography (EEG) monitoring is widely used to monitor depth of anaesthesia. Entropy is a new EEG-based technology, to measure the depth of anaesthesia. Sufficient adequate depth of anaesthesia, for most surgical procedures with low probability of recall, using M-Entropy module is between 40 and 60.

Several studies have shown, McCoy laryngoscope produces significantly less rise in haemodynamic parameters, as compared to Macintosh laryngoscope, during laryngoscopy and intubation. The McCoy laryngoscope has a hinged tip, controlled by a lever on the handle, that allows elevation of epiglottis, while decreasing the overall laryngoscope movements and the force applied. Hence overall laryngoscopic visualization is improved and it reduces the stress response.

Many studies are available on the haemodynamic and entropy responses to laryngoscopy and tracheal intubation, in non neurosurgical patients. Similar studies in neurosurgical patients are very few. There is no literature about the haemodynamic responses, during laryngoscopy and intubation, by maintaining uniform depth of anaesthesia (entropy between 40 and 60). Therefore we carried out a prospective, randomized controlled trial to compare haemodyamic responses to laryngoscopy and intubation, between Macintosh and McCoy blades, by ensuring uniform depth of anaesthesia.

We hypothesized that McCoy laryngoscope produces significantly less rise in haemodynamic parameters, as compared to Macintosh laryngoscope during laryngoscopy and intubation, if uniform depth of anaesthesia is maintained.

This study conducted on a total of 60 patients, aimed at comparing the haemodynamic changes elicited by laryngoscopy and endotracheal intubation, with Macintosh and McCoy blades, albeit maintaining uniform depth of anaesthesia with entropy monitoring. This study demonstrated that, haemodynamic responses, consisting of an increase in heart rate, SBP, DBP and MAP was statistically not significant ($p>0.05$), with both the blades, if depth of anaesthesia is uniform. This is in contrast to several studies where McCoy blade produces less stress response, than the Macintosh blade.

Our study was supported by the following three studies, on non neurosurgical patients, without entropy monitoring.

Jin Soo Joo et al [18] compared the haemodynamic responses during thiopentone - fentanyl induction, to laryngoscopy and intubation, in elective general surgical patients with Macintosh and McCoy blades and found no significant differences in arterial pressures and heart rate.

Tae Soo Hamn et al [19] also conducted a similar comparison of haemodynamic responses during thiopentone - fentanyl induction, in elective gynaecological patients, between the two blades and found no significant differences between the two blades. Hyun Jung Shin et al [20] conducted a similar comparison study of haemodynamic responses, during propofol- remifentanil induction, in elective general surgical patients, between the two blades and found no significant differences between the two blades.

The two groups consisting of 30 participants each, were comparable in terms of age, sex, height, weight, intubation & baseline haemodynamic parameters. It was also observed that, the laryngeal visualization was better and insertion of an ETT was easier in Group B. Thus laryngoscopy and intubation time was reduced with Mcoy blade (Group B).

After the induction of anaesthesia, and prior to laryngoscopy , the SBP, DBP and MAP in both groups, showed a decrease from the pre induction values. A fall of 24.42% & 21.46% , 19.37% & 19.81%, 21.77% & 20.30% in Group A & Group B for SBP, DBP and MAP was noted respectively. The heart rates in both groups showed an increase, from the pre induction values ie. by 15.22% & 10.03% in Group A and Group B respectively. These results were similar to those observed in previous studies, where it was shown that arterial pressure decreased significantly and heart rate increased significantly after induction of anaesthesia. This effect could be attributed to the hypotensive effect of the induction drugs used.

The HR, SBP, DBP and MAP were significantly elevated after laryngoscopy and insertion of the endotracheal tube, in both groups compared to the pre-laryngoscopy values. Rise in HR during laryngoscopy and intubation, from pre-laryngoscopy values was 6.62% & 16.14% in Group A and 5.76% & 13.77% in Group B respectively. Rise in SBP during laryngoscopy and intubation, from pre-laryngoscopy. values were 12.24% & 24.94% in Group A respectively and 9.79% & 23.92% in Group B respectively. Rise in DBP during laryngoscopy and intubation, from pre-laryngoscopy values was 13.75% & 29.21% in Group A and 11.21% & 26.83% in Group B respectively. Rise in MAP during laryngoscopy and intubation, from pre-laryngoscopy values was 13.07% & 26.42% in Group A and 11.14% & 26.37% in Group B respectively. The elevation persisted for a period of 5 minutes, after which the parameters returned to the pre-laryngoscopy values.

These results were similar, to those found by Millar [21], who found that in normotensive patients, laryngoscopy and insertion of a tracheal tube, is immediately followed by an average increase, in mean arterial pressure of 25 mmHg. The study done by Russell [13], also demonstrated a significant increase in arterial blood pressure after intubation. The observed changes, were probably due to the sympatho-adrenal response, caused by stimulation of the supraglottic region and that of the trachea.

Entropy values showed a decrease, from the pre induction values after induction .i.e, by 50.98% & 51.81% for RE and 47.36% & 49.07% for SE in Group A & Group B respectively. This could be attributed to depressant effects of anaesthestic agents on the cortical signals.

During laryngoscopy & intubation, there was only a modest elevation in the entropy values .ie. by 2.55% & 8.78% for RE and 2.26% & 3.81% for SE in Group A. In group B there was further decrease for RE by 3.76% & 2.30% and by 3.11% & 2.95% for SE during laryngoscopy & intubation respectively. Post intubation, uniform depth of anaesthesia was maintained (entropy values kept between 40 and 60), by altering the isoflurane concentration. Thus increase in all EEG-derived indices after tracheal intubation, was suppressed by ensuring uniform depth of anaesthesia.

The RE-SE values (good indicator of nociception) increased after tracheal intubation and this increase in RE-SE was also suppressed by maintaining uniform depth of anaesthesia. Thus, in our study, haemodynamic responses were comparable between the Macintosh and the McCoy groups and the rise in haemodynamic values, on comparison, were statistically not significant ($p>0.05$), when the depth of anaesthesia was kept uniform, (between 40 and 60) by entropy monitoring.

Conclusion

Through this study we conclude that, although McCoy blade was superior in terms of better glottic visualization, ease of intubation and overall operability, the haemodynamic responses produced during laryngoscopy, intubation and post intubation were similar and comparable with the Macintosh blade and statistically insignificant ($p>0.05$), when depth of anaesthesia is uniform and adequate.

The stress responses were also short lived in both groups, as uniform depth of anaesthesia using entropy monitoring, blunted the overall responses to laryngoscopy and intubation, and the awareness component, which could have occurred if not monitored. The response to laryngoscopy and intubation might be of no clinical importance in the healthy, normotensive patients, but might be harmful in patients with cerebral aneurysm, raised intracranial pressure, compromised intracranial compliance or other cardiovascular diseases. In such cases, the attenuated response can be achieved, with an adequate depth of anaesthesia, followed by maintaining uniform planes of anaesthesia later on.

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Original Research Article

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A Comparative Evaluation of Dexmedetomidine and Midazolam in Monitored Anaesthesia Care for Tympanoplasty

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Abstract

Introduction: Monitored Anaesthesia care (MAC) has been defined by the American Society of Anaesthesiologists as a diagnostic or therapeutic procedure done under local anaesthesia along with sedation and analgesia. Advantages of performing tympanoplasty under MAC with local anaesthesia are less bleeding, improved post-operative analgesia, early and smooth recovery and discharge from hospital with least expenditure. The biggest advantage is intra-operative communication and assessment of hearing in the patient.

Aim: The study was done to evaluate the efficacy of dexmedetomidine and midazolam for intra-operative sedation and analgesia in monitored anaesthesia care and to compare and assess any adverse effects in different groups of study.

*Methodology:*The study was Conducted in the Department of Anaesthesiology, Gandhi Medical College and Hamidia Hospital, Bhopal on ASA Grade I and II patients scheduled for tympanoplasty. 90 patients of either sex of ASA Grade I and II, aged between 16 and 40 years were studied.All patient were premedicated with injection glycopyrolate 0.01mg/kg IV and Inj pentazocine 0.3 mg/kg over 1 min. Group A received Dexmedetomidine: Bolus dose 1mcg/kg IV followed by 0.4mcg/kg per hour, and Group B received Midazolam: Bolus dose of 0.04 mg given over 1 min. Oxygen supplementation through nasal catheter was given. Sedation was titrated to Ramsay Sedation score of ≥3. Rescue sedation with Midazolam 0.01mg/kg was given if RSS was <3 . Surgery was allowed to commence when Visual Analogue Scale (VAS) was <3. Sedation was assessed using Ramsay sedation Scale.

Result and Conclusion: Sedation with Dexmedetomidine was found to be better alternative to midazolam in monitored anaesthesia care performed in minor ENT surgical procedures. It provides a calm sedated patient. Also, fall in the HR and MAP was seen in more number of patients of Group A than in Group B. This caused decreased bleeding, thus providing bloodless surgical field comfortable for the surgeon.

Keywords: Dexmedetomidine; Midazolam; Monitored Anaesthesia Care; Tympanoplasty.

Introduction

Monitored anaesthesia care includes sedation, anxiolysis and analgesia [1]. A number of diagnostic and therapeutic procedures are performed under MAC including Middle ear surgeries (MESs)

Advantages of performing tympanoplasty under MAC with local anaesthesia are less bleeding, improved post-operative analgesia, early and smooth recovery and discharge from hospital with least expenditure [2]. The biggest advantage is intra-operative communication and assessment of hearing in the patient.

Commonly used medication for MAC are benzodiazepine opioids and propofol [3]. The aim of this study was to assess the efficacy of two different drugs viz Dexmedetomidine [4] and Midazolam for use in MAC with respect to sedation, haemodynamics, effect on respiration and need for

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rescue analgesia. Assessment of patient satisfaction and surgeon satisfaction were secondary aims. Analgesic property of α2 agonists like dexmedetomidine with its opiate-sparing properties has been documented by studies carried by Smith H et al [5] and has also been reported in studies conducted in general anesthesia with dexmedetomidine by Keniya [6].

Materials and Methods

A prospective comparative study was conducted in the Department of Anaesthesiology, Gandhi Medical College and Hamidia Hospital, Bhopal on ASA Grade I and II patients scheduled for tympanoplasty. After thorough physical examination and investigation, and informed written consent from patients, 90 patients of either sex of ASA Grade I and II, aged between 16 and 40 years were categorised randomly into 2 groups viz:

I. *Group A:* Dexmedetomidine group: Bolus dose 1mcg/kg IV followed by 0.4mcg/kg per hour maintainance dose was used for MAC.

II. *Group B:* Midazolam group: Bolus dose of 0.04 mg given over 1 min.

A fasting status of 6 hours was maintained. Monitoring of NIBP, ECG, SpO_2 and capnography were done. IV fluid was given through IV cannula . All patient were premedicated with injection glycopyrolate 0.01mg/kg IV and Inj pentazocine 0.3 mg/kg over 1 min. Group A received Dexmedetomidine: Bolus dose 1mcg/kg IV followed by 0.4mcg/kg per hour, and Group B received Midazolam: Bolus dose of 0.04 mg given over 1 min. Oxygen supplementation through nasal catheter was given. Sedation was titrated to Ramsay Sedation score of >=3. Rescue sedation with Midazolam 0.01mg/kg was given if RSS was <3. After postioning, painting and draping, local anaesthetic infiltration was performed by the operating surgeon using 2% Lignocaine with adrenaline. Surgery was allowed to commence when Visual Analogue Scale (VAS) was <3 . Rescue analgesia was provided with IV infusion of Paracetamol 1g in case of intra-operative pain (VAS >3). Patients were kept in PACU for 3 hrs after the end of surgery. The intensity of post operative pain was recorded for all patients using VAS scale at 1, 1.5, and 2, 2.5 and 3 hrs. after surgery. Patients were also observed for adverse effects like hypotension, bradycardia, respiratory depression, nausea and vomiting. Sedation was assessed using Ramsay sedation Score [7].

Result

The patient characteristics were as shown in the table

Table 1 shows that mean age in years of study participants in group A was 25.23± 5.2 while that of group B was 26.5±4.8 years. P value was calculated for gender which came out to be non significant.

Table 1:

Study variables		Dexmedetomidine (Group A) (n=45)	Midazolam (Group B) (n=45)	P value
Mean age		25.23±5.2	26.5±4.8	
Gender	Male	15	11	>0.05
	Female	30	34	
BMI	Underweight	14	13	>0.05
	Normal	27	29	
	Preobese/ Obese	4	3	
Duration of surgery (min)		90	97	

Table 2:

Parameter	Number of Patients Dexmedetomidine (Group A) (n=45)	Midazolam (Group B) (n=45)	P value
Fall in MAP	21	12	<0.05
Fall in HR	18	2	<0.05
Rescue Analgesia	2	7	<0.05

Table 3:

Parameter	Dexmedetomidine (Group A) (n=45)	Midazolam (Group B) (n=45)	P value
Ramsay Sedation Score	3.42±0.27	3.03±0.21	<0.05

Group A had a greater number of patients who had fall in MAP i.e 21 out of 45, than group B in which 12 out of 45 patients showed fall in MAP. Group A patients had significant reduction in MAP from the respective baseline values.

The mean sedation score in group A was 3.42±0.27 and that in group B was 3.03±0.21 p value observed was <0.05 hence it was significant.

Discussion

Monitored anesthesia care (MAC) is useful for various clinical fields such as minimally invasive surgery, gastrointestinal endoscopy, and interventional or radiological procedures. It not only provides appropriate intra operative conditions but is also comfortable for the patients. Advantages of performing tympanoplasty under MAC with local anaesthesia are less bleeding, improved post-operative analgesia, early and smooth recovery and discharge from hospital with least expenditure.The biggest advantage is intra-operative communication and assessment of hearing in the patient.

Group A patients had significant reduction in MAP and HR from the respective baseline values. Also, more number of patients of Group A (18 out of 45) had fall in MAP than of group B(12 out of 45 patients) . This lower HR and MAP in Group A in comparison to the midazolam-fentanyl group could be explained by the markedly decreased sympathetic activity as previously explained in the study carried by Kamibayashi et al [8].

Dexmedetomidine is a highly selective α2-adrenoceptor agonist with eight times higher specificity for the receptor compared to clonidine [9]. It provides excellent sedation and analgesia with minimal respiratory depression [10].

Dexmedetomidine can be safely and effectively used for procedural sedation and surgeries done under MAC.

Since the approval of Midazolam by FDA in 1985, practitioners of all medical disciplines embraced the versatility provided by Midazolam though the risk of losing airway control, hypoxia and hypotension with higher doses of Midazolam has also been recognized [11].

Midazolam is the most frequently used sedative and has been reported to be well tolerated when used in MAC [12]. Dexmedetomidine has both sedative and analgesic properties and has been used as a single agent in many painful procedures [13]. A loading dose of 1 mcg/kg of Dexmedetomidine was used in our study. Since dexmedetomidine has a short distribution half life of 5 min. , it is necessary that the loading dose is followed by a maintainance dose of 0.4 mcg/kg per hour.

A prospective randomized double-blind study study which was conducted by Parikh DA et al comparing dexmedetomidine vs. combination of midazolam-fentanyl for tympanoplasty surgery under monitored anesthesia care also showed a similar results [14]. Another study conducted by Na HS, Song IA et al. showed Dexmedetomidine to be effective for monitored anesthesia care in outpatients undergoing cataract surgery [15].

Dexmedetomidine is unique in that it does not cause respiratory depression because its effects are not mediated by the γ- aminobutyric system [16]. However, Alhashemi et al. [17], had observed a higher ventilatory frequency in patients receiving midazolam in their comparative study of dexmedetomidine with midazolam for cataract surgery. Zeyneloglu et al [18] have reported better sedation scores with midazolam-fentanyl combination as compared to dexmedetomidine in extracorporeal shock wave lithotripsy (ESWL) when used alone.

Conclusion

The fall in heart rate and mean arterial as well as sedation were more in the patients of Group A than that of the patients in Group B. This caused decreased bleeding in GroupA patient,thus providing blood less surgical field comfortable for the surgeon.

Hence, our study concludes that in case of monitored anaesthesia care performed for minor ENT surgeries, dexmedetomidine appears to be a superior alterative to midazolam.

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Comparision of 0.5% Ropivacaine and 0.5% Bupivacaine for Supraclavicular Brachial Plexus Block in Upper Limb Surgeries

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Abstract

Introduction: Supraclavicular approach to brachial plexus block produces the most complete upper limb block as it blocks the brachial plexus at the level of the trunks formed by C5-T1 nerve roots.Ropivacaine is a pure S enantiomer with greater differentiation between sensory and motor block with better margin of safety due to reduced toxic potential. The aim of this study was to compare sensory and motor block effectiveness of 0.5% ropivacaine to that of 0.5% bupivacaine for supraclavicular brachial plexus block in upper limb surgeries.

Materials and Method: In this prospective randomized study total 60 patients undergoing upper extremity surgeries were given block using a peripheral nerve stimulator. Group A received 0.5% ropivacaine, 30ml and Group B received 0.5% bupivacaine, 30ml. Sucess of the block was assessed by determining loss of shoulder abduction and loss of pinprick in the C5-T1 dermatomes. The onset of action (sensory and motor) and duration of action (sensory, motor) were recorded. Post operative analgesia was assessed by using visual analog scale. The results were tabulated and statistically analyzed.

