Indian Journal of Anesthesia and Analgesia

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The Indian Journal of Anesthesia and Analgesia (IJAA) is official peer-reviewed scientific journal addresses all aspects of anesthesia practice, including anesthetic administration, pharmacokinetics, preoperative and postoperative considerations, coexisting disease and other complicating factors, cost issues, and similar concerns anesthesiologists contend with daily. The Journal seeks a balance between outstanding basic scientific reports and definitive clinical and management investigations. The Journal welcomes manuscripts reflecting rigorous analysis, even if unusual in style and focus.

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Perioperative Glycemic Control: An Overview

K.K. Mubarak

Professor & Head of Anaesthesiology, Govt. Medical College, Thrissur, Kerala.

Diabetic patients are more likely to undergo surgical procedures, which can disrupt their routine glycemic control. Perioperative dysglycaemia (hyperglycaemia, hypoglycaemia, stress-induced hyperglycaemia and glucose variability) is common in these patients. Perioperative glycaemic control include preoperative optimization of diabetes, identification of undiagnosed diabetes and other forms of dysglycaemia, intraoperative glucose control, and postoperative care with return to their regular diabetic management.

The American Diabetes Association (ADA) describes three categories of inpatient dysglycemia:

1. Previously diagnosed diabetes
2. Unrecognised diabetes with inpatient hyperglycemia persisting after discharge
3. Hospital related (Stress-induced) hyperglycemia (SIH) which returns back to normal, when the counterregulatory hormone surge is abated.

In addition, the prediabetes states of Impaired Fasting Glucose (IFG), Impaired Glucose Tolerance (IGT) and gestational diabetes mellitus (GDM) are continuum with overt diabetes and can manifest with hyperglycemia in the perioperative setting. They can have stress-induced hyperglycemia perioperatively, which can worsen their glycemic state.

Hyperglycemia is associated with adverse outcomes in surgical patients, irrespective of whether the patient is a known diabetic or not. A fasting blood glucose or HbA1c if fasting values are doubtful is an essential preoperative test, which also screen for diabetes in an otherwise healthy patient. Preoperative HbA1c above 7% has a high risk for postoperative wound infections. There is impaired neutrophil function if blood glucose level is above 200 mgm% with a strong association between perioperative hyperglycemia and nosocomial infections.

Although current anesthetic and surgical techniques have minimal impact on the metabolic stress producing hyperglycemia, the benefits of good glycemic control during the perioperative period offers a better surgical outcome. Anesthetic agents can affect glucose metabolism by modulation of the sympathetic tone. Inhalational anaesthetic drugs can suppress insulin secretion causing hyperglycemia, particularly in those with insulin resistance, raising the risk of ketoacidosis. The use of regional anesthesia or peripheral nerve blocks may mitigate these concerns, but no data suggest that it will improve the postoperative outcome.

Targets for Perioperative Glycemic Control

The optimal blood glucose target in the perioperative setting depends on the clinical conditions like type and duration of surgery, presence of infection, cardiopulmonary bypass and pregnancy. Elective surgeries should be postponed if the preoperative glycemic control is poor (HbA1c ≥8%). The aim is to achieve a near normal glucose metabolism, avoiding hypoglycemia and maintaining blood glucose levels at 90-180 mgm%. For this, surgical units should have facility for bedside glucose monitoring and to infuse glucose – insulin infusions as required.

Type I / Type II Diabetes

Type I diabetic patients are prone for ketosis if insulin is withheld, especially during stressful conditions like perioperative period, due to increased secretion of counter regulatory hormones. Type II diabetic patients can also develop ketosis, when there is a relative deficiency of insulin, especially in those who are on insulin therapy. To prevent hyperglycemia, they should be controlled with insulin preoperatively.

Minor / Major surgery

Regarding diabetic control, day care surgeries are

considered as minor surgery, as these involves little interruption of their routine dietary and drug regime. Surgeries which require overnight admissions and those with disruption of their routine diet and diabetic therapy are considered as major and managed accordingly.

Principles of Management

As the preoperative glycemic control significantly alters the surgical outcome, elective surgery should be done only when the diabetic status is under reasonable control, with neither hypo nor hyperglycemia, and $HbA_1C<8\%$. Diabetic gastroparesis should be sought for, as they have a high risk of pulmonary aspiration due to increased residual gastric contents and require longer period of preoperative fasting. Due to nausea and vomiting, they may not resume oral feeds which may complicate their postoperative glycemic control postoperatively. Preoperative fasting, interruptions to the routine dietary and drug regimen along with the stress of anaesthesia and surgery contribute to the poor perioperative glycemic control, leading to prolonged hospital stay with increased morbidity and mortality. These patients have to be taken up for surgery in the morning itself, preferably as the first case, to avoid prolonged fasting and hypoglycemia. Clear instructions regarding blood glucose monitoring and insulin adjustments should be given prior to surgery. Prolonged preopeoperative fasting increases catabolism and promotes insulin resistance. These patients require glucose-insulin infusion during the fasting period itself. Patient should be adequately hydrated prior to the induction of anaesthesia.

Diet Control

In those diabetic patients on diet control with HbA1c <6.5%, no specific therapy is needed. However, they require frequent blood glucose monitoring in the perioperative period. If blood glucose is above 180mg%, glucose insulin infusion is started and continued till they resume oral feeds.

Oral Hypoglycemic Agents

Oral antidiabetic drugs are stopped on the day of surgery and restarted once the patient resumes their normal feeds. Secretagogues (eg, sulfonylureas) can cause hypoglycemia and interfere with ischemic myocardial preconditioning increasing the risk of myocardial ischemia. These patients require short-acting insulin perioperatively depending on the type and duration of surgery. Glucose insulin infusion is administered if blood glucose >180 mg%, if surgery is prolonged or if they are on more than one oral antidiabetic agent. Metformin need not be stopped before minor surgery. But before major surgery it is discontinued due to the risk of lactic acidosis, especially in conditions of high lactate production like hypotension and myocardial ischemia. As prolonged stoppage may result in hyperglycemia, it is stopped on the day of major surgery and resumed 24 hours postoperatively, provided the serum creatinine level is acceptable. Glucose insulin infusion is given if withdrawal of metformin results in poor glycemic control.

Insulin

Diabetic patients on insulin require perioperative insulin therapy. Patients are advised to reduce their usual insulin dose the night before surgery to prevent hypoglycemia.

Maintenance insulin may be needed, based on the glucose levels and discretion of the clinician. Patients should be monitored to detect hyper / hypoglycemia.

Minor Surgery

The usual insulin and diet is maintained till the night before surgery. Patient is fasted overnight and the morning dose of insulin is delayed, if the procedure will be over by around 10 AM and the patient is able to take oral feeds with their routine insulin. If the procedure goes late, a reduced dose of insulin may be given. Glucose insulin infusion is started if the blood glucose is above 180mg %. If the diabetic status is under poor control, glucose insulin infusion has to be started in emergency situations even for minor surgeries.

Major Surgery

Patient is fasted overnight and the morning dose of insulin is skipped. Glucose insulin infusion is started prior to the induction of anaesthesia and continued postoperatively, till the patient is able to take oral feeds. Blood glucose is monitored hourly intraoperatively and postoperatively, till they are stable.

Subcutaneous Insulin Pumps

For minor surgeries, the usual basal infusion rate is continued, with hourly blood glucose monitoring. During major surgery, subcutaneous insulin

absorption may be erratic due to hemodynamic fluctuations and increased counter regulatory hormones. Hence they should be converted to glucose insulin infusion for proper glycemic control.

Glucose Insulin Infusion

This is the best way to maintain tight glycemic control in the perioperative period without producing hypoglycemia. It requires blood glucose monitoring, every 1-2 hours. If the initial blood glucose is high, glucose infusion is not started until the blood glucose level is controlled. Otherwise, insulin is not infused without glucose infusion, to avoid hypoglycemia.

Post-Operative Period

Glucose insulin infusion is continued till the patient is able to take oral feeds. When solid food is started, the usual subcutaneous insulin is given and the glucose insulin infusion stopped within 1-2 hours. Oral antidiabetic therapy is also started once the patient starts their oral feeds. Glucose levels may fluctuate during this period due to the metabolic stress of surgery, pain, infection and altered food intake and diabetic management. Removal of infective source or delivery of fetus may bring down the glucose level, causing hypoglycemia in the postoperative period. In such cases, insulin dosage is reduced and the whole regimen is reviewed. If oral intake is variable and cannot be relied, glucose insulin infusion is resumed till the oral intake is steady. Patients who are not detected to be diabetic, but required insulin perioperatively often requires continued insulin therapy, which has to be converted to subcutaneous injections postoperatively. If their HbA1c is >7%, it is likely that they had undetected diabetes preoperatively.

"Sliding Scale" Insulin

This was traditionally used to manage perioperative hyperglycaemia. It involves administration of insulin when the blood glucose is within specified ranges, with insulin being withheld when the blood glucose is within the normal range. It is retrospective and aimed at correcting rather than preventing hyperglycaemia. When used as sole therapy, it can lead to inappropriate insulin administration, resulting in large swings in blood glucose levels. "Correction insulin," is the use of additional short or rapid acting insulin in conjunction with the scheduled insulin doses to treat blood glucose levels above desired targets. Prolonged therapy with sliding scale is ineffective and potentially dangerous, especially in type 1 diabetes.

Intensive Insulin Therapy (IIT)

American College of Physicians (ACP) defines it as the use of intravenous insulin to achieve target blood glucose level with frequent blood glucose testing and adjustment of insulin dose. In intensive care unit (ICU) settings, the usual target is 80 to 110mg/dL, whereas in non-ICU settings it is <200 mg/dL. IIT is associated with risk of hypoglycemia, extended hospital stay and increased mortality. However, poorly controlled hyperglycemia is associated with increased morbidity and mortality due to poor immune response, increased cardiovascular events, thrombosis, inflammatory changes and delayed wound healing.

While evidence is not sufficient to give a precise range for blood glucose levels, target values of 140 to 200 mg/dL is a reasonable option, as this is associated with similar mortality as IIT targeted at blood glucose levels of 80 to 110 mg/dL with lower risk for hypoglycemic episodes. Although hypoglycemia is higher with lower target glucose values, it can also occur in patients on insulin with target blood glucose levels of 140 to 200 mg/dL.