Results: There was statistically significant difference in the mean onset time to achieve maximum sensory level between group A(7.87+/-2.13mins) and group B(9.53+/-2.45mins). Duration of sensory block and analgesia was similar in both the groups. However motor block was more prolonged in group B(556+/-93.7mins) as compared to, group A(467+/-92.5 mins).

Conclusion: Ropivacaine is a suitable alternative to bupivacaine in supraclavicular brachial plexus block for upper limb surgeries.

Keywords: Supraclavicular Block; Ropivacaine; Bupivacaine.

Introduction

Brachial plexus block is a valuable and safe alternative to general anaesthesia for upper limb surgeries. Supraclavicular approach to brachial plexus block produces the most complete upper limb block as it blocks the brachial plexus at the level of the trunks formed by C5-T1 nerve roots.Today with the use of peripheral nerve stimulator (PNS), there has been a good success rate in brachial plexus block along with reduction of drug requirement [4].

Bupivacaine has many side effects which include prolonged motor weakness, cardiovascular and central nervous system toxicity [5]. Ropivacaine is a newer long acting amide linked local anaesthetic agent. It is a pure S enantiomer with greater differentiation between sensory and motor block with better margin of safety due to reduced toxic potential [1,3]. This study was conducted to compare onset of action,duration of sensory, motor block and analgesia and incidence of side effects with 0.5% Ropivacaine and 0.5% Bupivacaine in supraclavicular brachial plexus block for upper limb surgeries.

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Material and Methods

After obtaining institutional ethical committee approval our prospective randomized double blind study was carried out in orthopaedic and plastic surgery operation theatre of our hospital. 60 patientswith age above 18yrs, of either sex and ASA grade I and II requiring brachial plexus block for upper limb surgeries were selected and randomised into two groups.Group A received 30 ml of 0.5% Ropivacaine and Group B received 30 ml of 0.5% Bupivacaine.Patients with weight<50kg, known allergy to local anaestheticdrugs, coagulation-disorder, peripheralneuropathy, pregnancy and lactating mother were excluded from the study.

On arrival in the operation room, baseline heart rate, blood pressure, respiratory rate and oxygen saturation were recorded. An intravenous line was secured in the unaffected limb and Ringer's lactate was started. The local anaesthetic was provided in non-identified syringes, labelled with the patient's serial number, prepared by another anaesthesiologist, not related to this study. The randomization was done by doing the computerized chart and selecting one of them blindly. Under all aseptic precautions all the patients received brachial plexus block through the supraclavicular approach. Neural localization was achieved by using a nerve locator connected to a 22 G, 50-mm-long stimulating needle (Stimuplex, Braun, Germany). The location end point was a distal motor response with a current of 0.5 mA.Following negative aspiration, 30 mL of a solution containing local anaesthetic was injected in 3ml increments.

Assessment of sensory block was done by pinprick method at each minute after completion of drug injection in C5,C6,C7,C8 &T1 dermatomal areas till complete sensory blockade. Sensory onset was considered when there was a dull sensation to pin prick (grade 1) along the distribution of above dermatomes. Complete sensory block was considered when there was complete loss of sensation to pin prick.

Sensory block was graded as-

Grade 0: Sharp pin felt

Grade 1: Analgesia, dull sensation felt

Grade 2: Anaesthesia, no sensation felt.

Assessment of motor block was carried out by the same observer at each minute till complete motor blockade after drug injection. Onset of motor blockade was considered when there was Grade 1 motor block. Motor block was determined according to a modified Bromage scale for upper extremities on a 3-point scale.

Grade 0: Normal motor function with full flexion and extension of elbow, wrist and fingers

Grade 1: Decreased motor strength with ability to move the fingers only

Grade 2: Complete motor block with inability to move the fingers

The block was considered incomplete when any of the segments supplied by median, radial, ulnar and musculocutaneous nerve did not have analgesia even after 30 min of drug injection. When more than one nerve remained unaffected, it was considered a failed block and omitted from statistical analysis. In this case, general anaesthesia was given.

Patients were monitored for haemodynamic variables such as heart rate, blood pressure, respiratory rate and oxygen saturation every min for 5mins; every 5mins till first 30mins and then every 15mins till 2hrs and every 30mins till surgery lasted. They were also monitored in postoperative period every hourly for 6hrs and 2 hourly for 12hrs.

The patients were assessed for the total duration of sensory as well as motor block and duration of analgesia. The duration of sensory block was defined as the time interval between the onset of sensory block (grade 1) upto the complete resolution of anaesthesia on all nerves.

The duration of motor block was defined as the time interval between the onset of motor block (grade 1) upto the recovery of complete motor function of the hand and forearm. The duration of analgesia was defined as the time interval between the onset of sensory block upto time of rescue analgesia.Rescue analgesia was given in form of Inj Diclofenac sodium 75mg intramuscularly when VAS score was >5. All patients were observed for any side-effects like nausea, vomiting, dryness of mouth and complications like pneumothorax, haematoma, local anaesthetic toxicity and post-block neuropathy in the intra- and post-operative periods.

The data thus obtained was tabulated & statistically analyzed by -

- Unpaired t test, paired t test , Mann whitney test and chi square test.
- The p value of < 0.05 was considered as statistically significant and the p value < 0.001 was considered as statistically highly significant.

Results

Data was collected in both groups for following parameters and observations of the analysed data were tabulated as follows.

Demographic characteristics and duration of surgery were comparable in both the groups.

Onset of sensory blockade was faster in group A(7.87 +/- 2.13 min) compared to group B (9.53 +/ - 2.37 min).By applying Mann Whitney Test this difference was found to be statistically significant (p=0.018)(Figure 1).

Mean time of onset of motor blockade was 11.1 +/- 2.5 mins in group A and 11.9 +/- 2.9 mins in group B which was comparable and there was no statistical difference (p value 0.273>0.05) (Figure 2).

The mean duration of sensory blockade in group A was 457.00 +/- 82.51 mins and in group B was 493.00 +/- 81.37 minsand this difference was statistically not significant (p=0.086) (Figure 3).

The mean duration of motor blockade was longer in group B (467.33 ±92.51min) compared to group A (556.00 ± 93.79min) and this difference was statistically significant (p=0.00035). Ropivacaine has less duration of motor blockade than Bupivacaine. (Figure 3).

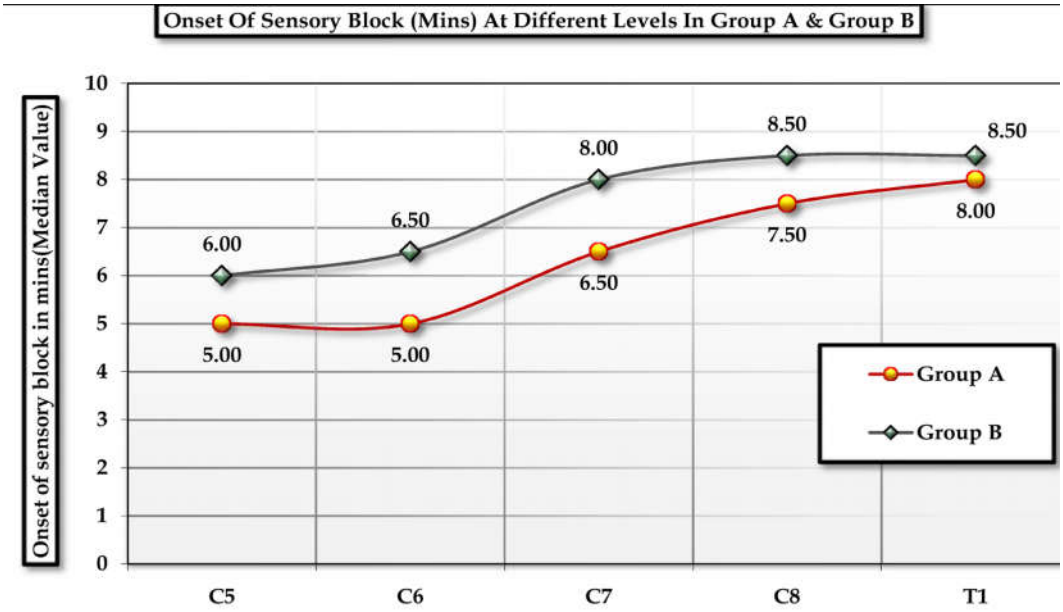

Fig. 1:

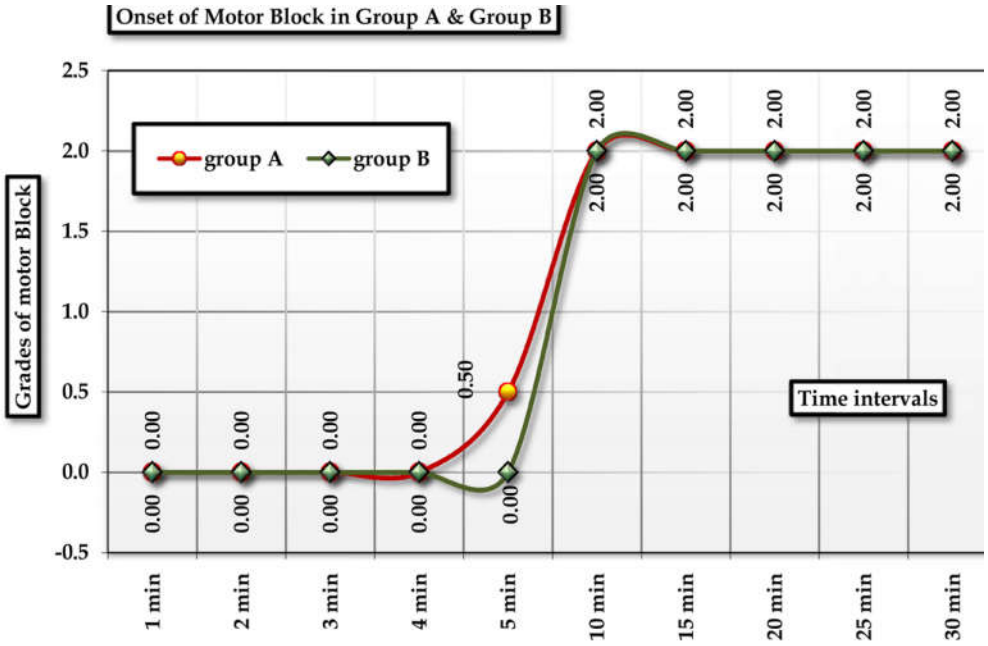

Fig. 2:

Fig. 3:

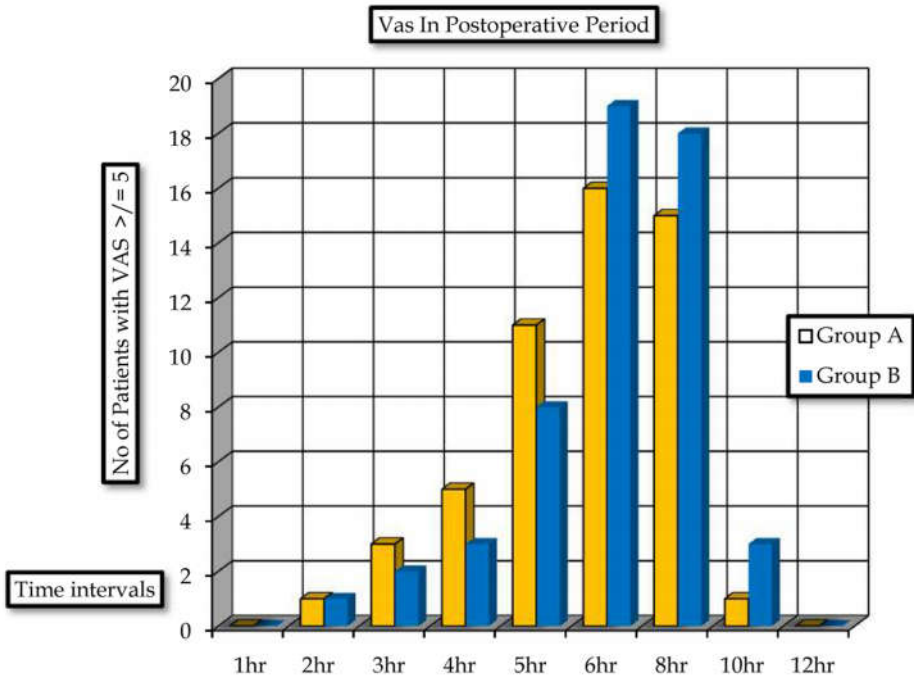

Table 1: Comparison of total duration of action

Total Duration (min)	Group A			Group B			Unpaired t-test applied		
	Mean	SD	Median	Mean	SD	Median	t-value	p-value	Difference is-
Sensory Block (mins)	457.00	82.51	435.00	493.00	81.37	480.00	-1.719	0.086	Not significant
Motor Block (mins)	467.33	92.51	420.00	556.00	93.79	600.00	-3.58	0.00035	Significant
Analgesia by VAS(mins)	521.67	76.30	525.00	557.33	81.96	555.00	-1.745	0.09	Not significant

*p<0.05:significant

Table 2: Comparison of vas score in postoperative period in group a & b

Time interval	No of Patients with VAS Score >/= 5	
	Group A	Group B
1hr	0	0
2hr	1	1
3hr	3	2
4hr	5	3
5hr	11	8
6hr	16	19
8hr	15	18
10hr	1	3
12hr	0	0

The mean duration of analgesia in group A was 521±76.30mins and in group B was 557.33±81.96 mins. This difference was statistically not significant (p= 0.09). Ropivacaine and Bupivacaine have similar duration of analgesia (Figure 3).

No significant difference in VAS Scores of two groups was observed at any time interval.At 6hrs, 16 patients in group A (53.3%) had VAS score > 5 and required rescue analgesia while in group B, 19 patients (61%) had VAS score of > 5 and did require rescue analgesia.At 8hrs, 15 patients in group A(50%) had VAS score > 5 andrequired rescue analgesia while in group B, 18 patients (60%) had VAS score of > 5 and did require rescue analgesia (Figure 4). So there was analgesia for 6-8 hrs in the postoperative period in both the groups and the total duration of analgesia was similar in both the groups (Figure 5).

There was no statistically significant difference between two groups in terms of haemodynamic

parameters at different time intervals till 12 hours of administration of brachial plexus block.

Discussion

Brachial plexus block provides an useful alternative to general anesthesia for upper surgeries. It avoids airway instrumentation, use of large number of anesthetic drugs and hemodynamic consequences of general anesthesia. Patient satisfaction, a growing demand for cost effective anesthesia and a favorable postoperative recovery profile have resulted in increased demand for regional techniques. Supraclavicular brachial plexus block is the preferred regional anaesthesia technique for upper limb surgeries. Here, the brachial plexus is presented most compactly at the proximal division or at the trunk level that provides most reliable anaesthesia for upper limb surgeries by anaesthetising the middle and lower plexus over 80% of the times (median, radial and ulnar). Existing local anesthetic, Bupivacaine, is known for its propensity for neurotoxicity and cardiotoxicity when large volume of the drug is required. Ropivacaine is a long acting amide local anesthetic agent with greater differentiation between sensory and motor block and potentially improved safety profile when contrasted to Bupivacaine [6,10].

In this study we found that the onset of sensory block was faster in patients receiving Ropivacaine than Bupivacaine.Similar result was observed in the study by Modak S & et al. who compared 0.5% ropivacaine and 0.5% bupivacaine for brachial plexus block by supraclavicular approach for upper limb surgeries [12]. Onset of sensory blockade was significantly faster in Ropivacaine group than bupivacaine. Mean time of onset of motor blockade in the present study was comparable in both the groups. The results in our study correlate with the study done byMisiolek, H.D. & et al. [11]. They compared 0.75% Ropivacaine and 0.5% Bupivacaine in brachial plexus block for the formation of arteriovenous fistula in patients with end-stage renal failure and found that 0.5% Bupivacaine and 0.75% Ropivacaine have a similar onset time of motor blockade.

The duration of sensory block was defined as the time interval between the onset of sensory block upto the complete resolution of anaesthesia on all nerves. The mean duration of sensory blockade in group A was 457.00 +/- 82.51 mins and in group B was 493.00 +/- 81.37 minswhich was statistically not significant (p=0.086). This result was comparable to the study done by S Patel et al [9] who compared the efficacy of 0.5% Ropivacaine with 0.5% Bupivacaine for supraclavicular brachial plexus block for upper limb surgeries.There was no statistically significant difference in onset and duration of sensory block.

The duration of motor block was defined as the time interval between the onset of motor block upto the recovery of complete motor function of the hand, forearm and arm. The mean duration of motor blockade was longer in group B (467.33±92.51min) compared to group A (556.00±93.79min). Ropivacaine had less duration of motor blockade than Bupivacaine.Thisresult is comparable with the study done by Misiolek, H.D. et al.whocompared 30 mL of 0.75% Ropivacaine and 30 mL of 0.5% Bupivacaine in supraclavicular brachial plexus block for the formation of arteriovenous fistula in patients with end-stage renal failure [11]. In this study Ropivacaine had less duration of motor blockade than Bupivacaine.

The duration of analgesia was defined as the time interval between onset of sensory block upto the time of rescue analgesia. The mean duration of analgesia in group A was 521±76.30mins and in group B was 557.33±81.96mins. In our study we found that Ropivacaine and Bupivacaine had similar duration of analgesia. D.C. Tripathi & et al. [14]compared Ropivacaine and Bupivacaine in supraclavicular brachial plexus block for upper limb orthopedic surgery. Both 0.5% Bupivacaine and 0.75% Ropivacaine provided comparable duration of postoperative analgesia.When the various studies were compared, it was observed that ropivacaine in concentration of 0.5% and 0.75% provide similar duration of post operative analgesia [8,15].

There was no significant difference in postoperative VAS score in both the groups.There was analgesia for 6-8 hrs in the postoperative period in both the groups. In our study there was no difference in the incidence of side effects in both the groups. S Patel & et al [9] compared 30 mL of 0.5% Ropivacaine and 30 mL of 0.5% Bupivacaine in supraclavicular brachial plexus block.They didn't observe any side effects in both the groups.There was no clinically important difference between using 0.5% Ropivacaine and 0.5% Bupivacaine for supraclavicular brachial plexus block.

Conclusion

Ropivacaine is a suitable alternative to bupivacaine in supraclavicular brachial plexus block for upper limb surgeries.

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Original Research Article

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Comparision of Analgesic Efficacy of Two Dissferent Doses of Intrathecal Buprenrphine

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Abstract

Pain is the most common symptom that brings the patient to a health care provider. The fear of pain during and after surgery affects the psychological state of the patient immensely. The technical skills and the extensive pharmacological knowledge on pain relief places the anesthesiologist in an ideal position to treat pain in the perioperative setting. Comparisonof analgesic efficacy and safety of two different doses of intrathecal buprenorphine (30 µg and 60 µg) along with bupivacaine (2.2 ml) in geriatric patients 60-80 years undergoing hemiarthroplasty.

Keywords: Inthtraecal; Hemiarthroplasty; Buprenorhine.

Introduction

Neuraxial blockade is the preferred method of anaesthesia for surgeries on the lower half of the body. It provides effective pain relief in the initial postoperative period. But additional analgesics are required as the effect of neuraxial blockade wears off. Additives added to the local anaesthetics while producing block not only improves the quality of analgesia but also prolong the analgesia compared to local anaesthetics alone, thus decreasing the need for frequent rescue analgesics.

Related Works

In 1900, matas discovered that the adverse effects of intrathecally administered cocaine could be mitigated with the addition of morphine. He used 1.5 mg of morphine intrathecally to reduce the CNS effects of cocaine. In 1901 a Japanese anaesthesiologist *Otojiro Kitagawa*, used 10 mg of morphine with local anaestheticeucaineintrathecally for cancer pain relief.

With the discovery of opioid receptors in the spinal cord, interathecal opioid administration quickly spread to perioperative care in a wide array of surgical procedures.

The pioneering animal studies conducted by *Yaksh and Rudy (1976)* showed spinal site of action. Thus, intrathecally administered opioids ushered in a new and exciting era in clinical pain therapy. Extension of this concept of intrathecal and epidural injection in man by *Behar et al (1979) and Wang et al (1979)* was subsequently followed by many clinical reports and scientific studies to determine the specific action, dose – response relations, pharmacokinetics and long-term effects of spinal opiate administration.

In recent years, studies have been done using buprenorphine, an opioid analgesic with agonist-antagonist properties, as an additive to spinal lignocaine or bupivacaine. Many studies have been done with intrathecal buprenorphine mostly in

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adult patients. Only very few studies were done in elderly patients with intrathecal buprenorphine. Hence this study was done in geriatric patients undergoing elective hemiarthroplasty of hip surgery who usually suffer from pain postoperatively due to tissue damage.

A comparative study was done with two different doses of intrathecal buprenorphine 30µg and 60 µg along with bupivacaine (2.2 ml) with an intention of reducing the incidence of side effects and to study whether considerable post operative analgesia was provided with minimal dosage. This study was conducted in our hospital settings who presented for elective hemiarthroplasty of hip.

Objectives of the Study

Primary Objective

- To compare the post operative analgesic efficacy of Intrathecal buprenorphine in two different doses (30µg/60µg).

Secondary Objective

- To compare the hemodynamic Instability.
- To compare the incidence of side effects like Nausea, vomiting, shivering, pruritus and respiratory depression.

Opioids

The term opioid refers to all compounds related to opium derived from juice of opium poppy, papaver somniferum. Opiate is the term used for drugs derived from opium. Morphine is the prototype opioid. Opioid compounds can be classified as naturally occurring, semisynthetic and synthetic opioids. With the development of synthetic drugs with morphine like effects, the term opioid is now used to refer all exogenous substances natural and synthetic that bind to opioid receptors and produce some agonistic effect.

The presence of opioid binding sites in the nervous system was reported in the year 1973. Immunohistochemical studies have demonstrated opioid receptors in various areas of the central nervous system. These include the amygdala, the mesencephalic reticular formation, the periaqueductal gray matter, and the rostral ventral medulla.

Mechanism of Analgesic Action

Opioids act as agonists at stereo specific opioid receptors at presynaptic and postsynaptic sites in the central nervous system (CNS) and also outside the CNS in the peripheral tissues.

Opioid agonists bind with the opioid receptors, leading to activation of the G-protein. Activity of adenylatecyclases and the voltage-dependent Ca^{2+} channels is suppressed on the other hand, inward rectifier K^+ channels and mitogen – activated protein kinase are activated.

Pain Pathways

The spinothalamic tract: the axons of most second order neurons cross the midline close to their level of origin (at the anterior commissure) to the contralateral side of the spinal cord before they form the spinothalamic tract and send their fibres to the thalamus, the reticular formation, the nucleus raphe magnus, and the periaqueductal gray matter.

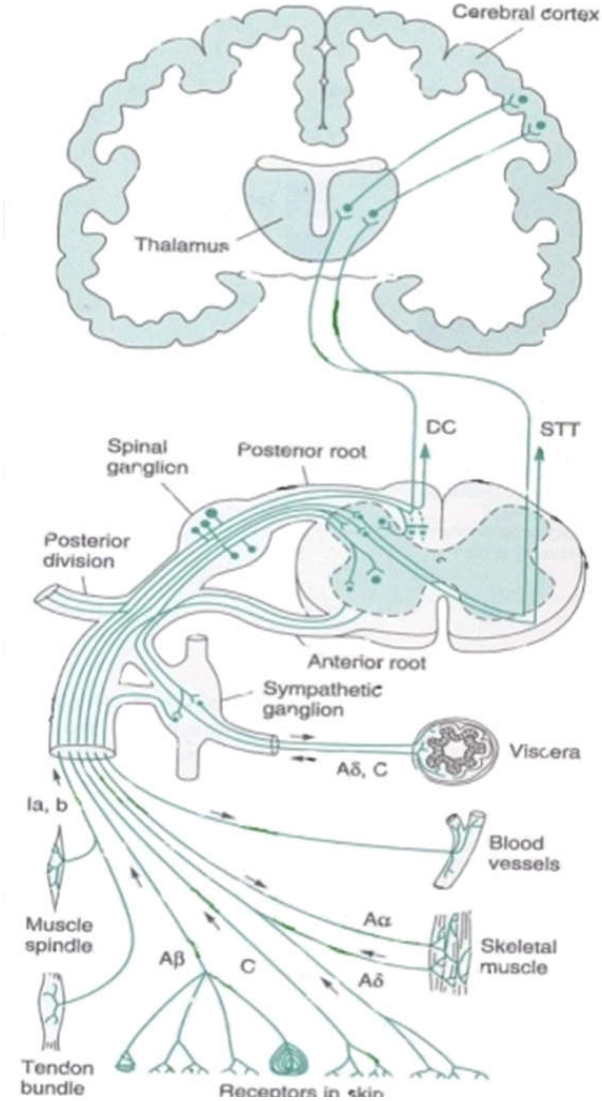


Fig. 1: Pain Pathways

Alternate Pain Pathways

These include the spinoreticular tract, the spinomesencephalic tract, the spinohypothalamic, the spinotelencephalic tract and the spinocervical tract.

Integration with symapathetic and motor systems: somatic and visceral afferents are fully integrated with the skeletal motor and the sympathetic systems in the spinal cord, brainstem and the higher centers. Afferent dorsal horn neurons synapse both directly and indirectly with anterior horn motor neurons.

Buprenorphine

Buprenorphine was first synthesised in 1966. It is an oripavine derivative of the alkaloid thebaine. It is a narcotic analgesic having powerful agonist and partial antagonistic action and low addiction potential. The antinociceptive effect of buprenorphine in mice is μ-opioid receptor-mediatedyet severely compromised by concomitant activation of opioid receptor like-1receptors.

Buprenorphine affects nociceptive processing by acting at both supraspinal and spinal μ and ORL1 receptors.In terms of spinal and supraspinal effects of buprenorphine, it is likely that buprenorphine facilitates the C-fiber reflex via a supraspinal mechanism that acts on sensory and/or motor components of the reflex arc although the depression of the reflex involves a spinal mechanism.

Observations and Results

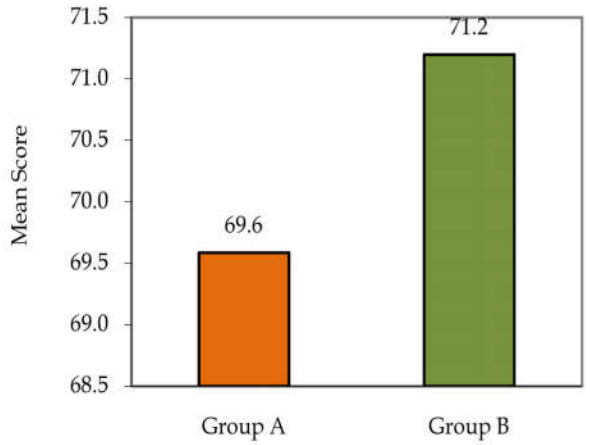
Demographic Data

The graph above clearly indicates that the mean age in Group A is 69.6±6.0 and the mean age in Group B is 71.2±5.4 No significant difference between the two groups with respect to age.

Table 1: Comparison of Age based on Group

Age	Group I		Group II	
	Count	Percent	Count	Percent
60-70	42	56.0	35	46.7
71-80	33	44.0	40	53.3
Mean ± SD	69.6 ± 6.0		71.2± 5.4	

t = 1.79, p > 0.05



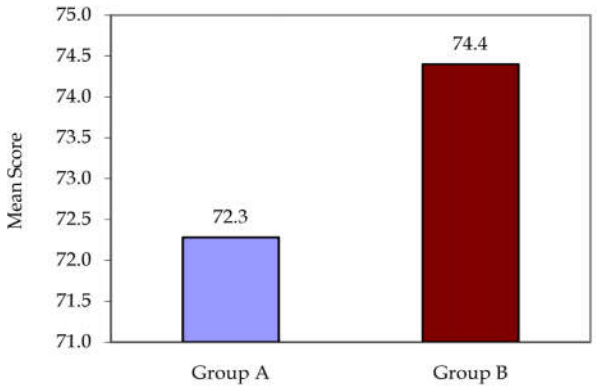
The graph clearly shows that the mean pulse rate in Group 1 is 72.3±13.2 and the mean pulse rate in Group 2 is 74.4±13.2. p value is 0.328>0.05. No significant difference between the two groups with respect to mean baseline pulse rate.

The graph shows that the mean baseline Respiratory rate in Group A is 14.9±0.9 And the mean Baseline Respiratory rate in Group B is 14.8 ±0.9. p value is 0.410 which is >0.05. The two groups are comparable with respect to mean baseline respiratory rate.

The graph above shows that the mean baseline BP in Group A is 104.3±5.3 and the mean baseline BP in Group B is 103.7± 5.5 . p value is 0.48 which is greater than 0.05. The two Groups are comparable with respect to mean baseline BP.

Table 2: Comparison of PR_Baseline based on Group

	Mean	SD	N	t	P
Group A	72.3	13.2	75	0.98	0.328
Group B	74.4	13.2	75		



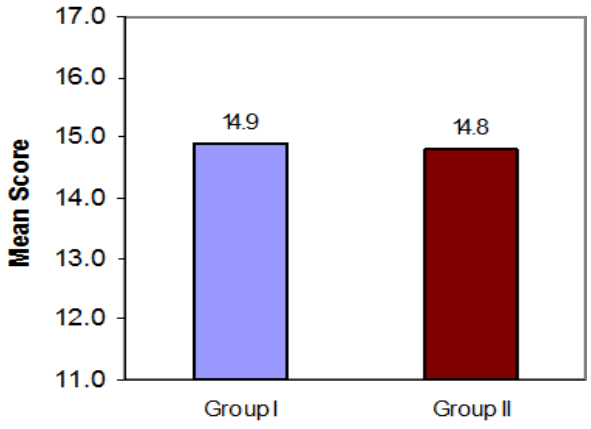
The above graph clearly tells that in Group A 61.6% were of female patients and in Group B 57.3% were of female patients whereas, male patients in Group A are 38.7 % and in Group B are 42.7%.

No significant difference was found between the two groups with respect to gender (p = 0.618).

The Graph shows that in Group A- 42.7% of Patients belongs to ASA 1 Grading and in Group B- 54.7% of patients belongs to ASA1 Grading.

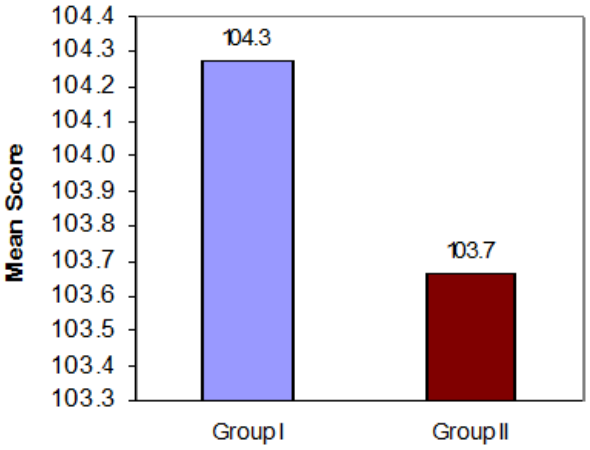
Table 3: Comparison of RR_Baseline based on Group

	Mean	SD	N	T	P
Group I	14.9	0.9	75	0.826	0.410
Group II	14.8	0.9	75		



Comparison of Mean Baseline BP based on Group

	Mean	SD	N	T	p
Group I	104.3	5.3	75	0.7	0.488
Group II	103.7	5.5	75		



Comparison of Gender Distribution based on Group

Gender	Group I Count	Group I Percent	Group II Count	Group II Percent	χ^2	p
Female	46	61.3	43	57.3	0.249	0.618
Male	29	38.7	32	42.7		

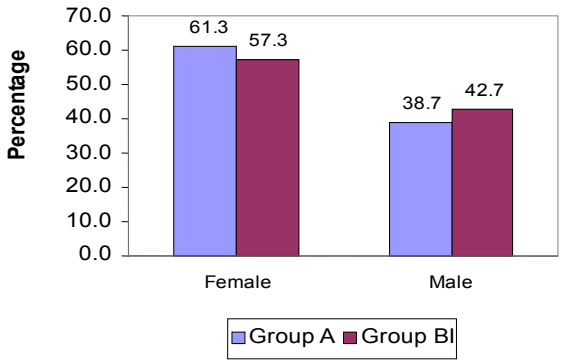


Table 4: Comparison of ASA Distribution based on Group

ASA	Group A Count	Group A Percent	Group B Count	Group B Percent	χ^2	p
Grade I	32	42.7	41	54.7	2.16	0.142
Grade II	43	57.3	34	45.3		

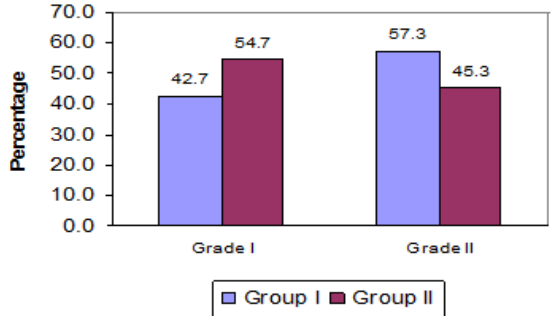
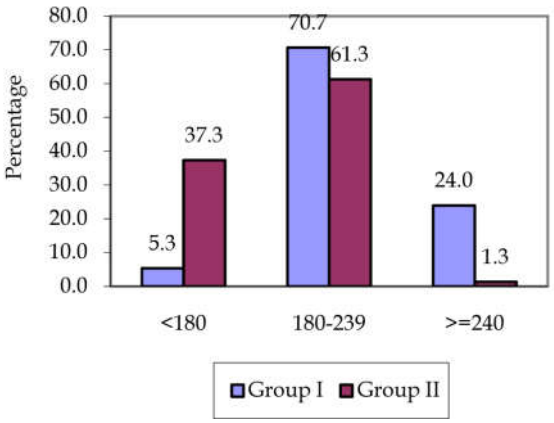
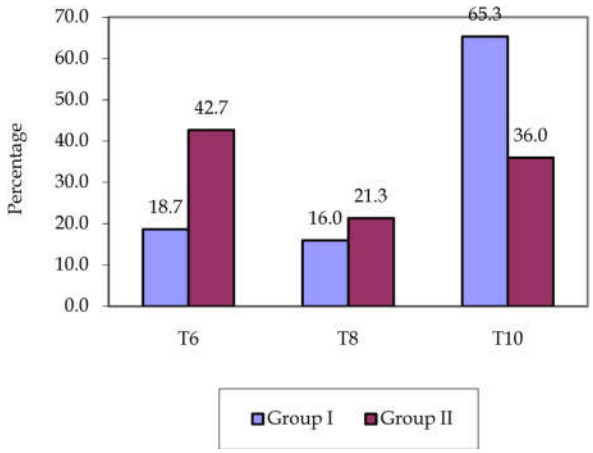


Table 5: Comparison of Time of Onset based on Group

Time of onset seconds	Group A		Group B	
	Count	Percent	Count	Percent
<180	4	5.3	28	37.3
180-239	53	70.7	46	61.3
>=240	18	24.0	1	1.3
Mean ± SD	211.9± 25.5		186.4± 24.0	

t = 6.3, p < 0.01





The graph also clearly depicts that in Group B 57.3% of patients belongs to ASA2 Grading and 45.3% of patients belongs to ASA2 Grading. p value is 0.142 which is greater than 0.05. The two groups were comparable with respect to ASA Grading.