Insulin Infusion

Separate intravenous access for a "piggyback" infusion of regular insulin (100 U per 100 mL 0.9% saline) is recommended. The infusion rate is determined as insulin (U/hr) =serum glucose (mg/dL)/150. Intra-arterial catheter is recommended for checking blood glucose concentrations 1-2 hours intraoperatively and postoperatively. A second intravenous catheter is used for intravascular volume replacement.

Conclusion

Management of patients with diabetes mellitus in the peri-operative period requires cooperation and communication between surgeons, physicians and anaesthesiologists. To keep blood glucose levels within the target range, medications need to be tailored during this period. There may be individual variations in the impact of surgery and adjustments made to the therapy, depending on the pre-existing diabetes status, nature and duration of surgery and perioperative complications.

Although optimal target glucose ranges remain controversial, the era of "tight" glycemic control has been changed to "less-tight" glycemic control, focusing on patient safety and efficacy oftherapy.

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Original Article

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Comparison of Air, Normal Saline and Lignocaine for Inflation of Endotracheal Tube Cuff

S.A. Bakshi*, V.R. Ankalwar*, N.G. Tirpude, T.M. Pendharkar*****

Abstract

The study design was a prospective, randomized, double blind. Ninety patients of either sex, ASA I and II were randomly divided into three groups according to the medium used for inflation of endotracheal tube cuff. The study was conducted to correlate the changes in intra-cuff pressure and post-operative incidence of tracheal morbidity in form of hoarseness, sore throat and dysphagia. We observed close relationship between rise in intracuff pressure and incidence of tracheal morbidity. The present study concluded that incidence of postoperative sore throat, hoarseness & dysphagia was significantly less (p 0.05) when Normal Saline & Lignocaine were used as medium for an endotracheal tube cuff inflation as compared to air.

Keywords: Lignocaine 2%; Endotracheal Tube (ETT) Cuff Inflating Medium; Intracuff Pressure of Endotracheal Tube; Post Intubation Tracheal Morbidity.

Introduction

The intubation with cuffed endotracheal tube is a gold standard in long term airway care and surgery under general anesthesia. It provides 100% airway protection against aspiration because of inflated cuff. However, the lateral pressure exerted by an inflated cuff on the tracheal mucosa may cause a range of complications like loss of mucosal cilia [1], inflammation, ulceration [2,3,4,5] , hemorrhage [3,5,6], tracheal stenosis [3,4,5,7], tracheo-esophageal fistula[3,8] and ischemic mucosal necrosis[9,10,11]. More often patients complain of symptoms like sore throat [2,8] hoarseness[2,8] and dysphagia[2] in the immediate postoperative period [12,13]. These complications or tracheal morbidity can lead to patient dissatisfaction and discomfort, if they last few days after operation. This significantly influences satisfaction as well as delays patient's return to normal routine activities.

Although the exact patho-physiology of post intubation airway symptoms is not fully elucidated, mucosal damage occurring at the cuff level is thought to be an important causative factor for tracheal morbidity. Decrease in tracheal mucosa perfusion occurs when the cuff exerts pressure greater than 30 cmH2O. This is probably the first step in the development of mucosal damage [14,15] . The magnitude of cuff pressure related complications depend on the amount of pressure exerted by the cuff on tracheal mucous membrane, duration of intubation and the area of cuff trachea contact [11,16,17]. Ideally pressure exerted against the tracheal wall by a cuff should be low enough to allow adequate tracheal capillary mucosal blood flow and prevent tracheal dilation, yet high enough to avoid aspiration and eccentric positioning of endotracheal tube in trachea. Hence, it is essential that a correct size of cuffed endotracheal tube is chosen with optimal diameter and circumference which will affect a seal with minimal in folding of excess cuff material [18]. An endotracheal tube in situ (i.e. in trachea) & cuff inflated with air represents a gas filled pocket in the body and the cuff wall acts as a diffusion area for nitrous oxide used for general anesthesia. This leads to increase in volume of cuff, ultimately resulting in rise of intra-cuff pressure.

Different methods have been recommended for controlling the intra-cuff pressure during balanced general anesthesia especially when nitrous oxide is a component. These include regular cuff pressure measurement and adjustment, Lanz pressure

Author's Affiliation:
*Associate Professor, ** Professor and Head, ***Resident, Dept of Anesthesiology, Govt Medical College, Nagpur - 440009 Maharashtra.

Corresponding Author: Dr. Vrishali R. Ankalwar, Associate Professor, Dept of Anesthesiology, Govt. Medical College, Nagpur-440009, Maharashtra, India
E-mail: vriankalwar@yahoo.com

regulating system[19] , Brandt anesthesia tube [20] , but all these techniques and devices are complicated, cumbersome or expensive. Hence these are not routinely accepted methods. Various other studies advocated the use of liquid medium like normal saline [2,9,22] or 2% lignocaine [21, 22] for inflating the cuff as it prevents significant rise in intra-cuff pressure and gives greater endotracheal tube tolerance and lowers the incidence of postoperative sore throat.

Present study was carried out to study Air, Normal Saline and 2% Lignocaine as a medium for inflation of endotracheal tube cuff & to compare the changes in intra-cuff volume, intra-cuff pressure and post intubation tracheal morbidity e.g. hoarseness, sore throat and dysphagia.

Materials and Methods

Institutional ethical committee approval was sought. The study was conducted on 90 patients of either sex, age 18- 65 years, ASA grade I & II. The written informed consent was taken from all the patients. This was a prospective, randomized double blind study carried out at tertiary care centre of Central India.

Patients were randomly allocated in to three groups of 30 patients in each group according to medium used for inflation of cuff of endotracheal tube. Air in group 'A', normal saline in group 'NS and Lignocaine 2% in group 'L' was used as medium for inflation of endotracheal tube cuff. Each time new pre-packed, pre- sterile high volume and low pressure cuff type endotracheal tube (size of endotracheal tube 7-8 F in women; 8.5-9.5 F in men) was used in all the cases under study. The patients posted for surgery below neck, surgery lasting for more than 60 minutes and surgeries of elective as well as emergency nature were included in the study. Patients with history of smoking, laryngo-tracheal disease or anomalies, naso-gastric tube in situ, oropharyngeal airway introduced preoperatively, more than one trial of intubation, surgery in any position other than supine and patients at risk for pulmonary aspiration were excluded from the study. Detailed pre-anesthetic check up and relevant investigations were done.

Preoperatively, all patients were kept fasting for 6 hours prior to surgery. In the operation theatre, monitors were attached to patient and vital parameters like heart rate, NIBP, ECG and SpO_2 were note d before premedication.

Intravenous access was set up and maintenance fluid dextrose normal saline (DNS) was set up. All patients were premedicated with intravenous inj. Ranitidine 50 mg, Glycopyrrolate 0.2 mg, Midazolam 1 mg and Pentazocine 0.5 mg/ kg. Before induction of anesthesia, endotracheal tube was tested for any leakage in the cuff. In Lignocaine group, cuff of endotracheal tube was prefilled with Lignocaine 2% for a period of 90 minutes prior to procedure to enhance diffusion of drug across the cuff and the then cuff was deflated just before intubation. Anesthesia was induced with injection Propofol 2 mg/ kg and Succinyl choline 2 mg/kg intravenously. Gentle endotracheal intubation was done with adequate size Polyvinyl chloride (PVC) portex cuffed endotracheal tube by experienced anesthesiologist. After intubation, tube cuff in all the three groups was inflated with adequate quantity of air just sufficient to prevent paratubal leak. This was checked by palpation method i.e. keeping the fingers over trachea & giving positive pressure ventilation. After fixing the endotracheal tube, it was connected to closed circuit and general anesthesia was maintained with on O_2 (50%) + N_2O (50%) + Sevoflurane and IV intermittent doses of inj. Vecuronium.

After 10 minutes of intubation, cuff pressure monitor was attached to the endotracheal tube through extension tubing containing three way. Three way was attached to the pilot balloon of endotracheal tube. 10 cc syringe was attached to third end of three way. After withdrawing all the air from endotracheal tube, cuff pressure was checked by cuff pressure monitor (Hansraj cuff pressure monitor) which was supposed to be 0 cmH2O. Later on the cuff of endotracheal tube was inflated with the medium as per allotted group. The cuff inflation medium used to inflate cuff of endotracheal tube was air for group 'A', normal saline for group 'NS' and Lignocaine for group 'L'.

Following Observations were Noted

- Initial volume of medium required for re-inflation of cuff.
- Final volume of medium aspirated from cuff just before extubation.
- Initial intra cuff pressure value at re-inflation.
- Every hour intra-cuff pressure value monitoring.
- Final intra-cuff pressure value just before reversal.
- Duration of intubation (From time of intubation to extubation).

At the end of surgery, after adequate recovery, reversal of residual neuromuscular block was done with inj. Neostigmine 0.05 mg/ kg and Glycopyrrolate 0.01 mg/ kg. On regaining consciousness, adequate skeletal motor tone & spontaneous respiration, patient was extubated.

Endotracheal tube cuff was checked for any damage. Patients were observed for 24 hours for symptoms of tracheal morbidity e.g. hoarseness, sore throat and dysphagia.

Hoarseness: - graded in to 4 points. Grade 0:- none, Grade 1:- noted by patient, Grade 2:- obvious to observer, Grade 3:- aphonia. Sore throat : - graded in to 4 points. Grade 0 - none, Grade 1 – mild (scratchy throat), Grade 2 – moderate (similar to that noted with cold), Grade 3 – severe (more severe than with cold). Dysphagia: - Difficulty or pain in swallowing which was recorded as absent or present.

The person keeping record of intra-cuff pressure and post operative tracheal morbidity was blind about the medium used for inflation of cuff of endotracheal tube.

Statistical Analysis

All the observations of the study were subjected to statistical analysis. Continuous parameters were presented as mean ± S.D. and categorical variables were expressed in percentages. Continuous variables were compared in three groups by analysis of variance (ANOVA) with multiple comparisons by Bonferroni test. Categorical variables were compared by chi square analysis. Volume of cuff inflation and deflation and intra-cuff pressure initial and final were compared in 3 groups by paired t-test for each group. Mean changes of these parameters were compared among 3 groups by ANOVA. P-Value < 0.05 was considered as statistically significant.

Results

The mean age of patients in Group 'A' was 38.63 ± 7.16 years, in Group 'NS' was 35.36 ± 10.19 years and in Group 'L' was 33.32 ± 11.63 years. Sex ratio (male: female) of Group 'A' was 15:15, Group 'NS' was 21: 9 and Group 'L' was 18:12. There were no statistically significant differences among the three groups regarding characteristics of the patients (Table 1).

Table 2 and Figure 1 showed comparison of initial volume of cuff inflation medium, final volume of medium at cuff deflation and total change in intra-cuff volume of medium of the three groups. Mean intra-cuff volume at inflation to make the cuff just leak proof was 5.05 ± 0.66 ml in Group 'A', 5.63 ± 0.73 ml in Group 'NS' and 5.58 ± 0.63 ml in Group 'L'.

There was no statistically significant difference in intra-cuff volume amongst three groups (p value-0.384). There was rise in total change in intra-cuff volume in Group 'A' (4.08 ± 1.12 ml) as compared to Group 'NS' and Group 'L'. There was a fall in intra-cuff volume in Group 'NS' and Group 'L' as -0.096 ± 0.14 ml and -0.35 ± 0.23 ml respectively. It was observed that medium volume at deflation of cuff in Group 'A' was significantly more than the medium volume used for inflation (p value - 0.000).

Similarly, intra-cuff pressure was increased in Group 'A' (7.2 ± 2.35 cm H_2O) as compared to Group 'NS' and 'L', (0.65 ± 0.77 and 0.5 ± 0.77 cm H_2O respectively). Rise in intra-cuff pressure was maximum in Group 'A' at first, second and third hour of inflation of cuff. Figure 2 represent the progressive rise in intra-cuff pressure than the baseline intra-cuff pressure in all the three groups. It was found to be statistically significant, (P value-0.0261) when compared with Group 'NS' and Group 'L'. The comparison of initial intra-cuff pressure, final intra-cuff pressure and total change in intra-cuff pressure in three groups were shown in Table 3 and Figure 3. It was observed that final intra-cuff pressure in Group 'A' was significantly more than the initial intra-cuff pressure (p value- 0.000).

The incidence of hoarseness of voice, sore throat and dysphagia were lowest in 'Lignocaine' group as compared to air and normal saline groups. Incidence of hoarseness of voice- Grade 1 was maximum in Group 'A' (70%) as compared to Group 'NS' (16.6%) and Group 'L' (10%). The incidence of sore throat of Grade 1 in Group 'A' was much higher i.e. 83.3%. In Group 'NS' & Group 'L' the incidence of sore throat was 20% and 10% respectively. None of the patient had developed hoarseness of voice and sore throat of grade 2 and grade 3. Dysphagia was observed significantly in more number of patients in Group 'A' (86.6%) as compared to only 2 patients (6.6%) in Group 'NS' and Group 'L' each. This was statistically significant (p value- 0.000) (Table 4).

The mean rise in intra-cuff pressure and the incidence of hoarseness, sore throat and dysphagia was more in Group 'A' as compared to Group 'NS' and Group 'L'.

Thus there was a significant correlation between

Table 1: Demographic data of patients

Group	Age (years) Mean ± S.D.	Sex wise distribution of patients Male	Female
Air (Group A)	38.63 ± 7.16	15 (50%)	15 (50%)
Normal Saline (Group NS)	35.36 ± 10.19	21 (70%)	9 (30%)
Lignocaine (Group L)	33.32 ± 11.63	18 (60%)	12 (40%)

Table 2: Comparison of Initial volume of CIM at cuff inflation, Final volume of CIM at cuff deflation & Total change in intra-cuff volume

Group	Volume at inflation of cuff (ml)	Volume at deflation of cuff (ml)	Change in volume (ml) Increase	Decrease
Air (Group A)	5.05 ± 0.66	9.13 ± 1.38	4.08 ±1.12	-
Normal Saline (Group NS)	5.63 ± 0.73	5.53 ± 0.71	-	-0.096 ± 0.14
Lignocaine (Group L)	5.58 ± 0.69	5.23 ± 0.63	-	-0.35 ± 0.23

Cuff inflation medium(CIM) Data are Mean ± SD.

Table 3: Comparison of Initial intra-cuff pressure, Final intra-cuff pressure & Total change in intracuff pressure in three groups

Group	Initial intracuff pressure (cm H2O)	Final intracuff pressure (cm H2O)	Change in intracuff pressure
Air (Group A)	21.2 ± 3.03	28.4 ± 3.97	7.2 ± 2.35
Normal Saline (Group NS)	20.46 ± 2.48	21.36 ± 2.74	0.65 ± 0.77
Lignocaine (Group L)	20 ± 2.21	20.5 ± 2.31	0.5 ± 0.77

Data are Mean ± SD.

Table 4: Correlation between Rise in intra-cuff pressure & Incidence of post-operative tracheal morbidity

Group	Rise in intracuff pressure	Hoarseness (%)		
		Gr 0	1	>1
Air (Group A)	7.2 ± 2.35	30	70	0
Normal Saline (Group NS)	0.65 ± 0.77	83.3	16.6	0
Lignocaine (Group L)	0.5 ± 0.77	90	10	0
Group	**Rise in intracuff pressure**	**Sore throat (%)**		
		Gr 0	**1**	**>1**
Air (Group A)	7.2 ± 2.35	16.6	83.3	0
Normal Saline (Group NS)	0.65 ± 0.77	80	20	0
Lignocaine (Group L)	0.5 ± 0.77	90	10	0
Group	**Rise in intracuff pressure**	**Dysphagia (%)**		
		Present	**Absent**	
Air (Group A)	7.2 ± 2.35	86.6	13.3	
Normal Saline (Group NS)	0.65 ± 0.77	6.6	93.3	
Lignocaine (Group L)	0.5 ± 0.77	6.6	93.3	

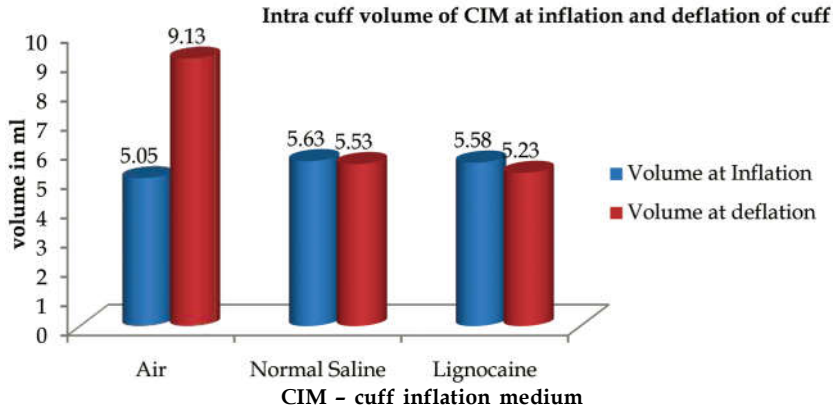

Fig. 1: Diagrammatic presentation of intra-cuff volume of CIM at inflation & Deflation of cuff in three groups

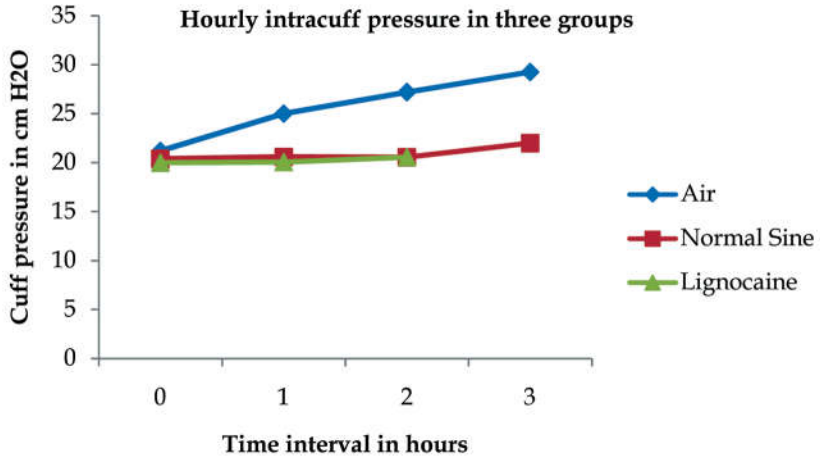

Fig. 2: Represent hourly intracuff pressure in three groups

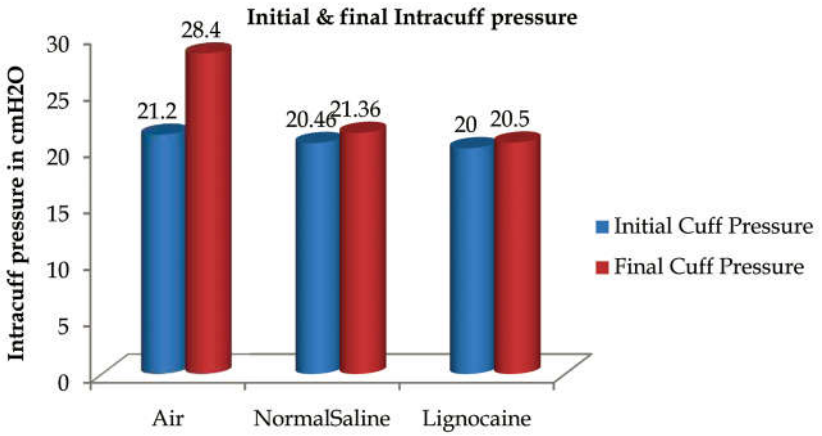

Fig. 3: Diagrammatic presentation of initial and final intracuff pressure in three groups

the rise in intra-cuff pressure and the incidence of post operative tracheal morbidity amongst three groups in relation to the medium used for endotracheal tube cuff inflation (Table 4).

Discussion

The present study was carried out to know whether the use of Normal Saline and 2% Lignocaine as a medium for cuff inflation offers any benefit over routinely used medium i.e. air. Considering possibility of toxicity of local anesthetic the amount of lignocaine used in the present study was less i.e. 2% Lignocaine 5 ml - 7 ml (100-140 mg) for patients weighing between 35 to 60 kg.

In our study, mean intra-cuff volume required for leak proof inflation of cuff was statistically comparable in all three groups (p value 0.384). This finding supports the study of Malhotra S. at al [22]. While Helena L [23] et al demonstrated that the median intracuff volume at inflation of cuff was 5.0 ml in group A and 6.5 ml in group L. The intra-cuff volume at inflation was more in group L as compared to group A. This was not observed in the present study and in the study of Malhotra S et al which may be because in these studies cuff was inflated preoperatively with lignocaine 2% for 90 min. to saturate the receptors which was not followed by Helena L et al [23].