Time of Onset.

The Time taken to reach the maximum level of sensory block.

Group A 211.9±25.5 Seconds

Group B 186.4±24.0 Seconds

The data was analysed using the 't' test and the p value was found to be <0.01 which is statistically significant between the two groups. Time taken to reach the maximum level of sensory block was shorter in Group B.

P value is 0.01 which is statistically significant

Maximum sensory block:

Group A

18.7 % of patients had maximum level of sensory block upto-T_6

16 % of patients had maximum level of sensory block upto-T_8

65.3% of patients had maximum level of sensory block upto-T_{10}

Group B

42.7% of patients had maximum level of sensory block upto-T_6

21.3% of patients had maximum level of sensory block upto-T_8

36% of patients had maximum level of sensory block upto-T_{10}

The data analysed using t test found p value to be 0.001 which is statistically highly significant.

Table 6: Comparison of Maximum Sensory Block based on Group

Max sensory	Group A		Group B		χ^2	p
	Count	Percent	Count	Percent		
T6	14	18.7	32	42.7	13.98**	0.001
T8	12	16.0	16	21.3		
T10	49	65.3	27	36.0		

**: - Significant at 0.01 level

Maximum level of sensory block was noted in Group B patients who were administered 60 µg of intrathecal buprenorphine.

The graph clearly states that,

Group A-

8% of patients had a sedation score of 1

62.7% of patients had a sedation score of 2

29.3% of patients had a sedation score of 3

Group B

4% of patients had a sedation score of 1

26.7% of patients had a sedation score of 2

69.3% of patients had a sedation score of 3

Patients in Group 2 had excellent intra operative sedation. But the p value is 0.220. Hence the two groups are comparable in terms of sedation score.

Mean Duration of Analgesia

Group A - 3.7± 0.41 hrs

Group B - 7.6± 1.1 hrs

p value is < 0.01 which is statistically significant between the two groups.

The graph clearly tells that mean duration of analgesia was prolonged in Group B.

P value>0.05. There was no statisticallysignificant side effects noted in either of the groups

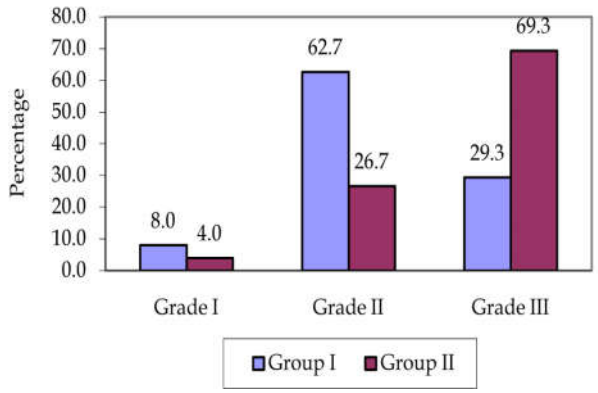
Table 7: Comparison of Sedation Score based on Group

Ng sedation	Group I		Group II		χ^2	p
	Count	Percent	Count	Percent		
Score 1	6	8.0	3	4.0	1.51	0.220
Score II	47	62.7	20	26.7		
Score III	22	29.3	52	69.3		

Table 8: Comparison of Duration of Analgesia based on Group

Duration of Analgesia	Group A		Group B	
	Count	Percent	Count	Percent
2-4 Hr	57	76.0	0	0.0
4-6 Hr	18	24.0	4	5.3
6-8 Hr	0	0.0	40	53.3
>8 Hr	0	0.0	31	41.3
Mean ± SD	3.7± 0.41		7.6± 1.1	

t = 26.1, p < 0.01



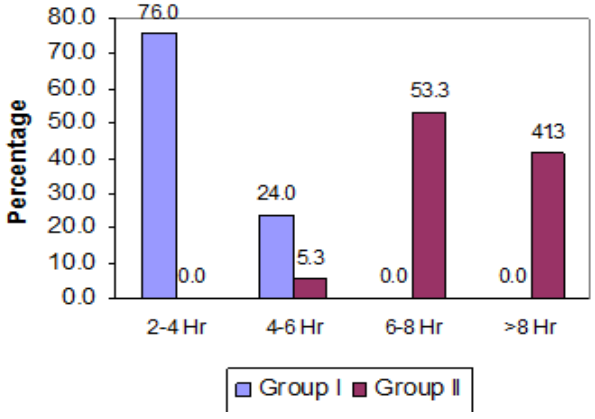
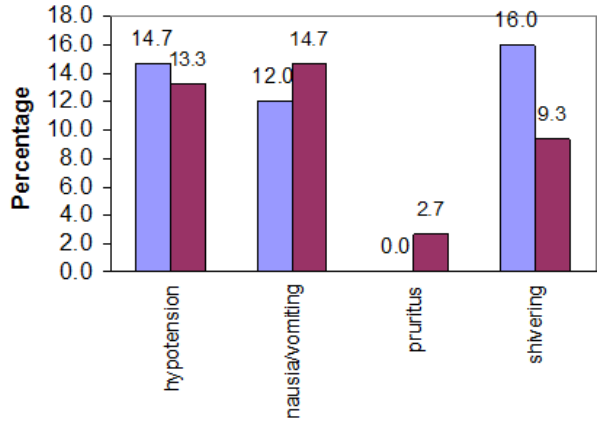


Table 9: Comparison of Side Effects based on Group

Hypotension	Group I		Group II		χ^2	p
	Count	Percent	Count	Percent		
Hypotension	11	14.7	10	13.3	0.05	0.814
nausea/vomiting	9	12.0	11	14.7	0.23	0.631
Pruritus	0	0.0	2	2.7	-	-
Shivering	12	16.0	7	9.3	2.03	0.155



Conclusion

The study done with the addition of two different doses of intrathecal buprenorphine, 30 µg and 60 µg along with bupivacaine 2.2ml (0.5%) clearly proves that,Post operative analgesia is prolonged with higher dosage of buprenorphine 60 µg given intrathecally along with bupivacaine. No increase in side effects were noted with the addition of buprenorphine in two different doses studied (30µg, 60µg). Use of 30µg of buprenorphine intrathecally also provideconsiderable prolongation of post operative analgesia. Since the side effects are incomparable between the two groups, 60µg of intrathecal buprenorphine can be safely administered to geriatric patients.

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Original Research Article

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Mechanical Complications during Insertion of Central Venous Catheter in Subclavian Vein and Internal Jugular Vein: A Comparative Study

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Abstract

Background: Central venous catheters (CVC) are an essential component of modern critical care. They allow delivery of medications, intravenous fluids, parenteral nutrition, hemodialysis and monitoring of hemodynamic variables. Thus, percutaneous placement of a catheter into a central vein is a frequent procedure in many clinical settings.

Aims: To compare the ease of insertion between Internal jugular vein (IJV) and Subclavian vein (SCV) catheterisation, frequency of mechanical complications between the two routes like- Arterial puncture, Pneumothorax, Hemothorax/Hydrothorax, Subcutaneous hematoma, Misplacement of catheter.

Materials and Methods: 100 patients admitted to The Trauma Care Unit of our institution requiring CVC divided into two groups of 50 each. Group A Patients had CVC via IJV and Group B Patients had CVC via SCV. A prospective randomized double blinded clinical study has been conducted in patients of either sex fulfilling the inclusion and exclusion criteria after taking ethical committee approval and informed consent from the patients. The data was analysed using statistical methods like Chi square test, independent samples T test.

Results: The age, sex in the two groups were found to be comparable. Ijv catheterisation was significantly easier than scv (P value <0.05) and the mechanical complication like pneumothorax and misplacement of catheter was less in Ijv (P value <0.05) compared to scv although arterial puncture, subcutaneous hematoma more in scv (P value <0.05) than Ijv.

Conclusion: According to the observations and analysis of this study, catheterisation in IJV was significantly easier than SCV and has significantly lower risk of catheterisation related complications.

Keywords: Central Venous Catheters; Internal Jugular Vein (IJV); Subclavian Vein (SCV); Mechanical Complications.

Introduction

Central venous catheters (CVC) are an essential component of modern critical care. They allow delivery of medications, intravenous fluids, parenteral nutrition, hemodialysis and monitoring of hemodynamic variables [1]. Thus, percutaneous placement of a catheter into a central vein is a frequent procedure in many clinical settings. There has been an explosion of interest in the area of central venous catheterisation recently. The traditional use of catheters in anaesthesia, critical care, surgery and acute medicine continues and there is also a rapidly increasing requirement for medium or longer term central venous catheterisation for parenteral nutrition, cancer chemotherapy, prolonged antibiotics and other interventions. Recently Ultrasonography-guided catheterization has also made the procedure easy and less complicated [3]. A wide variety of different professionals are involved with the insertion, care and removal of such devices. The Inferior Vena Cava and Superior Vena Cava are generally too difficult to catheterize directly, unless imaging is

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used, because they lie deeply protected within the chest and abdomen. Therefore, they are usually catheterized more peripherally ('upstream') often with the help of a guide wire.

Four veins are commonly catheterized for percutaneous central venous access they are Subclavian, internal jugular, femoral, basilica veins [4]. The tip of most central catheters should lie in the central veins near the heart. The anatomy of these vessels is both variable and invisible to the naked eye. Therefore, a sound knowledge of the normal anatomy and common variants is an important aspect of competence for the clinician involved in the placement of such catheters. Though peripherally inserted central lines (through antecubital vein) can be done with fewer complications [7], it may not be possible in patients with severe dehydration or edema over limbs, which are commonly encountered in emergency and intensive units. The most frequently used anatomical sites for CVC insertion are the Internal Jugular and the Subclavian vein. This study is designed to compare the different mechanical complications arising during the insertion of CVC through Internal Jugular Vein and Subclavian Vein commonly used routes for central venous catherisation.

Aims and Objectives

To compare the ease of insertion between IJV and SCV catheterisation. To compare the frequency of mechanical complications between the two routes (Internal Jugular Vein and Subclavian Vein) of insertion like- Arterial puncture, Pneumothorax, Hemothorax/Hydrothorax, Subcutaneous hematoma, Misplacement of catheter.

Material and Methods

This study was conducted in Trauma care unit, Tertiary care Hospital after getting approval from Ethical Committee. Written informed consent was taken from all the patients in this study. 100 patients admitted to The Trauma Care Unit of our institution requiring Central Venous Catheterization (CVC) and fulfilling the inclusion criteria were included in the study.

Type of Study

A prospective randomized Double blinded interventional type of Hospital based controlled study.

Methods of Study

After ethical committee approval and informed consent, a clinical study has been carried out on 100 patients of either sex, aged 18 to 80 years, requiring Central Venous access. Hundred patients were randomly allotted in two groups containing fifty patients in each group.

Group A: Patients in group A had CVC via Internal Jugular Vein (IJV).

Group B: Patients in Group B had CVC via Subclavian Vein (SCV) The patients were monitored closely for any complications arising from the procedure.

Inclusion Criteria

1. Age 18 to 80 years
2. Either sex
3. Patients requiring Central Venous Access for any purpose.

Exclusion Criteria

1. Refusal of consent
2. Coagulation abnormalities
3. Infection at local site of insertion

Insertion in Internal jugular vein – Landmark Technique [8]

After applying monitors like electrocardiogram, pulse oxymetry, patient positioned with 10 degree head down (trendeleneburge position) to help distend the vein and reduce the risk of air embolism. The surface marking of the IJV was identified by placing the thumb on the mastoid process and the middle finger on the head of the clavicle. The index finger then falls on a point one-third of the way along this line, which is the approximate point of entry for the needle. The carotid artery was palpated with the non-dominant hand, adjusting the point of skin entry to be just lateral to the arterial pulse. The cannulation needle was angled downwards at about 30–40%. The needle was directed outwards towards the ipsilateral nipple, avoiding pointing it in a medial direction. Gentle suction was applied to the needle as it was slowly advanced. Recognition that a needle is in the vein was made by observing the dark colour of venous blood and non-pulsatile nature of the filling of the syringe. Guide wire passed through the vein then a dilator passed over guide wire for dilatation of the track, then catheter

was threaded over the guide wire. Once the CVC was inserted, it was sutured into place and covered with a sterile dressing. Catheter position was preliminarily confirmed by return of blood and free flow of fluid through all ports. All patients were observed for mechanical complications. The patients suspected clinically of having pneumothorax, hemothorax or misplacement of catheter tip were confirmed by bedside radiographs after procedure. All complications were managed as clinically indicated.

Insertion in Subclavian Vein (infraclavicular route) – Landmark Technique [9]

The patient was positioned supine and slightly head down. This distends the vein and reduces the risk of air embolus. A finger was inserted in the Subclavian groove and pressed medially until resistance was felt. This corresponds to the subclavius muscle. The needle was inserted below the clavicle at this point, which would be at the junction of the medial and middle thirds of the clavicle. The needle was passed towards the sternoclavicular joint and suprasternal notch. Aspiration with the syringe during passage of the needle ensured that puncture of the vein was recognized. As the vein could be transfixed with the needle, aspiration was continued on withdrawal of the needle. A wire was passed through the needle and thereafter a standard Seldinger technique was used.

The number of percutaneous punctures (needle traversing skin) was recorded. Catheterization by single percutaneous punctures by 1 operator at 1 site was considered as Easy insertion. Catheterization by multiple percutaneous punctures by 1 operator at 1 site was recorded as difficult insertion. If the puncture by one operator at one site was unsuccessful, then the site should change or the operator should cease, in which case the attempt was recorded as a Failure. A pulsatile bright red coloured blood flow through the needle was used as an indicator for arterial puncture. Other complications like pneumothorax, hemothorax, hydrothorax, subcutaneous hematoma and misplacement of catheters were diagnosed clinically and by radiographs.

Results

The age, sex in the two groups were found to be comparable. Ijv catheterisation was significantly easier than scv (P value <0.05) and the mechanical complication like pneumothorax and misplacement of catheter was less in Ijv (P value <0.05) compared to scv although arterial puncture, subcutaneous hematoma more in scv (P value <0.05) than Ijv.

Table 1: Demographic profile

	Group A (IJV); n=50	Group B (SCV); n=50	P value
Age in yrs	45.0 (mean) 16.7 (SD)	45.6(mean) 17.8(SD)	0.17
Gender	24:26	26:24	0.4

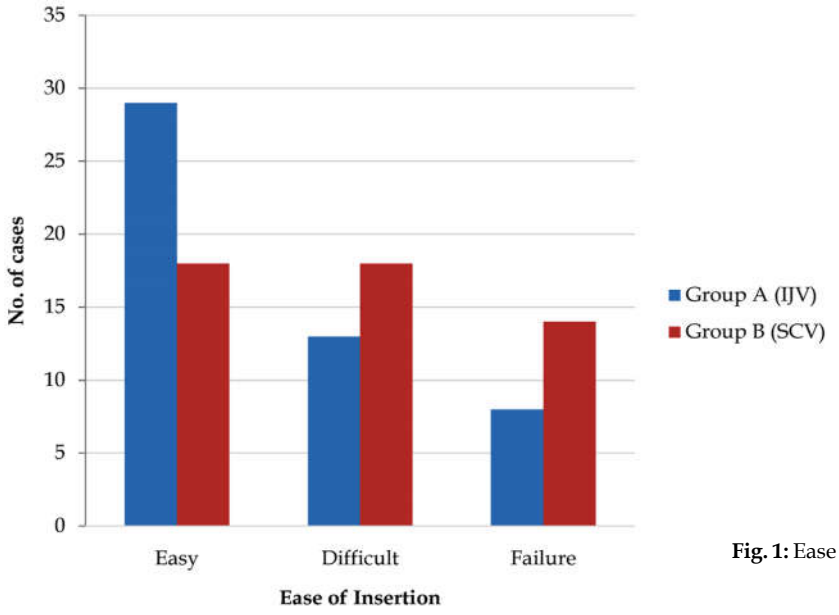

Fig. 1: Ease of Insertion

Table 2: Comparison of ease of insertion

Ease of Insertion	Group A (IJV); n=50	Group B (SCV); n=50	p value
Easy	29 (58%)	18 (36%)	0.02
Difficult	13 (26%)	18 (36%)	0.28
Failure	08 (16%)	14 (28%)	0.15
Total	50	50	

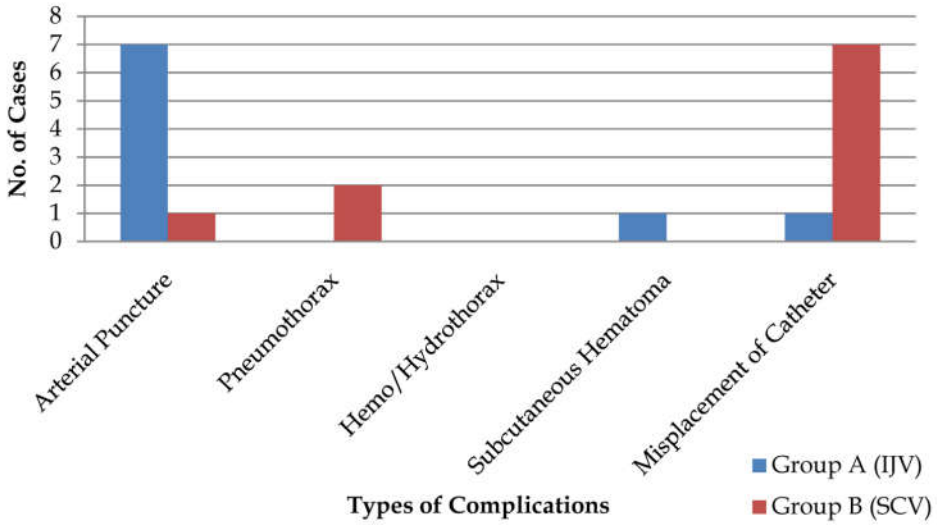

Table 3: Comparison of mechanical complications

Types of Complications	Group A (IJV); n=50	Group B (SCV); n=50	P value
Arterial Puncture	7 (14%)	1 (2%)	0.04
Pneumothorax	0	2 (4%)	0.15
Hemo/Hydrothorax	0	0	Na
Subcutaneous Hematoma	1 (2%)	0	0.69
Misplacement of Catheter	1 (2%)	7 (14%)	0.04
Total	9 (18%)	10 (20%)	0.8

Discussion

In many institution, the anatomical site of CVC insertion is chosen on the grounds of personal experience or local policies rather than on evidence-based guidelines. The aim of this study is to clarify some of the controversies that exist on the relative risk of internal jugular compared with Subclavian access [8,9]. If there is an evidence for an increased risk of specific complications with one approach, then clinicians may take advantage of that knowledge for insertion of a CVC in an individual patient.