We found statistically significant increase in intra-cuff volume at the time of extubation in group A which was in accordance with study of Malhotra S [22] and Helena L et al [23]. However, the fall in intra-cuff volume at the time of extubation in group 'NS' and 'L' observed in present study can be attributed to diffusion of normal saline and lignocaine from the endotracheal tube cuff which was also seen in study of Sconozo JM [24] , Altintas F et al [25] .This fall in intra-cuff volume at the time of extubation was statistically insignificant. However, Helena L et al [23] also observed fall in intra-cuff volume in group L at the time of extubation which was stastically

significant as they did not practice technique of presaturation of cuff receptors.

Initial intra-cuff pressure in all the three groups of present study was comparable (in range of 20-21.5 cm H2O) as well as with Helena et al [23] . According to Mehta S et al [18], the intra-cuff pressure of 25-30 cm of H_2O prevents aspiration of gastric contents. However in present study as well as in that of Helena L et al [23] the intra-cuff pressure was not adjusted exactly to 25-30 cm of H2O and its mean was in the range of 20-21.5 cm H2O and 20 cm of H2O respectively, still none of our patient had obvious evidence of aspiration.

In our study, we reported statistically significant progressive rise in intra-cuff pressure in group A when measured at hourly intervals (p - value 0.0281) also at the end of surgery (from 21.2 ± 3.03 to 28.4 ± 3.97 cm of H_2O). This finding correlates with the findings of Benette MH et al [26], Nguyen TU et al [27], Malhotra S et al [22] and Helena L et al [23]. This is because air inflated cuff within trachea represents a gas filled pocket in the body. The blood/gas solubility coefficient is 0.468 and 0.013 for nitrous oxide and nitrogen respectively which facilitates the diffusion of nitrous oxide into the cuff. Nitrous oxide diffuses inside an air space faster than nitrogen can escape. This leads to increase in both volume and pressure inside an air filled cuff [28] .

The final rise in intra-cuff pressure observed in normal saline and lignocaine 2% group was not significant. Our observations support the findings others [22], [25], [26]. Under ideal circumstances, there should be no change in intra-cuff pressure in the normal saline and lignocaine groups. The reason for this minimal rise in intra-cuff pressure could be explained by a small amount of air, which can be present in the PVC tube cuff even after deflation of cuff and when the cuff was inflated with liquid, air bubble was difficult to remove. So, Nitrous oxide gas diffusion into the air bubble may be responsible for small rise in intra-cuff pressure.

Nitrous oxide is 34 times more soluble than nitrogen in blood. The blood/gas solubility coefficient is 0.468 and 0.013 for nitrous oxide and nitrogen respectively which facilitates faster diffusion of nitrous oxide into the cuff especially in air space. The water / gas solubility coefficient of nitrous oxide is 0.435 hence it is obvious that the blood / water solubility coefficient of nitrous oxide (0.468/0.435) is near unity hence there is no net influx of nitrous oxide if liquid is used to inflate the cuff. Hence water or saline can be used to inflate the cuff of the tracheal tubes, the change in cuff volume and pressure would be minimal [9] .The findings in present study support it. Liquid medium with local anesthetic (e.g. 2% Lignocaine) can offer same benefits of stable intracuff pressure [25] and the cuff acts as a potential reservoir for local anesthetic allowing diffusion and subsequent anesthesia of the underlying mucosa [44] .This may help to reduce the incidence of postoperative tracheal morbidity because of diffusion from the cuff.

Postoperatively, after 24 hours the incidence of hoarseness of voice was maximum in group A as compared in group NS and in group L. The severity of hoarseness was grade 1 (noted by the patient). In all the three groups, none of the patient in the present study had hoarseness of grade 2 (obvious to observer) and 3 (Aphonia). When this incidence was correlated with the increase in intra-cuff pressure, it was obvious that the rise in intra-cuff pressure results in more incidence of hoarseness in group A as compared to group NS and group L. This supports the observations of Malhotra et al [22], Helena et al [23] and Ali et al [29].

However, the severity of hoarseness in the present study was less (Grade 1) as compared to Malhotra (Grade 2). The final rise in intra-cuff pressure in Malhotra's study was almost double as compared to present study, which may be responsible for the higher severity of hoarseness in their study.

Similarly, the severity of sore throat was grade 1 (mild-scratchy throat) in all the three groups. None of the patient in the present study had sore throat of Grade 2 (moderate, similar to that noted with cold) and 3 (severe, more severe than with cold). When this incidence was correlated with the increase in intra-cuff pressure, it was obvious that the rise in intra-cuff pressure results in higher incidence of sore throat as in group A compared to group NS and L. This observation in the present study supports the observation of Malhotra S et al [22] and correlate well with the findings of Combes X et al [2], Altintas F et al [25], Ali et al [29] and Navarro RM et al [19].

The occurrence of sore throat even when endotracheal tube cuff pressure was not significantly raised, suggest that this may due to the use of high volume low pressure cuffs. Loeser EA et al [12] in 1980 said that tracheal intubation with either cuffed or uncuffed disposable PVC tube produces a greater incidence and severity of post operative sore throat than mask anesthesia. Their findings support the results of present study.

The maximum number of patients from group A complained of dysphagia postoperatively as

compared to patients from group NS and group L. Thus the incidence of dysphagia also shows a close relation with the rise in intra-cuff pressure in the present study. Malhotra S et al [22] and Combes X et al [2] encountered patients of dysphagia in the post-operative period when they used air, saline as well as lignocaine for inflation of cuff. They were not able to demonstrate any correlation between the rise in intra-cuff pressure and the incidence of dysphagia as observed in the present study.

Conclusions

Inflating cuff endotracheal tube with air causes progressive and significant rise in intra-cuff pressure and volume as the duration of intubation increases.

Considering the findings & observations of the study, Normal saline and 2% Lignocaine seemed to be beneficial than Air for inflation of cuff especially when N2O is used as a part of balanced anesthesia in patients requiring prolonged duration of endotracheal intubation for general anesthesia to reduce the incidence of post operative tracheal morbidity.

If air is used for inflation of cuff, intra-cuff pressure should be monitored at regular interval and should be controlled to reduce the incidence and severity of post operative tracheal morbidity.

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Original Article

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The Effect of Intrathecal Dexmedetomidine as an Adjuvant to Spinal Anesthesia: Double Blind Study

Shah Bipin K.*, Chaudhary Asmita*, Chhanwal Heena, Chadha Indu A.*****

Abstract

Dexmedetomidine is a highly selective á$_2$adrenoreceptor agonist recently introduced to anesthesia. It produces dose dependent sedation, anxiolysis and analgesia without respiratory depression. *Methods*: This prospective randomized double-blind study was carried out on 100 patients, aged 20 to 70 years with American society of Anesthesiology (ASA) class I and II of either gender, for lower limb surgery, who met the inclusion criteria of spinal anesthesia. The randomly selected patients received Bupivacaine 0.5% 15 mg (3ml) + 0.5 ml of normal saline in group BS (n=50) and Bupivacaine 0.5% 15 mg (3ml) +Dexmedetomidine 10 mcg in 0.5ml NS in group BD(n=50). The onset time to reach sensory and motor level, the regression time of sensory and motor block, requirement of first rescue analgesic, hemodynamic changes and side-effects if any were recorded. *Result:* The onset time to reach T10 dermatome and modified bromage 3 motor blocks were not significantly different between the groups. Time to achieve sensory regression to L1 in Group BD (284.4±62.84 min) were prolonged as compare to Group BS (149.3±24.91min) (p=0.00). The regression time of motor block to reach modified bromage 0 was (379.5±75.42 min) and (231.6 ±44.55 min) in group BD and BS respectively (p=0.004). The first rescue analgesic was required at 200.90 ± 40.33 min and 327.60 ± 60.05 min in group BS and group BD respectively, were comparable (p=0.104). *Conclusion*: Intrathecal Dexmedetomidine as an adjuvant to intrathecal Bupivacaine prolong sensory and motor block with minimal side effects. So it is an attractive alternative choice for long duration surgery.

Keywords: Bupivacaine; Dexmedetomidine; Lower Limb Surgery; Spinal Anesthesia.

Introduction

Spinal anesthesia is a simple technique with rapid onset of action and usually used for patients undergoing below umbilical surgery. Various adjutants like Buprenorphine, Ketamin, Tramadol, Midazolam, Ramifentanyl, Sufetanyl, Pethidine, Various adjuncts have been used to prolong the analgesic effect of bupivacaine. Intrathecal use of clonidine and fentanyl has been shown to significantly increase the duration of spinal anesthesia. [1-5].

Intrathecal α_2 receptor agonists have antinociceptive action for both somatic and visceral pain. Dexmedetomidine shows more specificity towards á$_2$ receptor (α_2/α_1 1600:1) compared with clonidine (α_2/α_1 200:1) [6]. Several studies have shown that á$_2$ receptor agonists when administered intrathecal will enhance the analgesia provided by sub therapeutic doses of local anesthetics like bupivacaine due to synergistic effects with minimal hemodynamic effects [6,7,8.].

Materials and Methods

After approval from Institutional Ethics Committee a prospective randomized double blind study was conducted on 100 adults of either sex belonging to American Society of Anesthesiology (ASA) class I and II. The selected patients scheduled for lower limb surgery under spinal anesthesia. Patients with contraindication to spinal Anesthesia, history of spine surgery, infection at the injection site, coagulopathy, and pre existing cardiac disease, neurological disorders, allergic to

Author's Affiliation:
*Associate Professor, **Professor and Head, ***Professor, Department of Anesthesia, GCS Medical College, Hospital and Research Centre, Ahmedabad.

Corresponding Author:
Bipin K. Shah, 3, Navkar Bunglow, Merchant Park Society, Near Sejal Palace Flats, Jain Merchant Cross Road, Paldi, Ahmedabad- 380007.
E-mail: bipinkant@gmail.com. asmivip@yahoo.co.in

study drugs, psychiatric illness and pregnancy were excluded from the study.

All patients were examined and investigated a day prior to surgery, and were taught to scale their pain on VAS scale in post operative period [9]. They were advised fasting for 6 hours and Tab. Alprazolam 0.5 mg at night before surgery.

All patients were randomly divided in to two groups of 50 each. To provide double-blindness, three anesthesiologists were involved in the study. One anesthesiologist prepared the drug, another gave spinal anesthesia and data were recorded by an independent third anesthesiologist who was unaware of group allocation, patients were also unaware of the drug regimen received.

Group BS: received 3 ml of 0.5% Bupivacaine (15 mg)+0.5 ml NS.

Group BD: received 3 ml of 0.5% Bupivacaine (15mg) + Dexmedetomidine 10μg in 0.5 ml NS.

In the operation theatre ECG, pulse oximetry and non invasive blood pressure were attached and baseline parameters of each patient were recorded. Intravenous access was secured and all patients were preloaded with an infusion of 500 ml ringer lactate. Subarachnoid block was administered at the level L_{2-3} or L_{3-4} using 25G spinal needles with patient in the sitting position under aseptic and antiseptic precaution.

Demographic data such as age, weight, height, type and duration of surgery were noted. The sensory block was assessed by pinprick method (26G hypodermic needle) in mid-clavicular line bilaterally, loss of sensation to pin prick was considered as sensory block. Motor block was assessed according to the modified Bromage scale [10].

0: Patient able to move hip, knee, ankle.

1: Unable to move hip, able to move knee and ankle.

2: Unable to move hip and knee, able to move ankle.

3: Unable to move hip, knee and ankle.

Time to reach T10 dermatome sensory block and Bromage 3 motor block were noted. All time durations were calculated considering the time of spinal injection as time zero. Sensory and motor block level were recorded every 2 min for 20 min. Heart rate (HR), mean arterial blood pressure (MAP) and oxygen saturation were monitored and recorded after the block every 5 minutes for half an hour then every 15 minutes until the end of surgery.

Intraoperative sedation was measured every 15 min using Ramsay sedation score [11].

After operation HR, MAP, oxygen saturation, sedation score and VAS score were recorded during the first hour at 15 min interval, and thereafter every hour up to 8 hour then at 12hour and 24 hour. The time from intrathecal injection to sensory regression to L_1 dermatome and motor block regression to modified Bromage 0 were recorded. All time durations were calculated in relation to the time of spinal injection. Duration of pain relief was defined as the time from spinal injection to the first request for rescue analgesics. Post operative pain was accessed by VAS Score and if VAS score >3, Inj. Tramadol 100 mg diluted in 100 ml NS was given IV as a rescue analgesic. Occurrence of nausea, vomiting, pruritus and respiratory depression were recorded throughout the study duration. Hypotension (defined as adecrease in systolic blood pressure > 30% of the baseline value or systolic blood pressure < 90 mm Hg) was treated with Inj. Ephedrine 6 mg. Bradycardia defined as a pulse rate of < 50 beat/ min was treated with Inj. Atropine 0.3- 0.5 mg. Respiratory depression (RR <8 or SpO2 < 95%) was treated with oxygen supplementation and respiratory support if required. All data were observed and collected by third observer.

Statistical Analysis

Statistical analysis was done by SPSS version. Data was expressed as means and standard deviation (SD), medians and ranges. The comparison was studied using Fisher's exact test as appropriate, with P value reported at the 95% confidence interval (CI). $P \leq 0.05$ was considered statistically significant

Results

Both the groups were comparable with respect to age, height, weight, sex, and ASA physical status. There was no significant difference in the type and duration of surgery (Table 1).

Sedation was analyzed by Ramsay sedation score. In Group BS 45 (90%) patients achieved sedation score 2 and 5(10%) patients achieved sedation score 1. In group BD 40(80%) patients achieved sedation score 3 and 10(20%) patients achieved sedation score 2 (Table 2).

The time to reach T-10 sensory level (Group BS/ BD=3.55±0.71/2.75±0.85 min) was statistically not significant ($p > 0.05$). The median and range of the peak sensory level reached were T8 (T6 –T10) in group BS and T6 (T4-T10) in group BD, not statistically

different among the groups.

All patients in Group BD achieved modified bromage 3 motor block (4.020 ± 1.70 min), while in group BS 48 (96%) patients achieved modified bromage 3 motor block (8.268 ± 2.75 min),) which was statistically not significant (p=0.062), (Table3).

Time to achieve sensory level regression to L1 in Group BD (284.4±62.84 min) were prolonged as compare to Group BS (149.3±24.91 min), which was statically significant (p=0.00).

Time to achieve motor block regression to modified bromage 0 in Group BD (379.5±75.42 min) were significantly prolong as compare to Group BS (231.6 ±44.55 min) (p=0.004).

Post operative pain was accessed by VAS Score and if VAS score >3, Inj Tramadol 100 mg diluted in 100 ml NS was given intravenous as a rescue analgesic. Time of requirement of the first rescue analgesic in Group BS was 200.90 ± 40.33 min and in Group BD 327.60 ± 60.05 min were comparable, (p=0.104). The requirement of first rescue analgesic was prolonged in Group BD.

The mean values of MAP and HR were comparable between the two groups throughout the study. After 15 min of spinal anesthesia mean MAP was 74.9 mm Hg in Group BD and mean MAP 85.35 mm Hg in Group BS (non significant).

Both group showed a fall in HR after 15 min of spinal anesthesia. Mean HR in Group BS was 77.6 / min and in Group BD was 70.07/ min (non significant).

The most common intraoperative adverse effect were Hypotension /bradycardia, were observed 30% (n=15)/20 %(n=10) in Group BD and 16% (n=8) /6 %(n=3) in Group BS respectively. Inj Ephedrine 6 mg was used to treat hypotension in 8 patients from Group BD and 2 patients from Group BS. Inj Atropine 0.3-0.5 mg was used to treat bradycardia.

Incidence of vomiting was observed in 3 patients in Group in BS and 8 patients in Group BD at different intervals of time, which was treated with Inj Ondansetrone 4 mg.

Table 1: Demographic data

Patients data	BS group	BD group
Age (year)	41 ± 4	42 ± 6
Sex (M/F)	28/32	29/31
Weight (kg)	55 ± 4	58 ± 6
Height (cm)	156 ± 8	160 ± 7
Duration of Surgery	130 ± 35	138 ± 40

Table 2: Ramsay sedation score

Ramsay score	Group BS	Group BD
1	5(10%)	-
2	45(90%)	10(20%)
3	-	40(80%)

Table 3:

Variable (min)	BS group (n = 50)	BD group (n = 50)	F Test	p value
Time to reach T10 Sensory level	3.5510 ± 0.71	2.747 8± 0.85	1.748	.189
Time to reach BR-3	8.268 ± 2.75	4.020 ± 1.70	3.577	.062
Time to regression L1 sensory level	149.30 ± 24.91	284.40 ± 62.84	29.249	.000
Time to regression BR-0	231.60 ± 44.55	379.50 ± 75.42	8.768	.004
Time for rescue analgesic	200.90 ± 40.33	327.60 ± 60.05	2.693	.104

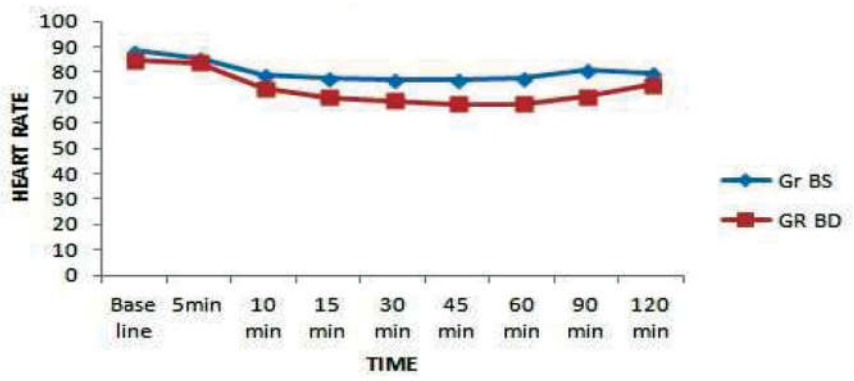

Fig. 1: Comparison of heart rate

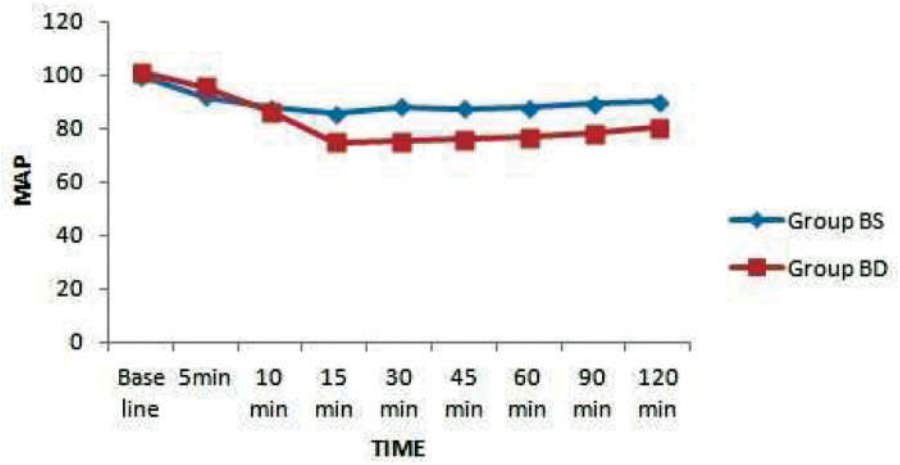

Fig. 2: Comparison of MAP

Discussion

In this study 100 patients were randomly divided in to two groups of 50 each. Group BS: received 3 ml of 0.5% Bupivacaine (15 mg) + 0.5 ml NS. Group BD: received 3 ml of 0.5% Bupivacaine (15mg) + Dexmedetomidine 10µg in 0.5 ml NS. Our study shows significant prolongation of the duration of spinal anesthesia by intrathecal administration of dexmedetomidine as an adjunct to hyperbaric bupivacaine for patients undergoing lower limb surgery.

Dexmedetomidine is a α_2 adrenoreceptor agonist which has about ten times higher affinity for α_2 adrenoreceptor than clonidine [12-14]. The intrathecal use of other α_2- agonist clonidine for postoperative analgesia alone [15]or co-administered with local anesthetics [3, 4, 5]or opioids [16] has been studied previously. It is thought that intrathecal Dexmedetomidine produces its analgesic effect by inhibiting the release of C fibers transmitters and by hyperpolarization of post-synaptic dorsal

Horn neurons [17] the prolongation of motor effect might be caused by direct impairment of excitatory amino acid release from spinal interneuron [18]. The complementary action of local anesthetics and α_2 adrenoreceptor agonists accounts for their profound analgesic properties. The prolongation of the motor block of spinal anesthetics may be the result of binding of α_2 adrenoreceptor agonists to the motor neurons in the dorsal horn[19,20].

In current study patients who received Dexmedetomidine shows significantly delayed requirement of rescue analgesic than those who received spinal bupivacaine alone. Hala et al concluded that intrathecal Dexmedetomidine in doses of 10µg and 15µg significantly prolong the anesthetic and analgesic effects of spinal hyperbaric bupivacaine in a dose- dependent manner which is similar to our study [21].