The study design was random, 100 patients were randomly allotted in two groups containing 50 patients in each group. Procedures performed by experienced operators.

Group A: Contained patients who had CVC via Internal Jugular Vein.

Group B: Contained patients who had CVC via Subclavian Vein.

All patients underwent thorough pre-procedure assessment including detailed history, clinical examination and necessary investigations in both emergency and routine patients . All catheters were inserted after visualization of landmarks by Seldinger technique. The demographic data, number of percutaneous punctures (needle traversing skin) and the complications were recorded. In our study, success rate of single percutaneous puncture is significantly greater through Internal Jugular Vein (58%) than through Subclavian Vein (36%), with a P value of 0.02. Lewis A. Eisen et al [5] had also found that the internal jugular approach was more likely to require 1 skin puncture, but their difference was not found to be statistically significant ($p = 0.38$). Success rate of two or more percutaneous punctures is more in SCV (36%) as compared to IJV (26%); showing more 'Difficult' insertion in SCV.

Eisen et al [5] had found that more than two attempts are often required in SCV route as compared to IJV, but they had also included failures in this group. Overall rate of failure of catheter placement in our study has been found to be 22%, which is comparable to what Lewis A. Eisen et al [5] had found (22.3%). The failure of catheter placement is found to be 16% through IJV as compared to 28% through SCV. Eisen et al [5]. had found failure rate of 26.1% in SCV route and 25% in IJV route. It is quite evident from the above results that the Subclavian route has more number of failures than Internal Jugular route.

One of the most frequently reported complications of CVC insertion is arterial puncture. Based on the observations of this study, the rate of arterial puncture when internal jugular vein was chosen is 14% and when Subclavian approach was chosen is 2%. This result is statistically significant with a p value 0.03. This result is comparable to the results of Eisen et al [5] with 5% arterial puncture in IJV catheterization and 3.2% arterial puncture through SCV route. Sibylle Ruesch et al [6] had also found similar result i.e. significantly more arterial punctures with jugular catheters compared with Subclavian (3.0% vs. 0.5%, RR 4.70 [95%CI, 2.05–10.77]).

This apparently significant increased risk of arterial puncture with the jugular access, could be due to an under-reporting of arterial punctures with the Subclavian approach; as puncture of a carotid artery is usually easier to detect than puncture of a Subclavian artery. Although the puncture of a carotid artery seems to happen more often, effective haemostasis is much easier (manual compression). It is unlikely that clinicians will abandon the internal jugular access based on these risk data. Only 2 cases of Pneumothorax have occurred through SCV route and none through internal jugular route. This result is not statistically significant (p=0.15).

Eisen et al [5] had also found 5 cases of pneumothorax in SCV and none in IJV, but the difference was not significant. No cases of Hemothorax or hydrothorax have occurred in either groups. So, no difference between Subclavian route and Internal Jugular route could be elicited with respect to these complications.

These results are comparable to the study of Sibylle Ruesch et al [6] and Eisen et al [5]. It may be somewhat unexpected because many clinicians believe that the Subclavian access is more prone to these complications. Thus, the conclusion must be that, in experienced hands, both accesses have the same low risk of hemothorax, hydrothorax and pneumothorax. Only 1 case of Subcutaneous Hematoma has occurred in Internal Jugular Vein catheterization and none in Subclavian Vein catheterization. This difference is not significant. Eisen et al [5] also found such a low incidence of subcutaneous hematoma (0.5%). In their study, a single case was found through Subclavian route only. Internal Jugular vein lies quite superficial to Subclavian vein. This might explain the fact that subcutaneous hematoma can be easily diagnosed in neck. Moreover such low incidence in both the studies make no significant comparison between the two routes. The data on catheter malpositioning may have more impact on clinical decision making. Malpositioning has been observed in 8% of CVCs, happening significantly less often with the internal jugular access as compared to Subclavian access [2% v/s 14%; P = 0.04]. Eisen et al [5] had also found less catheter malpositioning in insertions though internal jugular vein as compared to Subclavian vein. [0% v/s 6.4%; p=0.004] Also, malposition of a Subclavian catheter may include entry into the opposite Subclavian vein or the neck veins, whereas many jugular catheters may simply be pulled back if the tip lies in the right atrium. This is yet another argument in favour of the jugular approach. The jugular access should be chosen if a fast and correct catheter tip placement is mandatory (e.g., hemodynamic monitoring in a patient in shock). Malpositioning of a CVC per se, independent of the access may lead to serious complications. The positioning of catheter tips within the cardiac silhouette is associated with an increased risk of cardiac tamponade. It can be seen that the choice of approach can be a complicated process. Other factors like infectious and thrombotic complications, convenience of access, patient factors, the indication for the device, the experience of the operator plus the competence of the operator at each site; also needs to be considered which are beyond the scope of this study. The choice of access site should be individualised for each patient dependent on their characteristics. The aim is to achieve satisfactory function whilst minimising the risks which vary between both patients and approaches.

Conclusion

According to the observations and analysis of this study, catheterisation in Internal Jugular Vein is significantly much easier than SCV and has significantly lower risk of catheter misplacement.

Pneumothorax is also less common in IJV catheterisation. However, even though the risk of arterial puncture is significantly more in IJV route than in SCV route, effective haemostasis is much easier (manual compression) in carotid artery which is more superficial than Subclavian artery. As far as mechanical complications and ease of access are considered, Internal Jugular Vein catheterisation is better than Subclavian catheterisation. More studies with larger sample sizes are needed to determine methods to decrease complications rates further.

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Original Research Article

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Study on Epidural Analgesia during Labour to Control Labour Pain

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Abstract

The severity of labour pain was recognized by the Romans, who termed delivery the *poenamagna – the* "great pain" or "great punishment." Pregnancy, though is one of the most pleasant part of a woman's life is marred by the anxious awaiting of a painful labour. Although labour is painless in a few women, the vast majority considers it painful, and a clear majority rates it as severe pain. Melzack, one of the authors of the gate control theory of pain, developed a questionnaire to assess the intensity and emotional impact of pain. Using this tool, he observed that labour pain was rated as more painful than cancer pain and that, among nulliparous women with no prepared childbirth training; it was nearly as painful as amputation of a digit without anaesthesia.Traditionally a number of techniques have been employed to provide labour analgesia. But Epidural analgesia is considered to be the gold standard in labour analgesia.

Keywords: Poenamagna; Labour Pain; Epidural Analgesia.

Introduction

Among the current methods of obstetric analgesia, regional analgesia (the most widespread technique being epidural analgesia) offers the best effectiveness/safety ratio. Epidural anaesthesia is an effective means of providing analgesia during labour. The increased availability of epidural analgesia and the favourable experiences of women who have had painless labour with epidural block have reshaped the expectations of pregnant women entering labour. Compared with other forms of pain relief, epidural analgesia is associated with the highest level of maternal satisfaction.

Historical Review

Ancient Methods

Folklore, superstition, opposition from the church as well as members of the medical profession have all played a part in delaying the development of various techniques of pain relief. There is evidence that women have always sought relief from pain of childbirth by adopting various means and methods. These methods were mostly physical, psychological or pharmacological.

In Pago Pago, the strong men in the tribe were employed to assist the birth by pressing their heels into lower ribs of labouring parturients during the contractions.

Aburel and Cleland's discovery that uterine pathways entered the cord at 10^{th} and 11^{th} thoracic segments may have provided a pseudoscientific basis for this practice. Ancient Chinese employed opioids and soporific sponges for the relief of labour pains. Helen of Troy prepared herbal remedies that banished sorrow from the memory.

Hippocrates, the Father of Medicine, remarked "Divinumest opus sedaredolorem" (divine is the work to subdue pain). The new era of analgesia and

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anaesthesia was initiated in 1772 with Joseph Priestley's discovery of nitrous oxide.

Inhalational Methods

James Young Simpson was the first to use Ether to aid delivery of a dead foetus after internal podalic version on 19th January, 1847. He also used Chloroform for childbirth on 8th November, 1847. Nathan Colley Keep used Ether successfully for labour analgesia in April 1947. In February 1848 Gardner of New York used chloroform in obstetrics. On 7th April 1853, the successful administration of chloroform analgesia to Queen Victoria by John Snow for the birth of her eighth child, Prince Leopold is the most important milestone in the history of obstetric anaesthesia. In 1880 Stanislav Klikovich was the first to use a mixture of 80% nitrous oxide and 20% oxygen to provide analgesia for labour. In 1911 AE Guedel devised the first machine for self-administration of nitrous oxide and air in labour. Trichloroethylene was used in obstetrics for the first time in 1943 through Freedman's inhaler. This method was unreliable as some mothers received an apparent overdose. In 1933 Minnitt of Liverpool, designed a machine for the self-administration of N_2O and air in labour. In 1936 Wasley Bourne first used Divinyl Ether in obstetrics. In 1958 – Lucy Baldwin modified Walton's dental anaesthetic machine to allow the women self-administer varying concentrations of nitrous oxide. In 1961, Tunstall used a mixture of 50% nitrous oxide and 50% oxygen in one cylinder. In 1848 – Heeffelder first used Ethyl chloride. In 1953 – Virginia Apgar published description of a method to establish a simple, clear classification of newborn infants which can be used as a basis for comparison of the results of obstetric practices and types of maternal pain relief. Heaney first used Ethylene in obstetric practice and published a review article. In 1960 Artusio introduced Methoxyflurane which was widely used for obstetric analgesia. Concern about the depressant effects of all volatile agents on the foetus and gradual development of better techniques of pain relief in labour led to a decline in their use.

Parenteral Techniques

Parallel to the evolution of inhalational methods of pain relief in childbirth was the development of parenteral techniques. Parenteral techniques were pioneered by Alexander wood. 1860: Kormann administered Morphine to control the pain of labour by hypodermic needle. 1869: Oscar Liebreich used chloral hydrate. 1870: Guilbert used a combination of chloroform and morphine in obstetric practice. 1902: Von-Steinbuchel used a combination of morphine and scopolamine in labour to produce 'twilight sleep'. This method eventually fell into disrepute because of the high incidence of asphyxia neonatorum. 1923: Cleisz used barbiturates for labour. 1940: Benthen first used Meperidine in labour. 1954: Hershenson used chlorpromazine for labour analgesia because of its hypnotic effects. 1966: Filler and Filler used pentazocine to produce analgesia of rapid onset and short duration.

Rectal Preparations

1874: Pirogoff in Russia and Dupuy in France instilled Ether rectally. 1913: Gwathmey introduced Ether into the alimentary tract to produce analgesia. 1933: Gwathmey analgesia consisting of a combination of morphine and magnesium sulphate injected hypodermically and colonic Ether in a mixture of olive oil, alcohol and quinine was used.

Local Anaesthetic Techniques

1853: Alexander Wood refined a syringe for injections and began administration of drugs into the area of nerve trunks. He is referred to as the' Father- in-law' of nerve blocks. 1891: Qunicke described paramedian approach for performing lumbar dural puncture. 1899: August Bier used cocaine for spinal anaesthesia and was the first to describe post-dural puncture headache. 1901 The first caesarean delivery in UK using cocaine spinal anaesthesia was performed at Manchester Maternity Hospital. 1903: Braun used epinephrine in place of elastic bandages to decrease the rate of local anaesthetic absorption. 1937: Cosgrove and colleagues summarized the experiences of the use of spinal anaesthesia in labour. 1945: Tuohy modified Lemmon's technique using a ureteral catheter introduced into the subarachnoid space via a needle with a Huberpoint. 1908: Pudendal nerve block was first described by Muller via transperineal and trans- vaginal routes. 1926: Gellert described the paracervical nerve block for effective pain relief.

Epidural Technique

1901: Cathelin introduced caudal analgesia by injecting cocaine through caudal canal via sacral hiatus. 1909: Von Stoeckel used procaine in the caudal analgesia by injecting cocaine through sacral hiatus. 1930: Aburel traced the afferent pain fibres carrying the pain impulse from the uterus and

demonstrated that by blocking this plexus pain of early labour was relieved. 1931: Dogliotti, "Father of Obstetric Analgesia" rediscovered lumbar epidural loss of resistance technique. 1943: Greenhill used hyperbaric solutions with smaller doses for continuous spinal anaesthesia. 1949: Tosten Gordhindroduced lignocaine. 1957: Ekenstam synthesised Bupivacaine. The popularity of epidural anaesthesia was enhanced by headlines in the press proclaiming 'painless childbirth at last' after the Fourth World Congress of Anaesthesiogists in London in1968. Next was the concept of use of local anaesthetic and opioids either alone or in combination. Recent advance in the labour analgesia is the introduction of walking epidurals by using low concentrations of local anaesthetic making the parturient ambulant.

Review of Anatomy

Epidural space is the potential space between the spinal duramater and the periosteum and ligaments lining the vertebral canal. The duramater is made of two layers the endosteal and the meningeal layer. The two layers are closely fused within the cranium. Below the foramen magnum, these two layers are separate. The outer layer forms the periosteum lining the spinal canal. The inner layer forms the spinal duramater. Between these two layers is the epidural or the periduralspace. The epidural space is widest in the midline posteriorly with an average of 5mm between ligamentum flavum and the posterior surface of the spinal dura. The depth is slightly more, proximal to the inferior border of the lamina due to the obliquity of the vertebral lamina. Thus the epidural space is composed of a series of discontinuous compartments that become continuous when the potential space separating the compartments is opened up by injection of air or liquid. According to a study dorsomedian fibrous tissue connects the duramater and the ligamentum flavum in the lumbar region fairly frequently. Due to these fibrous strands, the injected fluid distends the space laterally rather than in the midline.This has been confirmed anatomically through epiduroscopy and epidurography. These fibrous strands are responsible for occasionally unilateral anaesthesia following apparently adequate epidural technique.

Table 1: Characteristics of Ligamentumflavum at Different Vertebral Levels

Site	Skin to Ligament (cm)	Thickness of Ligament(mm)
Cervical	-	1.5-3
Thoracic	-	3-5
Lumbar	3-8	5-6
Caudal	Variable	2-6

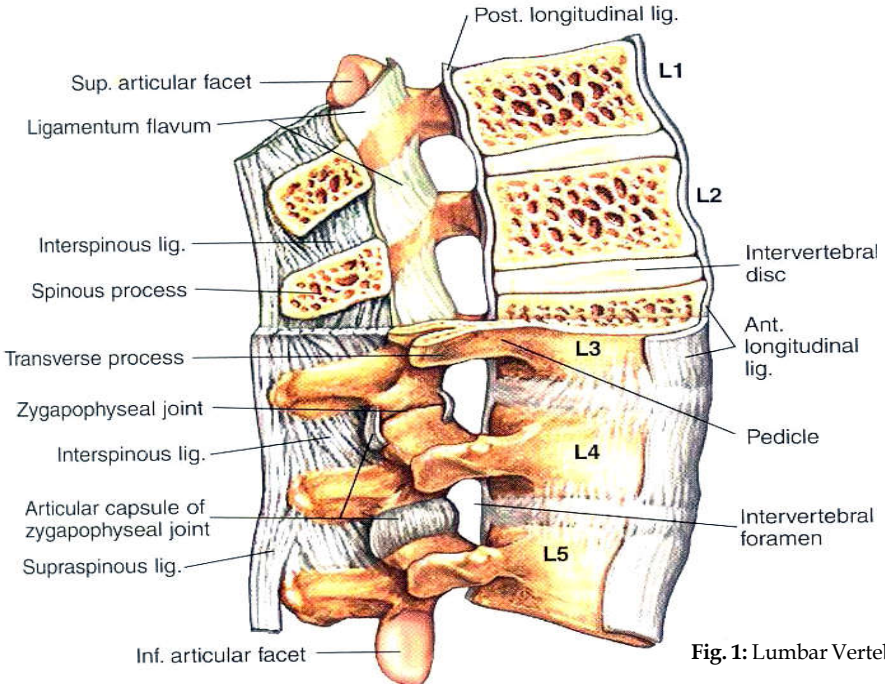

Fig. 1: Lumbar Vertebral Liagments

The epidural space is entered most safely and easily in the mid lumbar region.