Vidhi et al studied that intrathecal Dexmedetomidine is associated with prolonged motor and sensory block, hemodynamic stability, and reduced demand of rescue analgesics in 24 hours as compared to clonidine, fentanyl or lone bupivacaine [2].

Kanazi et al [19] reported that intrathecal dexmedetomidine 3 µg were equipotent to intrathecal clonidine 30 µg when used with bupivacaine for spinal anesthesia.

In our study intrathecal 10mcg of Dexme zdetomidine (group BD) achieved T10 sensory level at 2.75±0.85 min, which is very short compare to Hala (7.7±3.6 min) [21]. Intrathecal Dexmedetomidine as an adjuvant is beneficial for lengthy complex surgery as an alternative to epidural or prolonged general anesthesia.

Hem Anand et al studied the Dexmedetomidine and fentanyl along with low dose bupivacaine for lower abdominal surgery and concluded that Dexmedetomidine facilitate the spread of the block and offers prolonged post operative analgesia [1].

Most of the clinical experience gained in the use of intrathecal α_2 adrenoreceptor agonists has been described with clonidine [22, 23] and there has been a need for more clinical studies related to intrathecaldexmedetomidine to prove its efficacy, safety, and the suitable dose for supplementation to spinal local anesthetics. In our study, the intrathecal dose of dexmedetomidine selected was based on previous human studies wherein no neurotoxic effects

have been observed [20, 24].

In our study total duration to achieve motor block bromage 3 was 8.27±2.75 min in BS group and 4.02±1.7 min in BD Group (p =0.062).

Udita et al studied intrathecaldexmedetomidine group achieved motor block Bromage 3 was 6.61±2.18 min[25], which shows 10 mcg intrathecal Dexmedetomidine has fast onset of motor block as compare to 5 mcg of intrathecal Dexmedetomidine.

The most significant side effects were reported with the use of intrathecal α_2 adrenoreceptor agonists were bradycardia and hypotension [26].

We observed hypotension and bradycardia in 30% (n=15), 20%(n=10)in Group BD and 16% (n=8) ,6%(n=3) in Group BS respectively. Inj Ephedrine was used to treat hypotension in 8 patients from Group BD and 2 patients from Group BS. Inj Atropine was used to treat bradycardia. Incidence of vomiting was observed in 3 patients in Group in BS and 8 patients in Group BD at different intervals of time, which was treated with Inj Ondansetrone.

We noted significantly delayed requirement of rescue analgesic with 10 µg Dexmedetomidine when compared to Bupivacaine with NS (p=0.104)[24,27].

Intrathecal Dexmedetomidine as an adjuvant to intrathecal Bupivacaine prolong sensory and motor block with minimal side effects. So it is an attractive alternative choice for long duration surgery.

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Original Article

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A Prospective Randomized Double Blind Study for Comparative Evaluation of Bupivacaine with Two Different Doses of Clonidine for Pediatric Caudal Analgesia in Infra Umbilical Surgeries

Panwar Dinesh*, Sabharwal Nikki, Sahni Amita***, Diwan Sahil***

Abstract

Introduction: We designed a double blind randomized controlled trial to comparatively evaluate the efficacy of bupivacaine with two different doses of clonidine for pediatric caudal analgesia in infra umbilical surgeries. *Methodology:* 90 children, 2-10 years of age, weight < 20 kg of either sex, belonging to ASA grade I and scheduled for infra umbilical surgeries were taken up for the study. Patients were divided randomly into three groups of 30 each using the computer generated technique- Group 1- 0.75 ml/ kg of 0.25% bupivacaine and 1µg/ kg of clonidine; Group 2 - 0.75 ml/ kg of 0.25% bupivacaine and 2µg/ kg of clonidine. Group 3: 0.75 ml/ kg of 0.25% bupivacaine. 0.75 ml/ kg of the study drug solution was injected after administration of anaesthesia. Post operative monitoring for heart rate, blood pressure, respiratory rate, SpO_2; Post operative analgesia- using Modified Objective Pain Score. Post operative sedation score using the Four Point Sedation Score was done at the interval of 0, ½, 1, 2,4,8,12,24 hours. *Results:* Efficacy of Post operative analgesia assessed by MOPS score was found to be better in group 2 followed by group 1 and least in group 3. Also, post operative sedation score was highest in Group 2 as compared to group 1 & 3. *Conclusion:* We recommend a dose of 1µg/kg clonidine as an adjuvant to 0.25% bupivacaine (0.75ml/kg) for infra-umbilical surgeries to significantly prolong post-operative analgesia without causing significant sedation. Increasing the dose of clonidine to 2µg/kg didn't significantly prolong postoperative analgesia but did produce significant sedation, which might interfere with discharge criteria for day care surgery.

Keywords: Pediatric Caudal Analgesia; Infra Umbilical Surgeries; Clonidine; Bupivacaine.

Introduction & Background

Caudal epidural analgesia is a reliable and safe technique that can be used with general anaesthesia for infra umbilical and post operative analgesia in patients undergoing lower abdominal, urological and lower limb surgeries [1,2].

The major limitation of single injection technique is the relatively short duration of post operative analgesia (4-6 hr) that accompanies the use of even long acting local anesthetic agent like bupivacaine [2,3]. The most frequently used method to further prolong post operative analgesia following caudal block is to add different adjuncts to local anesthetic solutions each of which has its limitations including significant side effects like respiratory depression, nausea, vomiting, urinary retention, pruritis and neurotoxicity [1,2,3].

Clonidine, an α_2 adrenergic agonist, produces analgesia without significant respiratory depression after systemic, epidural or intrathecal administration. Although epidural clonidine has been associated with reduction in heart rate and arterial pressure in adults, these hemodynamic side effects appear to be less pronounced in children [2,10]. The analgesic action of intrathecal or epidural clonidine results from direct stimulation of pre and postsynaptic α_2 adrenergic receptors in the dorsal horn grey matter of the spinal cord, inhibiting the release of nociceptive neurotransmitters [2,6].

Many studies have shown that addition of clonidine to epidurally administered bupivacaine prolongs the duration of post operative analgesia in children. However doses of clonidine used by different authors are variable

Author's Affiliation:
*Attending Consultant, Anaesthesia, Max Superspeciality Hospital, Delhi **Senior Consultant *** Senior Specialist, Anaesthesiology, Safdarjung Hospital & VMMC.

Corresponding Author:
Dinesh Panwar, Attending Consultant, 86-A, Radheshyam Park, Parwana Road, Delhi 110051.
E-mail: drdineshpanwar@gmail.com, nikkisab71@hotmail.com

[1,2,3].

W. Klimscha et al (1998) studied the efficacy and safety of clonidine and bupivacaine combination in caudal blockade for pediatric hernia repair in 58 patients. These authors reported significantly longer duration of analgesia with 0.25% bupivacaine 0.75 ml/kg combined either with 1 µg/kg clonidine (median 360 minutes) or clonidine 2 µg/kg (median 360 minutes) as compared to bupivacaine with or without epinephrine 1: 200000 (300-340 minutes respectively) in a 6 hour observation period. They also observed that clonidine group in their study required significantly lesser supplementary analgesia within the first 24 hrs [1].

In 1993, a study by J.J.Lee et al in 40 children aged 1 to 10 years undergoing elective orthopedic surgeries assessed the efficacy of combining clonidine with bupivacaine for caudal analgesia. Their study revealed that addition of clonidine 2 µg/kg to 0.25% bupivacaine 1 ml/kg significantly prolonged the duration of caudal analgesia compared with that provided by bupivacaine alone (9.8 hrs. and 5.2hrs. respectively) , without an increase in the incidence of side effects in children undergoing orthopedic surgeries. However, the duration of analgesia was considerably shorter than that reported by Jamali and colleagues (mean of 987 mins) for the clonidine group, despite the administration of twice the amount of clonidine in their study [9].

Samir Jamali et al (1994) assessed the efficacy of clonidine with bupivacaine compared to epinephrine and bupivacaine for caudal analgesia in 45 pediatric patients of ages 1 to 7 years, scheduled for sub-umbilical surgeries. Their study demonstrated that addition of 1µg/ kg of clonidine to a caudal block with 0.25 % bupivacaine 1 ml/kg as compared with bupivacaine with and without epinephrine, increases the duration of post operative analgesia in pediatric patients, the mean duration of analgesia being 16.8 hrs, 4.7 hrs and 7.5 hrs for clonidine, epinephrine and plain bupivacaine groups respectively [7].

DA. H de Beer and M. L. Thomas (2003) in the review article on caudal additives in children had observed that caudal analgesia remained the most popular and commonly used regional block in pediatric Anaesthesia. They have stated that bupivacaine is the most widely used local anesthetic used for this technique and provides post operative analgesia lasting 4 to 8 hours. They have also stated that extended duration of analgesia that can be achieved by using caudal additives is significant but whether the perceived benefits justified the potential risks and which is the ideal agent needs further study. Clonidine as an additive to caudal bupivacaine, has been shown to improve the efficacy and duration of post-operative analgesia in children by several authors, however the duration of analgesia varies widely in these studies [2].

James Eisenaah et al (1993) studied the hemodynamic and analgesic action of epidurally administered clonidine (lumbar epidural) in nine adult volunteers. They monitored the BP/HR, finger and toe blood flow and response to cold pain testing while sampling CSF & arterial plasma for clonidine analysis. They correlated the effects to plasma and CSF clonidine concentration. They concluded that in comparison to potent opioid Alfentanyl administered as IV infusion to other volunteers, epidural clonidine produces a similar degree of analgesia but less respiratory depression [5].

A.M.EL.Hennaway et al (2009) studied the efficacy of addition of clonidine or dexmedetomidine to bupivacaine for prolonging paediatric caudal analgesia in 60 children. They concluded that addition of dexmedetomidine 2 µg/kg or clonidine 2 µg/kg to caudal bupivaciane 0.25 % of 1 ml/kg significantly promotes analgesia time after anesthetic recovery in children aged 6 months to 6 years, undergoing lower abdominal surgeries without increasing the side effects. Moreover, dexmedetomidine did not offer significant advantages over clonidnine with regard to the analgesia duration [8].

Archana Kaul et al (2009) evaluated the analgesic efficacy, hemodynamic and respiratory safety of clonidine 2 µg/kg with 0.25% bupivacaine 0.75 ml/kg for caudal block in 40 children undergoing inguinal hernia repair. They concluded that addition of clonidine in caudal block prolongs post operative pain relief in children (10.25± 3 hrs) and is a safe alternative to bupivacaine alone in pediatric day care surgeries [10].

We, therefore, designed a double blind randomized controlled trial to comparatively evaluate the efficacy of bupivacaine with two different doses of clonidine for pediatric caudal analgesia in infra umbilical surgeries.

Aims and Objectives

1. To evaluate the efficacy of two different doses of clonidine as an adjuvant to caudal bupivacaine for providing postoperative analgesia in pediatric patients undergoing infra umbilical surgeries.
2. To compare the above two groups with bupivacaine alone for caudal analgesia in

pediatric patients undergoing infra umbilical surgeries.

Materials and Methods

After obtaining approval of the hospital ethics committee, this randomized controlled double blind study was conducted in the department of Anaesthesia and Intensive care, Safdarjung hospital & VMMC, New Delhi.

Patient Selection

90 children, 2-10 years of age, weight < 20 kg of either sex, belonging to ASA grade I and scheduled for infra umbilical surgeries were taken up for the study. Patients were divided randomly into three groups of 30 each using the computer generated technique.

Group 1: 0.75 ml/ kg of 0.25% bupivacaine and 1µg/ kg of clonidine.

Group 2: 0.75 ml/ kg of 0.25% bupivacaine and 2µg/ kg of clonidine

Group 3: 0.75 ml/ kg of 0.25% bupivacaine.

Exclusion Criteria

- History of allergic reaction to local anesthetics.
- Bleeding diathesis.
- Pre existing neurological and spinal disease.
- Local and systemic infections.
- Parental refusal.

Pre Operative Preparation

A detailed pre anaesthetic check up was done for all patients as per standard protocol. Parents of children were explained about the procedure and nature of the study and informed consent was obtained from them explaining all the risk and benefits. All children were premedicated with Syrup Trichlofos 70 mg/kg two hours before procedure.

Anesthetic Technique and Intraoperative Management

Induction

All patients were administered general Anaesthesia with inhalational induction using O_2/ N_2O (50:50) and Sevoflurane 6-8 % using Jackson-Rees modification of Ayre's T piece and face mask. Intravenous line was secured immediately after induction. Fentanyl in a dose of 2 µg/ kg was administered intravenously. An appropriate sized Proseal LMA was inserted and proper positioning confirmed by auscultation and Capnography.

Caudal Block

The child was then turned to the left lateral position and caudal block was administered under aseptic precautions using a 23G hypodermic needle of short bevel and a total volume of 0.75 ml/kg of the study drug solution was injected after ensuring proper placement of the needle at 45° to the skin by repeated negative aspiration for CSF and blood.

Maintenance

Anaesthesia was maintained with O_2/N_2O (33:67%) and sevoflurane 2-4% with manual assistance and a fresh gas flow of 2-3 times the minute ventilation. Intravenous fluid given intra operatively was ringer lactate in standard doses. Any decrease in mean arterial pressure or heart rate more than 30% of baseline value was defined as severe hypotension or bradycardia respectively and treated with rapid infusion of intravenous fluid with injection ephedrine and atropine.

Rescue analgesia with syrup paracetamol (20 mg/ kg) or injection paracetamol (10 mg/kg IM) if patient not allowed orally, was given only on demand or if the pain score is more than equal to 4.The total dose of rescue analgesia administered in 24 hrs was noted.

Intraoperative Monitoring

Intraoperative monitoring included the following parameters which were recorded before operation and every five minutes until the end of surgery.

1. Heart rate
2. Blood Pressure
3. Respiratory Rate
4. SpO_2
5. Et CO_2
6. ECG

Reversal

At the completion of surgery, all anaesthetic agents were discontinued and LMA removed after patient was awake. Patient was then transferred to recovery room.

Post Operative Monitoring

Patient was monitored for two hours in the recovery room and subsequently in the pediatric ward for up to 24 hours after surgery. Following parameters were monitored at the interval of 0,1/2,1, 2,4,8,12,24 hours.

1. Vital parameters- heart rate, blood pressure, respiratory rate, SpO_2.
2. Post operative analgesia- Pain scoring was done using Modified Objective Pain Score (MOPS).
3. Post operative sedation score was assessed using the Four Point Sedation Score
4. Patient was evaluated for any other side effects like Pruritis, Nausea and vomiting, Urinary retention, Headache, Local hematoma and Motor block.

Post operative IV fluids were continued till patients were allowed orally.

Data Analysis & Results

The data was collected on a standard Proforma and tabulated. The data for continuous variables was analyzed in terms of Mean and Standard Deviation or Median with Interquartile Range. The Statistical significance of different variables was determined by Student's t- test/ non parametric Wilcoxon's Mann Whitney test as appropriate. The Chi- square/ Fisher exact test was applied for categorical variable. Statistical significance was determined at p- value < 0.05.

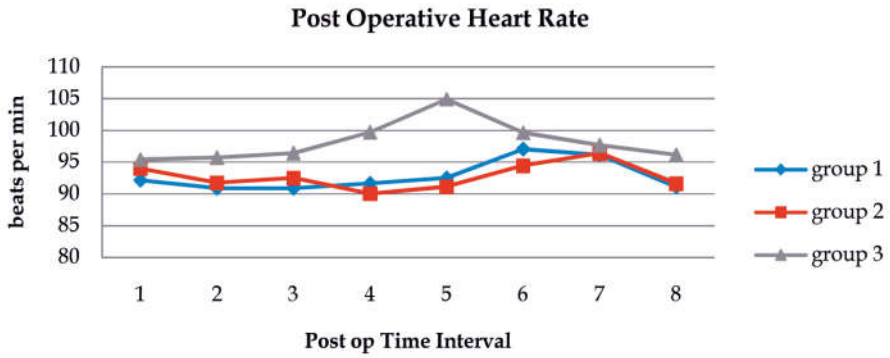
Baseline demographic parameters viz age (years), body weight(kg) and duration of surgery (min) of all three Groups was similar to each other. There is significant increase in post operative heart rate in Group 3 compared to Group 1 &2 at T2 (p=0.011) and T4 (p=0.000). Post operative heart rate in Group 1 &2 were comparable at all times. There is a significant increase in post operative mean arterial pressure in Group 3 compared to Group 1 & 2 at T4 (p= 0.046) and there is a significant increase in post operative mean arterial pressure in Group 1 compared to Group 2 & 3 at T8(p= 0.045). There is a significant increase in post operative respiratory rate in Group 3 compared to group 1 & 2 at T4(p=0.031) and there is a significant decrease in post operative respiratory rate in Group 3 compared to Group 1 & 2 at T8 (p= 0.001). Post operative respiratory rate of Group 1 &2 was comparable at all times.

Post operative analgesia as assessed by median of MOPS score showed that there was significant increase in Group 3 at T4 {5 (0-8)} as compared to Group 1{2 (0-6)} and group 2 {2(0-5)}. The median post operative sedation score from T0-T1 was highest in Group 2 as compared to Group 1 & 3 in which it was comparable. The total no. of rescue analgesics given in group 3 (46) was highest in comparison to Group 1 (22) & 2 (20).

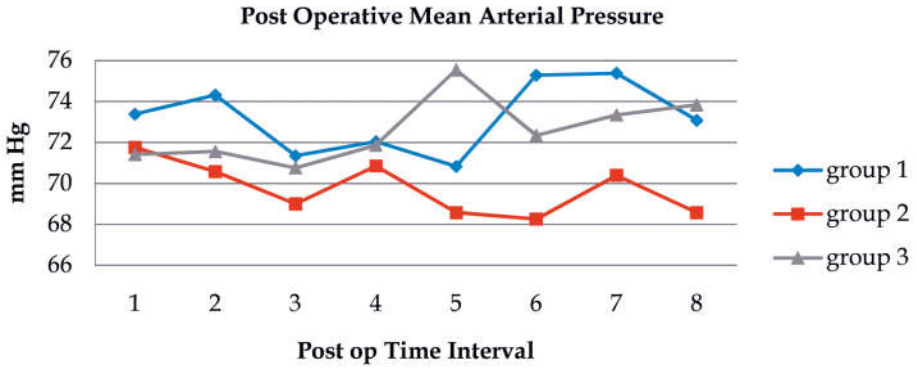
There was significant difference in the duration of analgesia between Group 1 and 3 and between Group

Table 1: Demographic distribution

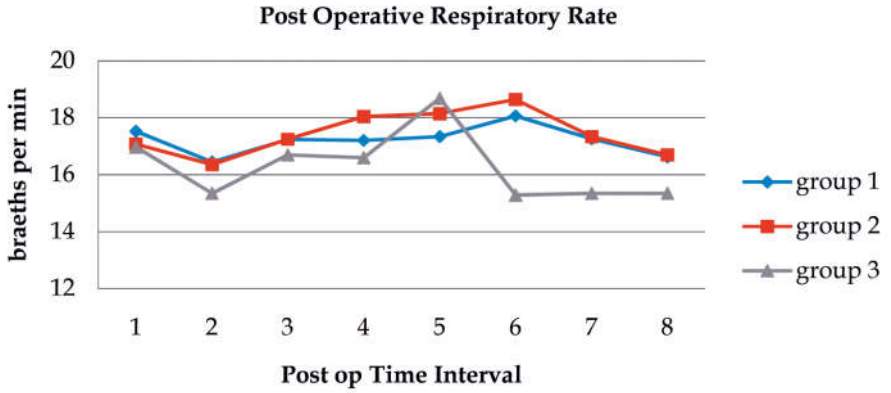
	Group 1	Group 2	Group 3	p-value
Age(years)	4.28±2.170	4.79±2.061	4.31±2.316	0.620
Weight(kg)	13.66±3.467	15.36±2.725	14.59±3.176	0.128
Duration of surgery (min)	38.55±13.341	35.89±12.914	36.55±17.066	0.773