The lumbar spine and the interspinous ligaments are widest in the mid-lumbar region making an easy land mark for insertion of the epidural needle.

Lateral View of Lumbar Vertebral Ligaments

Contents of Epidural Space

1. Fat: It is the ubiquitous material in the space and is highly vascular. The fat competes with the nervous tissue of the spinal roots, cord and blood vessels within the spinal cord for the drug. Drugs with high lipid solubility and lipoprotein binding characteristics tend to enter the fat phase and remain there for a period of time, depending on their pharmacodynamics and briskness of local blood flow competing for uptake.
2. Spinal arteries: The arteries that traverse the space arise from the vertebral, ascending cervical, deep cervical, intercostals, lumbar and ileo-lumbar arteries. They anastamose with those above and below and across the midline and lie mainly in the lateral parts of the epidural space.
3. Epidural veins: the venous plexus of the vertebral canal which drain the adjacent structures and the spinal cord lie in the anterolateral parts of the epidural space.

They form a network, which runs vertically within the epidural space. It can be subdivided into a pair of anterior venous plexus which lie on either side of the posterior longitudinal ligament into which basivertebral veins empty and a posterior venous plexus.

These are valveless (Batson's plexus) and afford a connection between the pelvic veins below with the intracranial veins above. These veins become distended during coughing and straining and also when the inferior venacava is obstructed by large abdominal tumours or in late pregnancy. When these epidural veins engorge, the epidural space is markedly reduced.

Aspiration tests may not always indicate intravenous position of a needle or catheter and subsequent injections of air or local anaesthetic will be carried directly to the heart. The appropriate dose of the drug should preclude this problem.

4. *Lymphatics*: The lymphatics run anteriorly from each intervertebral foramen. They drain the dural cul-de-sacs of the dural root sleeves and empty in the longitudinal channels in front of the vertebral column.

Connections between Epidural Space and Paraspinal Tissue Space.

The epidural space is not a closed space. Many of the tissue planes around the spinal canal connect to form an extended system of tracks.

There are 58 foramina in all. The areolar tissue around these foramina varies in density according to age. As age advances the soft and tenuous tissue undergoes increasing condensation to form a definitely recognizable structure. The fibrous tissue thickens and blocks the intervertebral foramina with aging.

This confines the solutions injected into the epidural space within the spinal canal and they escape less rapidly along the neurovascular bundles into the paravertebral spaces. Thus dosage should be reduced. The spread is greater in pregnant females.

Physiological Aspects of Epidural Space

Haldt and Moloney were the first to describe negative pressure in the epidural space in 1928. This negative pressure is maximum at points of firm attachments. It is maximum in the thoracic region, less in the lumbar region and least or absent in the sacral region.

Lower lumbar _ 0.5 cm H_2O

Upper lumbar _ 1.0 cm H_2O

Thoracic _ 1.0 to _ 3.0 cm H_2O

(Average_ 2.0 cm of H_2O)

Three theories have been put forth to explain the negative pressure.

1. The Cone Theory: Jonzen, 1926, Eaton in 1938 and Lawrence in 1948 put forward this theory. According to this theory, the needle introduced into the epidural space depresses the dura, creating a larger space. This theory was reviewed in the studies conducted by Aitkenhead in 1979 in experiments on dogs.
2. Transmission Theory: According to Macintosh and Bryce-Smith the negative pressure in the epidural space is caused by the transmission of the intrapleural negative pressure through intervertebral foramina to the epidural space. It varies with the depth of respiration. i.e., clinically this negative pressure will be diminished or absent if the patient is not relaxed or straining. Marked flexion at the spinal column increases the negative pressure. A rise in negative pressure may favour the spread of local anaesthetic solution in the epidural space.

3. *Flexion Theory:* This theory states that the negative pressure is directly proportional to the flexion of the spine.

Physiology of Pain in Labour

Pain is transmitted from the periphery by small 'A' delta and C fibres, the cell bodies of which lie in the dorsal root ganglia. From the dorsal horn central projections enter the grey matter. Except for a few A delta fibres that terminate in the marginal layer (Lamina I) the remainder synapse in the substantia gelatinosa (Lamina II), communicating by a series of interneurons with cells whose bodies reside in lamina V. These wide dynamic range neurons respond to both high intensity stimuli provoked by pain and also to low intensity light touch. Increased activity in these neurons results in impulse transmission in the anterolateral ascending columns.

Substance-P together with other peptides acts as neurotransmitter in the pain pathway. It is found in the cell bodies of dorsal root ganglia and released in the substantiagelatinosa in response to painful stimuli. The activity of a series of interneurons in the Lamina II inhibits substance-P release. These interneurons are activated by collaterals from the large sensory fibres and also by descending inhibitory fibres in the dorsolateral funiculus.

Stimulation of inhibitory neurons or opioid receptors in the substantiagelatinosa acts principally by reducing cyclic AMP levels in the opioid sensitive cells, resulting in presynaptic inhibition of release of substance-P and also by postsynaptic hyperpolarization of the dorsal horn neurons. Thus the increase in activity in Lamina V neurons and in the anterolateral ascending columns is prevented. Opioids are more effective in blocking activity produced by C than A delta fibres.

Labour – Anatomical and Physiological Aspects:

Labour is divided into 3 stages

The first stage: Begins with the onset of regular painful uterine contractions and ends at full dilatation of the cervix. Average duration in the primigravida is 8-10 hours and in multigravida 6-8 hours.The first stage of labour is divided into latent phase when the cervix slowly dilates upto 3 cm and an active phase when the cervix dilates from 3 cm to 10 cm.

The active phase is further divided into early active phase when the dilatation is upto 7 cm and the late active phase to full dilatation. During the active phase, the cervix dilates at the rate of about 1 cm per hour. The second stage: Extends from full dilatation of the cervix to the birth of the foetus and varies from a few minutes to about 2 hours. It is divided into the perineal stage and the expulsive stage.

The third stage: Is the period after the birth of the foetus to the expulsion of the placenta and membranes. The average duration is about 5 minutes

Prelabour: Prelabour is defined as the development phase of preparation for parturition. It occurs several weeks before the onset of true labour. The cervix begins to soften and dilate. Progesterone, oxytocin, prostaglandins (PGE2 and PGF2a), cortisol, prostacyclin, interleukin 8 and monocyte chemotactic peptide interact with each other producing the prelobour softening of the cervix.

The mother, the foetus and the placenta all contribute to the maintenance of pregnancy, the initiation of labour and finally the birth of the foetus. The key component in the initiation of labour is the foetal brain which influences the foetoplacental unit via the hypothalamopituitary –adrenoplacental axis.

The increase in the oestradiol levels at term causes a shift in the oestrogen to progesterone ratio in favour of estrogen, which leads to increase in the oxytocin sensitive receptors in the myometrium and decidua and activates amnion to produce prostaglandin. PGF2a is responsible for myometrial contractility. PGE2 is essential for cervical ripening. The main sources of these are the decidua for PGF2aand amnion for PGE2.

Uterine changes: The uterus is composed of smooth muscle (myometrium). During the transition from pregnancy to labour, the myometrial oxytocin sensitive receptors increase. There is increased frequency and amplitude of contraction of the myometrium and also increase in the concentration of myometrial gap junctions between these smooth muscle cells thereby facilitating synchronization.

Cervical changes: The cervix is mainly made of connective tissue collagen. Gradual softening of the cervix occurs 4 weeks prior to onset of labour (prelabour). This involves degradation of stromal collagen by changes in its proteoglycan complexes and increase in the water content of the ground substance leading to reduced tensile strength which eventually results in effacement and dilatation.

Foetal membranes: The decidua and the amnion are the main sources of arachidonic acid, the main precursor of prostaglandin. The decidua also produces prostaglandin synthetase enzyme.

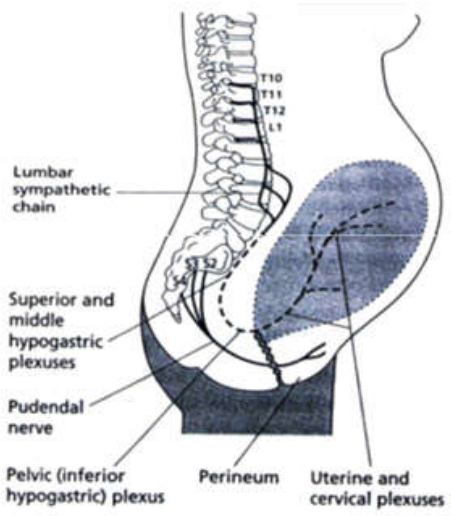

Fig. 2: Sensory Pathways

The Sensory Pathways Involved in Parturition

Beneficial Effects of Epidural Analgesia:

1. When analgesia is provided by opioids, the hyperventilation is decreased somewhat but the depressant effect of the opioid may still cause hypoventilation and hypoxia.1 Complete pain relief obtained with epidural analgesia prevents the transient period of hyperventilation during a contraction and thus prevents hypoventilation during uterine relaxation, so that the $PaCO_2$ remains in the range of 28-32 mm Hg and PaO_2 increases to 100 mm Hg.
2. Epidural analgesia, by blocking the nociceptive inputs and sympathetic efferents, reduces the release of catecholamines and cortisol. This reduces the work of the myocardium.
3. Epidural analgesia eliminates that portion of the increase in cardiac output and blood pressure which is caused by pain. It is thus beneficial to parturients, provided of course that maternal hypotension is avoided.
4. The relief of pain and anxiety with a continuous lumbar epidural analgesia decreases the total work of labour, maternal metabolism and oxygen consumption. Hence, it significantly reduces the maternal and foetal acidosis. In this aspect, epidural analgesia is far superior to the analgesia provided by systemic opioids.
5. Epidural analgesia blocks the reflex inhibition of gastric motility. Unlike opioids, it does not delay the gastric emptying. Thus it has a salutary effect on the gastrointestinal function as a whole.
6. Properly administered epidural analgesia will relieve most of the pain and thus obviate many of the psychological and emotional reactions to severe pain mentioned previously.
7. Effective analgesia, by reducing the sympathetic overactivity, can reduce or eliminate uterine hyperactivity or hypoactivity and can change incoordinate uterine contractions into a normal labour pattern. It also improves any placental hypoperfusion and any existing deterioration of uterine blood flow.
8. It has been shown that epidural analgesia, by its vasomotor blocking effect, increases intervillous blood flow in parturients. This is of value to all foetuses,but is particularly important to foetuses at risk such as those born to mothers with pregnancy-induced hypertension, heart disease and diabetes.

Maternal hypotension must be strictly avoided by appropriate prophylactic measures (e.g. intravenous infusion of fluids, leftward displacement of the uterus) to achieve these benefits.

Methods of Pain Relief in Labour

A variety of labour analgesia options are available, including psychoprophylaxis, transcutaneous electrical nerve stimulation (TENS), systemic medication, inhalational techniques and neuraxial blocks. In addition, other regional techniques such as caudal and paracervical blocks are used infrequently.

Psychoprophylaxis

"Natural childbirth" was a phrase coined by Grantley Dick-Read in 1933 who believed that childbirth was a painless procedure and did not need medical intervention. Fernand Lamaze popularised natural childbirth as an option for parturients. Other methods include hypnosis (which is effective in a small proportion of parturients but is not universally useful) and acupuncture (which does not seem to be of any use in labour).

Transcutaneous Electrical Nerve Stimulation

This is thought to reduce pain by nociceptive inhibition at a presynaptic leveling the dorsal horn by limiting central transmission. TENS is also thought to enhance the release of endorphins and dynorphins centrally. However, reports have failed to demonstrate its effectiveness in labour analgesia.

Systemic Medication

Opioids are the most commonly used class of drugs but they have various side effects like respiratory depression, nausea and vomiting and excessive sedation.

They cross the placenta freely and may cause respiratory depression in the newborn. The commonly used opioids include pethidine, fentanyl, butorphanol and remifentanil. Other systemic medications used in the treatment of labour pain include sedative-tranquilisers and ketamine.

Inhalational Analgesia

Inhalational analgesia involves the administration of sub anaesthetic concentrations of inhaled anaesthetics to relieve pain during labour. It provides a limited amount of pain relief. Entonox (50:50 N_2O/O_2 mixture) has been used for many years as both a sole analgesic and as an adjuvant to systemic and regional techniques of labour. Desflurane (0.2%), enfurane and isoflurane (0.2-0.25%) have also been used successfully.

Regional Analgesia Techniques

A variety of regional techniques are used in labour analgesia to provide optimal analgesia with minimal depressant effects.

Epidural Analgesia

Lumbar epidural analgesia offers a safe and effective method of pain relief in labour. Low doses of local anaesthetics and opioid combinations are administered to provide a T10-L1 sensory block. The benefits of epidural analgesia include effective pain relief without appreciable motor block and a reduction in maternal catecholamines.

Spinal Analgesia

A single shot subarachnoid injection of local anaesthetic or opioid provides effective and rapid onset of labour analgesia.

Combined Spinal-epidural Analgesia

The combined spinal-epidural (CSE) technique is widely used in obstetric practice and it offers effective, rapid-onset analgesia with minimum risk of toxicity or motor block. In addition, it provides the ability to prolong the duration of analgesia as required.

Conclusion

Epidural analgesia is used principally for pain relief during labour. It is estimated that some 20% of all parturients now receive epidural analgesia for pain relief in labour. Safe and effective relief of pain during labour and delivery accomplished by the skillful use of epidural analgesia prevents the stress response in the mother. Obstetricians and anaesthetists have always feared that incidence of instrumental deliveries in women receiving epidural analgesia could be higher than in those who do not receive it. Ideally pain relief with epidural techniques should be produced with the minimum disturbance to the progress of labour or to sympathetic functions, sensory functions (proprioception) and motor functions of the CNS. Thus it is intriguing to the obstetric anaesthetist to strike a balance between patient satisfaction by providing good analgesia, reduce motor block thus making the parturient participate in labour and decrease the instrumental deliveries due to prolonged second stage.

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Review Article

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Comparative Analysis of Bupivacaine and Ropivacaine during Epidural Analgesia

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Abstract

IASP defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of the actual damage." This definition embraces various concepts especially the subjectivity of the symptoms which is the basis of the non-pharmacologicaloptions in the treatment of labour pain. We conducted this study to compare the efficacy of the equipotent 0.125% Bupivacaine and 0.2% Ropivacaine in labour.

Keywords: Bupivacaine; Ropivacaine.

Introduction

Bupivacaine has been the widely used local anaesthetic drug for Labour epidural analgesia but Albright in 1979 published an alarming editorial which associated bupivacaine with cardiac arrest. The search for a long acting local anaesthetic devoid of cardio toxicity led to the synthesis of Ropivacaine a new amino amide local anaesthetic which has been shown to cause less intense motor blockade and less cardiotoxic and is rapidly evolving as local anaesthetic of choice in labour Analgesia.

Review of Literature

Evron S, Glezerman et al studied a prospective Randomised double blind study comparing low doses of Bupivacaine & Ropivacaine concluded that Ropivacaine 0.2% was equialgesic with 0.125% Bupivacaine & produced less motor block (P<0.001) without any difference in duration of labour, deliver type or neonatal outcome.Fernandez C Et al study compared the efficiency and extent of motor block with 0.2% Ropivacaine and Bupivacaine 0.125% on 60 women in labour and concluded that both the drugs are equally effective for pain control. Motor block was seen in 8 patients with Bupivacaine and 1with Ropivacaine (P<0.05). Ropivacaine reduced motor block and offers an advantage in situations when walking Epidural is desired.

W.D.R Writer et al showed a prospective meta analysis using 0.25% Bupivacaine & Ropivacaine and concluded that Spontaneous Vaginal delivery occurred more frequently with Ropivacaine than with Bupivacaine (58% vs. 49% P<0.05) & fever infants with NACS (Neurological and Adaptive Capacity Scores) less than 35 in Ropivacaine compared with Bupivacaine group (2.8% vs. 7.6% P<0.05). P.D.W Fettes Et study concluded that the intermittent group required fewer supplementary injections and less drug to maintain similar pain scores, Sensory and motor block compared with continuous group. Hence concluded that intermittent topups remain a more efficacious mode of analgesia.

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Stephen H. Halpem et al study a Meta analytical study in 2074 patients and concluded that there is no statistically significant difference between the two drugs in the incidence of any obstetrical or neonatal outcome.Bee Beng Lee et al Study a prospective Randomised double blind study examining the effectiveness of five different doses of Ropivacaine (10, 20, 30, 40 & 50 mg) in labour analgesia and concluded that in a traditional dose–response study, the ED50 of Ropivacaine required to initiate epidural analgesia in early labour was 18.4 mg (95% confidence Interval 13.4–25.4 mg). J.M Porter Et al study on Epidural Ropivacaine during labour and its protein binding, placental transfer and neonatal outcome. They concluded that there was no significant Correlation between Maternal unbound Ropivacaine concentration and neonatal (cord) Ropivacaine concentration and no association between mean (SD) Umbilical venous Ropivacaine concentration and NACS of the neonates.Nicola S Wallace Retrospective study of 100 random post natal women who had received labour analgesia 98% of those who had received epidural analgesia said they would request this in subsequent labours, compared with 76% of those who had used Entanox only and 66% of those who had received Pethidine.

They conclude that: Most women in labour wants epidural analgesia, Friends are more influential requesting Labour analgesia than prenatal classes, Anaesthesiologist should be flexible in the mode of Labour Analgesia, Maternal satisfaction with Epidural analgesia in labour means that anaesthesiology work load in labour ward will increase. Halpem S H et al this study was conducted to know the effect of labour analgesia on breast feeding success. It was concluded that Epidural labour analgesia with local anaesthetics and opioids does not impede breast feeding success. Beilin Y Anesth Analg the study concluded that, Epidural Bupivacaine is equally as safe as, of equal or less toxicity than and significantly more potent and more economical than Epidural Ropivacaine. They say that newer does not mean better. N. Fratelli et al, The study evaluated the effects of Epidural analgesic with bolus doses on Uterine artery Pulsatality index (UtA-p1) during labour and concluded Epidural Analgesia using Ropivacaine 1mg/ml (20 ml)significantly reduced placental blood flow only transiently during uterine contraction 30 minutes after the injection. These changes did not seem to affect neonatal outcomes. D. Benhamou et al, The study concluded that Ropivacaine 2mg/ml was effective and well tolerated when given as a continuous extradural infusion at 6-8 ml/hr and may be used as the sole analgesic during labour. Linda S. Polley et al, Analgesic potencies of Ropivacaine and bupivacaine for epidural analgesis, The minimum local analgesic concentration of Ropivacaine was 0.111% wt/vol, and the minimum local analgesic concentration of bupivacaine was 0.067% wt/vol. They concluded that Ropivacaine was significantly less potent than bupivacaine, with a potency ratio of 0.6(95% confidence interval, 0.49-0.74), for epidural analgesia in the first stage of labour.

Ropivacaine may be less cardiotoxic than bupivacaine yet bupivacaine induced cardiac arrest is an exceedingly rare event especially in the labouring patient or in clinical settings utilising dilute concentrations used to produce analgesia. The benefits of Ropivacaine are theoretical at best but they are not worth their cost. Michael P. Nageotte et al, study concluded that as compared with lumbar epidural analgesia, the combination of spinal and epidural analgesia is not associated with an overall decrease in the incidence of caesarean delivery. G. Capogna et al. Relative potencies of bupivacaine and Ropivacaine for analgesia in labour, The analgesic potency of Ropivacaine was 0.60 relative to bupivacaine. Claims for reduced toxicity and motor block must be considered with differences in analgesic potency in mind. D. Bruce Scott et al,The acute CNS and CVS effects of Ropivacaine and bupivacaine were compared in 12 human volunteers in a randomised double blind manner with IV infusions at a rate of 10mg/min up to a maximal dose of 150 mg. They concluded that Ropivacaine is a less toxic compound than bupivacaine, but their relative therapeutic ratios must await the results of clinical trials in humans to assess the potency of Ropivacaine compared with that of bupivacaine.

Pharmacology of Bupivacaine

Bupivacaine hydrochloride is a long-acting local anaesthetic of the amide type. It is an amide linked local anaesthetic synthesized by B.A.F Ekenstam in 1957 and introduced into clinical practice by Talivuo in 1963. Bupivacaine HCl which is chemically designated as 2-piperidinecarboxamide, 1-butyl-N-(2,6-dimethylphenyl)-monohydrochloride, monohydrate.

Bupivacaine occurs as a 50:50 racemic mixture of the R- and S-enantiomers and is commercially available as bupivacaine and levobupivacaine, the S-enantiomer of bupivacaine.

Bupivacaine hydrochloride is a local anaesthetic of the amide type with a long duration of action. Bupivacaine hydrochloride differs structurally from

mepivacaine hydrochloride only in the substitution of a butyl group for the Methyl group. Bupivacaine hydrochloride occurs as a white, odourless, crystalline powder and is freely soluble in water and in alcohol. The pKa of bupivacaine hydrochloride is 8.1

Mechanism of Action

The base form is in equilibrium with cationic form outside the axoplasmic membrane. Base form diffuses inside the cell and recalibrates with cationic form. It then reaches the local anaesthetic receptor in the Na channel by reversing channel pore while it is in an open state. It prevents Na ions moving intracellularly. In addition to this simple sodium channel blockade, it also affects second messenger system such as adenylatecyclase and guanylatecyclase and also inhibits synaptic transmission by modification of post synaptic receptor (or) presynaptic calcium channel blockade in epidural / subarachnoid blockade.

Physiochemical Properties

Property Value

- Molecular weight 288
- Potency ratio 15
- Toxicity ratio 10
- pKa (25.C) 8.16

Protein Binding in %

- Maternal 95
- Fetal 66

% Non Ionizedat

- pH 7.4 – 17, pH 7.2 - 11

Partition Co-efficient

- (25.C, pH7.4) 346, Anaesthetic index 3.0-4.0

Pharmacokinetics of Epidural Bupivacaine

The uptake of local anaesthetic into blood vessels in the area where it has been deposited and its subsequent transfer into systemic circulation is referred to as systemic absorption. A biphasic absorption pattern has been found for epidural bupivacaine. The rapid initial absorption following epidural administration is most likely related to high concentration gradient between the drug in the solution and in the blood. In addition profound increases in epidural blood flow observed during epidural administration of bupivacaine may contribute to its fast initial absorption rate. Later on, after the local anaesthetic has been taken up into local tissues such as epidural fat, absorption will become dependent on tissue blood partitioning, resulting in marked slowing of absorption. Estimated total fraction of the dose ultimately absorbed into general circulation is 0.94 with mean absorption time 8.6 hours.Absorption of local anaesthetic is directly related to the amount of drug injected, vascularity, site injected and tissue binding of local anaesthetic at injection site. Bupivacaine will produce lower Cmax than less potent and less lipid soluble agents.Distribution of local anaesthetic has special emphasis in the pregnant patient, because one of the organs that will be exposed to the absorbed drug is fetoplacental unit.

Adverse Effect and Complications

Central Nervous System Toxicity

Potentially toxic blood level can occur when a drug is injected intravenously, intra arterially or a large dose of drug is given into highly vascular area. Risk of CNS toxicity is more because bupivacaine is a highly protein bound drug. Pregnancy is associated with 30% reduction in protein binding. This allows for higher brain level of bupivacaine for a given dose of drug.

Symptoms

Slow speech, jerky movements, tremors, hallucination, and seizure.

Cardiovascular Toxicity

1. Dose dependant depression of contractility
2. Dose dependent depression of conduction and velocity in all conducting tissues.

Progressive Prolongation of Ventricular Conduction

3. Predisposition to re-entry phenomenon followed by sudden onset of ventricular fibrillation.
4. More affinity for cardiolipin

Toxic plasma concentration is 4-5µg/ml

Ropivacaine

Ropivacaine is a new aminoamide local anaesthetic. It is the monohydrate of the hydrochloride salt of 1-propyl-2',6'- pipecoloxylidide

and is prepared as a pure S enantiomer. Pipecoloxylidides were first synthesized in 1957 and have been in clinical use for more than 30 years. Ropivacaine has a propyl group on the piperidine nitrogen atom of the molecule. The pipecoloxylidides are chiral drugs because the molecules possess as asymmetric carbon atom and they may have left - (Sinister) or a right (rectus) handed configuration.

Ropivacaine is produced as the single "S" enantiomer. It has an enantiomeric purity of 99.5% and is prepared by alkylation of `S' enantiomer of dibenzoyl - L – tartaric acid.

The Physiochemical Properties of Ropivacaine are as Follows

1. Molecular weight (base) : 274
2. pKa: 8.1
3. Partition coefficient (N Heptane/ buffer):2.9
4. Mean uptake ratio (rat sciatic nerve): 1.8
5. Protein binding %: 94

The relative lipid solubility of Ropivacaine as measured by partitioning studies between N-heptane buffer and relative mean uptake into rat sciatic nerves, shows Ropivacaine to be intermediate between bupivacaine and lignocaine. Plasma–protein binding is marginally less than that of bupivacaine but the pKa is identical.

Onset: Moderate

Relative Potency: 6

Duration: Long acting

Ropivacaine blocks the generation and the conduction of nerve impulses, presumably by increasing the threshold for electrical excitation in the nerve, by slowing the propagation of the nerve impulse, and by reducing the rate of rise of action potential. The progression of anaesthesia is related to the diameter, myelination and conduction velocity of affected nerve fibres. is reached in regard to unbound concentration.

Metabolism

Ropivacaine is extensively metabolised in the liver, predominantly by aromatic hydroxylation mediated by cytochrome P4501A to 3- hydroxy Ropivacaine. Approximately 37% of the total dose is excreted in the urine as both free and conjugated 3-hydroxy Ropivacaine. Low concentrations of 3-hydroxyRopivacaine have been found in the plasma. Urinary excretion of the 4-hydroxy and both the 3-hydroxy and 4-hydroxy Ndealkylated metabolites accounts for less than 3% of the dose. An additional metabolite, 2-hydroxy methyl Ropivacaine has been identified but not quantified in the urine. Both 3-hydroxy and 4-hydroxy Ropivacaine have a local anaesthetic activity in animal models less than that of Ropivacaine. There is no evidence of in vivo racemization in urine of S (-) Ropivacaine to R (+) Ropivacaine.

Elimination

The kidney is the main excretory organ for most local anaesthetic metabolites. In total, 86% of the Ropivacaine dose is excreted in the urine after intravenous administration of which only 1% relates to unchanged drug. Ropivacaine has a mean total plasma clearance of 387±107 ml/min. The mean ±SD terminal half life is 1.8 ±0.7h after intravascular administration and 4.2±1.0h after epidural administration.

In-Vivo Studies

The effect of local anaesthetics on the electrophysiology of the heart has been defined. The maximal rate of increase in the cardiac action potential (Vmax) is largely dependent on sodium ion influx via the sodium channels. All local anaesthetics are known to depress Vmax in a dose dependent manner. Ropivacaine is intermediate between lignocaine and bupivacaine in decreasing Vmax. Exogenous progesterone has no additional effect on depression of Vmax.

Ropivacaine administered by the intravenous route was found to be less toxic than bupivacaine Mild CNS symptoms and minor cardiovascular toxicity occur at lower dosage and lower plasma concentrations with bupivacaine compared with Ropivacaine. Two human volunteer studies of lumbar extradural block using 0.1%, 0.2%, or 0.3% of Ropivacaine 10ml or 0.25% Bupivacaine 10ml followed by continuous infusion of 10ml/hr of the same drug for 21 hours showed a similar spread of sensory block, reduced intensity of motor block and quick recovery which offers a distinct advantage in the clinical setting during extradural analgesia for labour or post-operative pain.

Adverse Reactions

A major cause of adverse reactions may due to excessive plasma levels which may be due to over dosage, unintentional intravascular injection or slow metabolic degradation. Most adverse events reported were mild and transient.

Central Nervous System Reactions

These are characterized by excitation and/or depression. Restlessness, anxiety, dizziness, tinnitus, blurred vision or tremors may occur, possibly proceeding to convulsions. However, excitement may be transient or absent with depression being the first manifestation. This may quickly be followed by drowsiness, unconsciousness and respiratory arrest. Other effects may be nausea, vomiting, chills and constriction of pupils.

Cardiovascular System Reactions

High doses of accidental intravascular injection may lead to high plasma levels and related depression of myocardium, decreased cardiac output, heart block, and hypertension, bradycardia ventricular arrhythmias including ventricular tachycardia and ventricular fibrillation and possibly cardiac arrest.

Results

Data were analysed using SPSS 15 software. Descriptive analysis for nonparametric variables was expressed in *proportion* and parametric variables in *mean* and *standard deviation*. The treatment difference was assessed using *ttest*for independent samples for parametric variables and by *Chi square test* for non-parametric variables. Statistical significance was assessed using p at 0.05 cut off or 95% confidence interval. (95% CI).

The total duration of labour in both groups were comparable. The duration of first, second and third stage of labour were also comparable. Student T-test was done on duration on total and each stage of labour. The P-values were all >0.05 implying that differences were not statistically significant.

Table 1: Time for Onset of Analgesia

A - Group(Mean ± S.D)	B –Group(Mean ± S.D)	P - Value
11.9	11	0.406

A - Group		B -Group	
Minimum	Maximum	Minimum	Maximum
15	8	13	8

The time for onset of analgesia shows no statistical significance.p> 0.05

Table 2: No. of Rescue Boluses

A - Group(Mean ± S.D)	B – Group(Mean ± S.D)	P - Value
0.27± 0.521	0.40 ± 0.675	0.395

A - Group		B - Group	
Minimum	Maximum	Minimum	Maximum
0	2	0	2

The number of rescue boluses required showed no statistical significance in the t test.

Table 3: Maximum Sensory Level Achieved

A - Group(Mean ± S.D)	B – Group (Mean ± S.D)	P - Value
9.20± 0.761	9.03 ± 0.765	0.401

A - Group		B - Group	
Minimum	Maximum	Minimum	Maximum
8	10	8	10

The minimum and maximum sensory levels achieved in both Group A and Group B were T8 and T10 respectively and showed no statistical significance in the t test.

Table 4: Duration of Labour

Stage of Labour	A - Group		B - Group		P - Value
	Mean (Mins)	SD	Mean (Mins)	SD	
First Stage	314.20	71.604	302.13	50.469	0.454
Second Stage	63.07	8.242	65.13	8.283	0.337
Third Stage	6.93	2.318	7.37	2.076	0.449
Total	384.20	69.906	374.47	49.624	0.537

Stage of Labour	A - Group		B - Group	
	Minimum	Maximum	Minimum	Maximum
First Stage	185	480	200	365
Second Stage	50	79	50	89
Third Stage	3	12	3	11
Total	245	540	261	430

Conclusion

Bupivacaine has stood the test of time as bedrock of labour analgesia because of its longer duration of action and lesser degree of motor block for a comparable degree of sensory analgesia. The newer local anaesthetic Ropivacaine has advantages over Bupivacaine because of its motor-sparing properties and its lower systemic toxicity. Ropivacaine is a local anaesthetic with lower cardiotoxic potential [1,2,3,4,6] and higher threshold for neurtoxicological symptoms [4,5,6] than racemic bupivacaine. Themajority of published data on ropivacaine are on its use in the epidural space [8,9]. In the context of above mentioned developments we have undertaken a study to compare 0. 20% Ropivacaine with 0.125% Bupivacaine without any additives for epidural labour analgesia.

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Review Article

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Xenon: The Future Anaesthetic Agent

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Abstract

After the discovery of xenon in 1898, xenon anaesthesia has been studied for decades. The search for an inert gas to replace N_2O led to introduction of xenon in anaesthesia practice. Xenon's anaesthetic properties were discovered in 1939. Since then, a number of studies of xenon anaesthesia have been conducted. The anaesthetic properties of xenon is mainly conferred by the inhibition of *N*-methyl-D-aspartate receptors in the central nervous system. Xenon is an inert gas and, theoretically, is not metabolized to toxic metabolites, does not react with absorbent, and does not deplete vitamin B_{12}, as opposed to other inhaled agents. Xenon is described as having many of the characteristics of an ideal inhalational anaesthetic agent, including rapid induction and emergence, analgesic properties, cardiovascular stability, and neuroprotective qualities. It is non-flammable, non-explosive, non-toxic, devoid of teratogenic effects and does not contribute to the greenhouse effect. Clinically, there are certain disadvantages to xenon anaesthesia. Because of its high density, xenon was found to increase airway resistance and work of breathing in an animal study. Nevertheless, it may be a good choice for high-risk patients with unstable haemodynamics, cardiovascular diseases, expected prolonged recovery from anaesthesia, or advanced age. Moreover, the high cost of xenon associated with its production has discouraged more widespread use. This article reviews the benefits and drawbacks of xenon anaesthesia, and discusses future perspectives.

Keywords: Anaesthesia; Inhalational Agent; Inert Gas; Xenon.

The quest for the ideal anaesthetic agent has been continuous since the begining of anaesthesia. Inhalational anaesthetic agents have been used in the practice of anaesthesia for centuries. The first report of the use of inhalational anaesthetic agents such as ether (1846), chloroform (1847) and nitrous oxide (1844) began to emerge in 1840s. The inhalational anaesthetic agents used in modern practice include the fluorinated ethers isoflurane, sevoflurane and desflurane and gas nitrous oxide (N_2O) and these agents, from diethyl ether and N_2O to sevoflurane and desflurane, have been studied and compared extensively.

The search for an inert gas to replace N_2O led to introduction of xenon in anaesthesia practice. Recently there has been renewed interest in the use of xenon as an anaesthetic agent, as researchers have tried to find a safe and effective substitute for N_2O, which has caused environmental concerns because of its ozone depleting properties [1]. Several advantages of xenon, compared with other inahalational agents, have been demonstrated in various studies which include:

1. Rapid onset and offset of its action due to its low blood gas solubility coefficient.
2. Less CVS depression
3. Neuroprotection and
4. Profound analgesia.

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Xenon is a naturally occurring gaseous element. Xenon derives its name from the Greek word for "stranger" because of its rarity, as it represents 0.0000086% or 0.87 parts per million of air [2]. Xenon exists naturally as 9 isotopes, the most abundant of which is Xe132 [3]. It is discovered in 1898 by British chemists Sir William Ramsay and Morris W. Trave. It is manufactured by fractional distillation of air and is used commercially for lasers, high intensity of lamps, flash bulbs, jet propellants, x-ray tubes and in medicine. As xenon is naturally occurring element, it is not a pollutant or an occupationally hazardous gas, nor does it contribute to global warming or the greenhouse effect[2]. In contrast N_2O is 230 times more potent as a greenhouse gas than is CO_2, taking 120 years to break down. Xenon has many properties of an ideal anaesthetic agents, including the fact that it is odourless, nonpungent, nontoxic, nonexplosive, environmental friendly and unlikely to go biotransformation due to its stability [4]. Although xenon was discovered in the 1898, its anaesthetic properties were not discovered until 1939 by Behnke and Yarbourough [5,6]. In 1946, Lawrence JH reported its narcotic properties in mice [7]. Later in 1951, Cullen and Gross used xenon as an anaesthetic agent in human volunteers and concluded that xenon was capable of producing of complete anaesthesia [8]. It was until 1965, Eager and associates actually established the MAC of xenon at 0.71 or 71% indicating a greater potency [9].

Physiochemical properties

Atomic number	54
Atomic weight	131.293(6)
Melting point	111.74°C
Boiling point	108.09°C
Critical temperature	16.62°C
Density	5.366 g/L
Specific heat	0.158 J/g•K

Physical form Colorless nonflammable gas and does not support combustion.

Table 1: A Comparison of Xenon with Other Currently Used Inhalational Agents

Agent	MAC (%)	Blood/gas	Brain/blood	Muscle/blood	Oil/gas
Xenon	71	0.115	0.23	0.10	1.9
Nitrous oxide	104	0.47	1.1	1.2	1.4
Desflurane	6.0	0.42	1.3	2.0	18
Sevoflurane	2.0	0.69	1.7	3.1	53.4
Isoflurane	1.2	1.4	2.6	4.0	90

MAC - minimum alveolar concentration.

Table 1 compares Xenon's MAC and partition coefficients with that of other inhalational agents. It has lowest blood gas partition coefficient of any inhalational agent. Its favourable pharmacokinetics makes it suitable for faster induction and emergence [10,11]. Induction of anaesthesia with xenon is faster than with sevoflurane 71±21 vs 147±59 sec [12]. Emergence from xenon anaesthesia is 2-3 times faster than that from equi-MAC concentration of N_2O/isoflurane or N_2O/sevoflurane anaesthesia [13]. Xenon is found to be three times more efficacious than sevoflurane at blocking cardiovascular response to incision at equi-MAC concentration. It is additive with isoflurane and sevoflurane at MAC awake [14]. Xenon can diffuse freely through rubber, with significant losses of gas by this route during anaesthesia, thereby increasing the cost of xenon anaesthesia.

Xenon is a noble gas, but under special condition it is capable to form certain compounds with very low reactivity like clathrates, fluorides, chlorides, oxides, oxyfluorides, peroxynates and complex salts. However, it is unlikely that xenon is involved in any biochemical reactions when used in anaesthetic concentrations [15]. As xenon is Inert gas hence not metabolized. There is no renal or hepatic clearance. Xenon is mainly eliminated through lungs; approximately 95% of inhaled xenon is removed in first pass after discontinuation [2].

Mechanism of Action

Most inhalational anaesthetic agents act by increasing the activity of the GABA system. Xenon works by inhibiting excitatory N-methyl- D-aspartate (NMDA) receptors in the CNS with insignificant effect on GABA receptors or non-NMDA glutaminergic receptors [16,17]. The analgesic effects of xenon are also explained by its inhibition of NMDA receptors in the CNS as well as in the dorsal horn of spinal cord [3,18]. Similar to other volatile anaesthetic agents, it reduces the whole brain metabolism of glucose [19] or inhibits neurotransmission system in glycine receptors [20].

Pharmacodynamics

Cardiovascular

It is well known that inhalational agents disrupts haemodynamic stability and can have ionotropic effects. This can be dangerous for patient with high cardiovascular risk. Xenon anaesthesia is associated with cardiovascular stability with no significant changes in myocardial contractility, cardiac index, blood pressure or systemic vascular resistance. The haemodynamic stability was a result of less stress induced sympathetic stimulation, a theory supported by stable epinephrine levels during xenon anaesthesia. Compared with N_2O anaesthesia, much less fentanyl was required to maintain cardiovascular stability during xenon anaesthesia [1,21]. Xenon was found to depress both sympathetic and parasympathetic transmission [22]. The mechanism of autonomic action of xenon has yet to be explained. Xenon also attenuates myocardial depressant effect of isoflurane [23]. Ventricular functions, as assessed by transesophageal echocardiography, are unchanged during xenon anaesthesia [24,25]. Even in presence of compromised myocardium, xenon anaesthesia is remarkably stable [26].

CNS and Neuroprotection

As xenon is an NMDA receptor antagonist, it exhibit unique neuroprotective action without coexisting neurotoxicity. As activation of the NMDA receptors appear to be crucial to the initiation of neuronal injury and death from a variety of insults [27], its neuroprotective effects have been examined in a series of in vitro and in vivo studies. Xenon also attenuates cardiopulmonary bypass–induced neurocognitive dysfunction [28]. Xenon may therefore be a useful agent when protection against neurological injury required.

Another point to discuss is xenon's effect on cerebral blood flow when it used as neuroprotectant. Frietsch T et al reported that in the first 5 min of exposure, xenon increases cerebral blood flow; thereafter, xenon's effect on the cerebral blood flow appears to reverse [29]. In human beings xenon produced increased regional blood flow in all organs, largest percentage increase in the cerebral blood flow [1]. The global increase in cerebral blood flow may in turn increase the intracranial pressure (ICP), but preserves autoregulation, probably due to redistribution of blood from corticocerebeller to white matter [30]. Inhalation of 33% xenon, for 20 minutes in 13 patients, 3 days after severe head injury showed clinically significant increase in ICP and cerebral perfusion pressure [31]. Despite of these changes, there were no arteriovenous oxygen difference values which would be indicative of cerebral oligaemia or ischaemia. However, in monkeys, 33% xenon reported to reduce cerebral blood flow by 12% and cerebral oxygen consumption by 16% [32].

Analgesia

Xenon produced analgesia by inhibiting NMDA receptors. It also acts at the level of spinal cord, particularly in the dorsal horn. It manifests more potent analgesic action than N_2O, the only other anaesthetic gas with true analgesic efficacy. Various researchers compared xenon and N_2O. Peterson-Felix et al found that xenon has an analgesic potency 1.5 times that of N_2O [33]. Fentanyl requirement was lower in a xenon based anaesthesia compared with that of N_2O (fentanyl 0.05 vs 0.24mg) and fewer patients required fentanyl (35 vs 95%) [1]. Further studies have found that during xenon anaesthesia lower doses of propofol required to prevent movement than with N_2O [34]. The difference in analgesic potency between xenon and N_2O is more difficult to define when tested in volunteers with experimental pain. When heat stimulation was used to provoke pain, xenon and N_2O were equivalent analgesic [35]. When electrical stimulation is used to provoke pain, xenon is more potent than N_2O [33]. Xenon produces minimal stress response to painful stimuli. Xenon attenuates haemodynamic reactions caused by surgical stimulus and requires only one-fifth of fentanyl required by N_2O group [36]. Because of its potent analgesic properties, xenon is used for the treatment of angina pectoris and for change of painful dressings [37].

The mechanism of analgesic action for xenon differs from N_2O although both gases are NDMA antagonists [15,16,38]. N_2O produces analgesia by release of endogenous ligands for opiate receptors in the periaqueductal grey region, which indirectly activates inhibitory neurons in the spinal cord. Xenon acts at spinal cord dorsal horn and suppresses the effect of both pinch and touch on the firing of wide dynamic range movements [17, 39]. Furthermore, nitrous oxide induced analgesia can be antagonised by naloxone [40]. As for xenon, it was found that naloxone has no effect on the rise in pain threshold, suggesting that the analgesic effects are not mediated by opiate receptors [35].

Respiratory System

Xenon cause slowing of respiration secondary to central respiratory depression; but it maintains the

minute ventilation by compensatory increase in tidal volume. Lachman B et al demonstrated that peak airway pressure, PaO_2 and $PaCO_2$ remained unaffected during xenon anaesthesia but they suggested that xenon although safe, should be used cautiously in older patients with chronic lung disease [1].

Xenon is unlikely to cause diffusion hypoxia, as its blood/gas partition coefficient is much lower than that of N_2O and it diffuse in to the alveoli more slowly than N_2O.

Xenon has a density of approximately three times and its viscosity is twice that of N_2O. It can, therefore, be expected that xenon anaesthesia in high concentration will lead to an increase in airway resistance and need higher driving pressure for ventilation. Various animal studies have shown either a moderate increase in airway resistance with high xenon concentration or no change to airway resistance during xenon anaesthesia. However, some studies on humans have observed no significant increase in airway resistance under xenon anaesthesia [42].

Organ Perfusion

It has been shown that compared to other anaesthetic regimens, xenon anaesthesia produces the highest regional blood flow in brain, liver, kidney and intestine. All volatile anaesthetics currently used, cause a reduction in the regional blood flow which carries the potential danger of tissue hypoxia. Xenon, therefore, appears to be interesting alternative for anaesthetic in the transplant surgery.

Toxicity

As xenon is excreted through the lungs without any change by hepatic or renal system, it can be safely used for anaesthesia in patients with hepatic and renal dysfunction. Xenon exerts no effects on coagulation, platelet function or immune system [3]. In vivo and in vitro studies suggest that xenon does not trigger malignant hyperthermia in MH-susceptible swine [42,43].

Embryotoxic or teratogenic changes were not observed in pregnant Wistar rats, nor was xenon found to be allergenic [44]. Xenon has proven to increase pulmonary resistance due to its greater density [50]. This can increase work of breathing with increase the risk in patients with COPD, morbid obesity and in premature infants [2].

Environmental Effects

The major volatile anaesthetic agents used today are chlorofuorocarbon based and are known to deplete the ozone layer [46] and as such their emission is being banned by international agreement from 2030.

The montreal summit of 2007 accelerated this date for developed countries to 2020. As said earlier, N_2O is 230 times more potent as a greenhouse gas than CO_2, taken 120 years to breakdown and the amount released as an anaesthetic contributes 0.1% of greenhouse effect [47]. In contrast, xenon appears to be environmentally safe, nonreactive and has no deleterious ecological effects. Thus xenon has certain environmental and legal advantages.

Pharmacoeconomics

The major disadvantage of the xenon anaesthesia is its high cost. In UK, the cost of 2 hour of xenon anaesthesia using 20 L xenon is about £300 compared to £10 with volatile anaesthetic agents and £20 with propofol anaesthesia [48].

As xenon is an expensive gas, therefore, closed circuit delivery must be used. Methods to reduce the cost of xenon anaesthesia include decreasing consumption, recycling of used xenon and reducing manufacturing cost. The major cost is due to the priming and flushing of the delivery circuit; if the delivery system could be refined to avoid the need for priming and flushing [49] than xenon anaesthesia would cost more affordable, assuming the closed circuit delivery.

Another mean to improve the cost effectiveness of xenon anaesthesia are xenon recycling system [46]. The major disadvantage of this system is that anaesthesia would have to be maintained with another agent while xenon was recovered, thereby negating the beneficial emergence property of xenon [3]. Dingley and Masson recently developed a cryogenic device to recover xenon from waste anaesthesia gas [50].

An interesting note is that Nakata et al pointed out that xenon anaesthesia is financially viable with longer duration of anaesthesia [51]. After 4 hrs of xenon administration in a completely closed circuit, xenon becomes comparable in cost to other anaesthetics. This gives a closer edge in cardiac and neurological surgeries in which prolonged anaesthesia is required and rapid recovery is beneficial [3]. Unfortunately, even if the cost of xenon anaesthesia can be reasonable reduced, it is still unlikely to gain widespread use due to its limited availability [49].

Induction and Emergence with Xenon

Reports suggests that xenon anaesthesia being used routinely during general surgery, gynaecological surgery and orthopaedic surgery in Russia, Europe [52,53]. Burov NE et al [37] described four stages of anaesthesia with 70% xenon and 30% O_2

Stage 1 - Stage of paraesthesia and hypoalgesia with pins and needle sensation all over the body.

Stage 2 - Stage of euphoria with increased pshycomotor activity where patient struggles to remove facemask, does not obey commands but has full recollection of commands.

Stage 3 - Stage of analgesia and partial amnesia noted by 3^{rd}-4^{th} min.

Stage 4 - Stage of surgical stimulus shows a degree of muscle relaxation with pronounced diaphragmatic breathing.

Because of high cost and limited availability, xenon should be conserve during anaesthesia. The patient lungs should be denitrogenated with 100% O_2 for 5 min before xenon inhalation. The amount of xenon necessary for primary equilibrium is about 0.1 L/kg body weight and xenon expenditure of 50-70 mL/min during steady state anaesthesia, depending on diffusion loss via the circuits and tubings permeability [54]. As xenon possess rapid onset, consciousness lost within 3 min. Xenon has no effect on nondepolarising muscle relaxants. Xenon concentration should never be below 40% as the MAC awake of xenon is about 30% volume which is below the desired concentration for anaesthesia [8].

Recovery from xenon is rapid and found to be 2-3 times faster with equi-MAC concentration of N_2O-sevoflurane/isoflurane anaesthesia [13] and 8-10 times faster recovery with equivalent depth of propofol anaesthesia [55]. Burov et al observed that patients woke up in 2 min and were fully conscious in 4 min after xenon anaesthesia [37]. Because of these recovery properties, xenon anaesthesia is now recommended during day care surgical procedures, in ICU and during cardiac surgery where cardiovascular stability will improve the surgical outcome [56].

Replacing the N_2O and volatile anaesthetic agents by an inert gas, xenon, can reduce the pollution and environmental hazards. Despite the high cost and limited availability, xenon is a potent inhalational anaesthetic with many salubrious qualities. With a favourable phrmacodynamic and pharmacokinetic properties: quick onset and rapid emergence, cardiac, neuroprotective, analgesic properties and environment protective qualities, xenon could very well be the future anaesthetic agent.

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Erratum

Original Research Article

Article Titled "**Platelet Indices as Indicators of Severity of Sepsis**"

Gaargi Shashidhar[1], Roopa Rani K.[2], Usha M.[3]

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The original published version of this Article contained errors in the name of corresponding author mentioned, **Gaargi Shashidhar**. But corresponding author name is "**Roopa Rani K.**"

Now read as,

Original Research Article

Platelet Indices as Indicators of Severity of Sepsis

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Mistake is regretted **by Editor-in-chief**

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Indian Journal of Obstetrics and Gynecology	Bi-monthly	9500	9000	742	703
Indian Journal of Pathology: Research and Practice	Monthly	12000	11500	938	898
Indian Journal of Plant and Soil	Semiannual	65500	65000	5117	5078
Indian Journal of Preventive Medicine	Semiannual	7000	6500	547	508
Indian Journal of Research in Anthropology	Semiannual	12500	12000	977	938
Indian Journal of Surgical Nursing	Triannual	5500	5000	430	391
Indian Journal of Trauma & Emergency Pediatrics	Quarterly	9500	9000	742	703
Indian Journal of Waste Management	Semiannual	9500	8500	742	664
International Journal of Food, Nutrition & Dietetics	Triannual	5500	5000	430	391
International Journal of Neurology and Neurosurgery	Quarterly	10500	10000	820	781
International Journal of Pediatric Nursing	Triannual	5500	5000	430	391
International Journal of Political Science	Semiannual	6000	5500	450	413
International Journal of Practical Nursing	Triannual	5500	5000	430	391
International Physiology	Triannual	7500	7000	586	547
Journal of Animal Feed Science and Technology	Semiannual	78500	78000	6133	6094
Journal of Cardiovascular Medicine and Surgery	Quarterly	10000	9500	781	742
Journal of Forensic Chemistry and Toxicology	Semiannual	9500	9000	742	703
Journal of Geriatric Nursing	Semiannual	5500	5000	430	391
Journal of Global Public Health	Semiannual				
Journal of Microbiology and Related Research	Semiannual	8500	8000	664	625
Journal of Nurse Midwifery and Maternal Health	Triannual	5500	5000	430	391
Journal of Organ Transplantation	Semiannual	26400	25900	2063	2023
Journal of Orthopaedic Education	Triannual	5500	5000	430	391
Journal of Pharmaceutical and Medicinal Chemistry	Semiannual	16500	16000	1289	1250
Journal of Practical Biochemistry and Biophysics	Semiannual	7000	6500	547	508
Journal of Psychiatric Nursing	Triannual	5500	5000	430	391
Journal of Social Welfare and Management	Triannual	7500	7000	586	547
New Indian Journal of Surgery	Bi-monthly	8000	7500	625	586
Ophthalmology and Allied Sciences	Triannual	6000	5500	469	430
Otolaryngology International	Semiannual	5500	5000	430	391
Pediatric Education and Research	Triannual	7500	7000	586	547
Physiotherapy and Occupational Therapy Journal	Quarterly	9000	8500	703	664
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