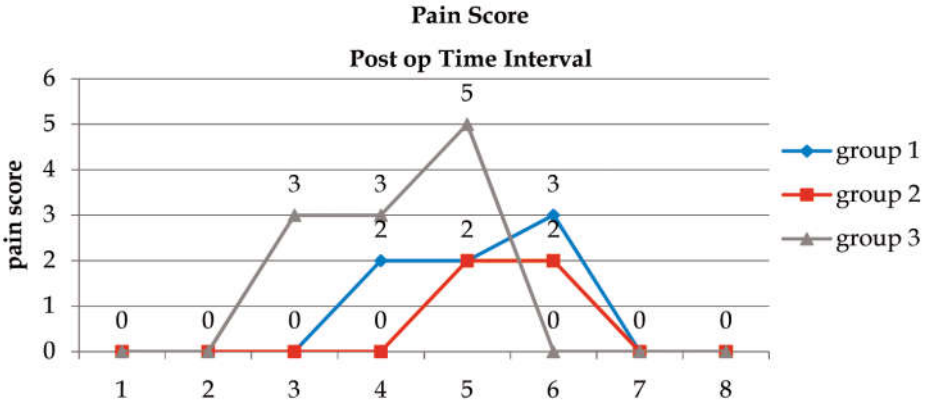
Graph 1: Comparison of Post operative heart rate in three groups



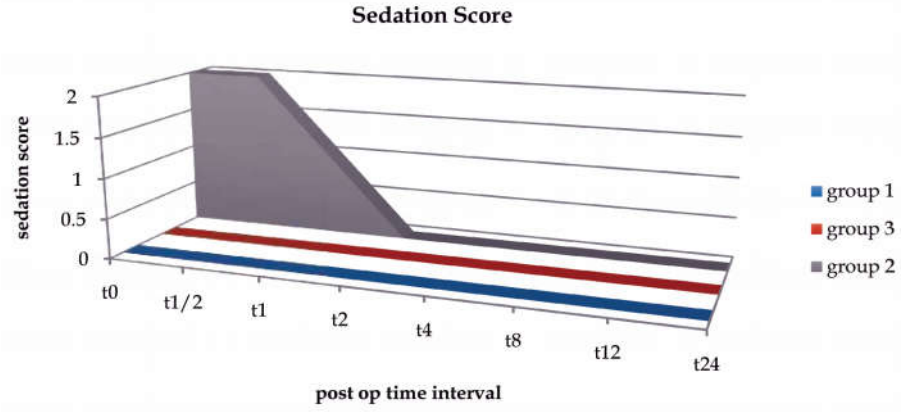
Graph 2: Comparison of Post operative Mean arterial Pressure in three groups



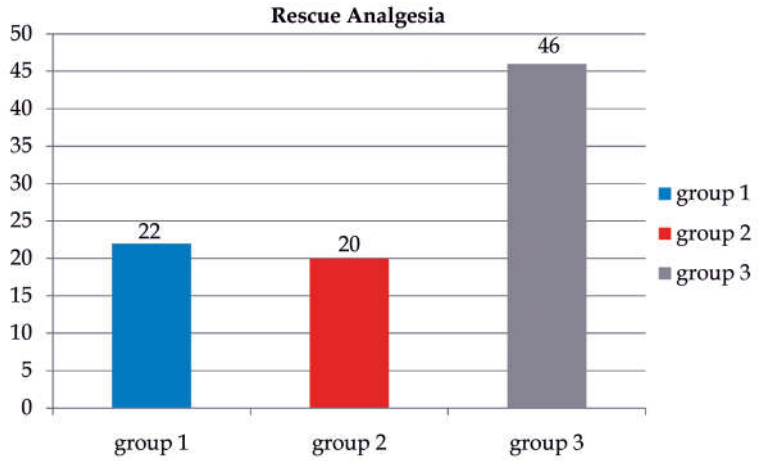
Graph 3: Comparison of Post operative Respiratory rate in three groups



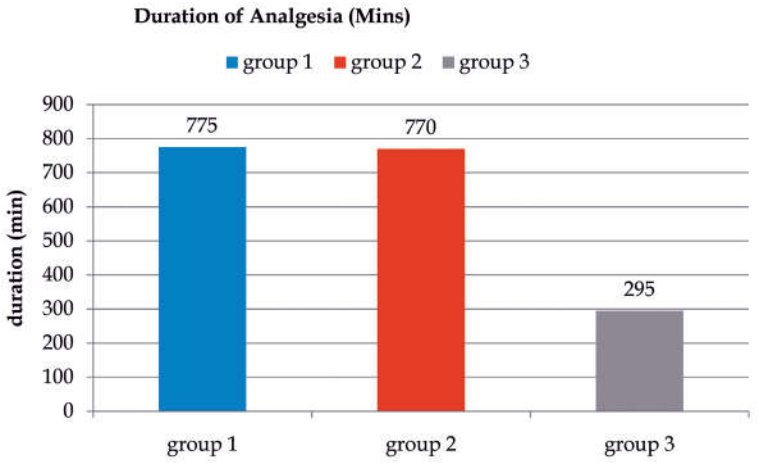
Graph 4: Comparison of Post operative Pain score in three groups



Graph 5: Comparison of Post operative sedation score in three groups



Graph 6: Comparison of rescue analgesia required in three groups



Graph 7: Comparison of duration of analgesia in three groups

2 and 3. ($p<0.05$). There was no significant difference in the duration of analgesia between group 1 and 2. ($p>0.05$).

Discussion

Caudal analgesia is a relatively simple technique with a predictable level of blockade, and is by far the most common regional anaesthetic used in paediatric surgery for lower abdominal, urological and lower limb surgery [1,2,9].

Clonidine, an α_2 adrenergic agonist produces analgesia without significant respiratory depression after epidural administration. Clonidines' analgesic effect is more pronounced after neuraxial injection, due to its action on spinal cord of inhibiting release of nociceptive neurotransmitters, and makes this route of administration preferable. The addition of clonidine prolongs the duration of action of bupivacaine after intrathecal and epidural administration in both children & adults (Klimscha 1995) [1].

Several authors have used clonidine as an adjuvant to 0.25% bupivacaine for caudal block in children with variable results [1,9,10,11,12]. In children, a mixture of 1 ml of 0.25% bupivacaine with 1-2 µg/kg clonidine significantly improves the duration and quality of caudal analgesia [1,9,12,13,15,21].

Although the results of different studies showed that clonidine when added to 0.25% bupivacaine for paediatric caudal analgesia prolonged the duration and improved the quality of post operative analgesia, the results differed widely. Moreover, clear advantages & disadvantages, if any, of the different doses of clonidine used, could not be ascertained. In an attempt to find out the optimal doses of caudal clonidine in children, we designed a double blind randomized controlled trial to comparatively evaluate the efficacy of bupivacaine with two different doses of clonidine for paediatric caudal analgesia in infra-umbilical surgeries.

In our study, the type of surgeries performed were mainly Herniotomies (n=34), Urethroplasties (n=23) and post burn split skin grafting (n=14) with others being Orchiopexy (n=6), phimosis(n=2), anal stenosis (n=3), Z- plasty (n=2) and cysto-lithotomy (n=2). All the three groups were comparable with respect to type of surgeries. The type of surgeries in the study groups of Klimscha et al [1] (hernia repair), Jamali et al [10] (sub-umbilical surgeries), Archna Koul et al(inguinal hernia repair) [13], Hennawey et al (lower abdominal surgeries) [8] and Parmeshwari et al (sub umbilical surgeries) were similar to our surgeries [11].

In our study, no statistically significant differences were observed between the three groups regarding intraoperative heart rate, mean arterial pressure, systolic blood pressure, diastolic blood pressure, respiratory rate, SpO_2, and $EtCO_2$,. All the three groups were comparable.

Post operatively, patients' vital parameters were monitored for 24 hours at time interval of 0, ½, 1,2,4,8,12 and 24 hours. The vital parameters monitored were heart rate, mean arterial pressure, respiratory rate, SpO_2, pain score, sedation score and duration of analgesia.

Efficacy of post operative analgesia assessed by MOPS score was found to be better in group 2 followed by group 1 and least in group 3. The distribution showed that median score of pain was highest in group 2 at T8 (Median 2 range 0-5) with maximum patients requiring analgesia between T4 to T8 i.e. between 4 to 8 hours post operatively. In group 1, the median score of pain was maximum at T8 (median 3, range 0-6) while for group 3 median score of pain was maximum at T4 (median 5 range 0-8). The reason for this is a shorter duration of analgesia i.e. 4 hours, for plain bupivacaine, used in group 3.

Duration of analgesia was assessed by the time from giving the caudal block to the first rescue analgesic. The median duration of analgesia (min) from application of caudal block to first rescue analgesic given to patients post operatively was 775min, 770 min and 295 min in group 1,2 and 3 respectively. There was a significant difference in the duration of analgesia between group1 and group3 and between group 2 and 3 but there was no significant difference between group 1 and 2. Klimscha too had shown in an earlier study that duration of analgesia was significantly longer {$p<0.05$} in bupivacaine and clonidine 1 µg/kg group and bupivacaine and clonidine 2 µg/kg group {median 360(range270-360)min.}and {median 360(355-360)min.} respectively, compared with the placebo {77(45-190)min.}, bupivacaine 0.25% {346(105- 360)min.} or bupivacaine & epinephrine group {300(75-360)min.} [1] . Similarly B. cook had shown that the median duration of caudal analgesia was 5.8 hr in bupivacaine with Clonidine 2 µg/kg group [13]. The variability in the duration of caudal analgesia in the above two studies as compared to our findings could be due to the fact that they used parental assessment for acute paediatric pain which is less objective than the ratings of professional health care providers. J J Lee et al had shown that the mean duration of caudal analgesia for clonidine 2 µg/kg was 588±150 min [9] and Aruna Prameswari had shown the mean duration of analgesia to be 593.4± 423.3 min for caudal clonidine 1µg/kg group [11] both of which are similar to our results.

There were significantly higher number of rescue analgesics required in Group 3 (n=46) as compared to Group 1 (n=22) and Group 2 (n=20). All the patients in Group 3 required post operative analgesia, however, 31% patients in group 1 and 28.5 % in Group 2 did not require any rescue analgesic for 24 hours. This result is supported by findings of Jamali et al who found that 46% of patients in clonidine group (1µg/kg) required no post operative pain medication as compared to 13% in control group during the first 24 hours after caudal Anaesthesia [7]. J J Lee in his study had shown that children in bupivacaine group were given 26 & 40 administrations of morphine & paracetamol respectively for 24 hrs and children in bupivacaine with clonidine 2 µg/kg group had a total of 16 & 29 administrations of morphine & paracetamol respectively for 24 hrs [9]. Similarly, Helmut Hegar found out that within 24 hr post operative period 16% of children in clonidine 1µg/kg and clonidine 2µg/kg Group required additional analgesia as compared to ketamine Group in which 63% of children required additional analgesics [6]. These studies therefore support our findings that clonidine 1µg/kg and 2µg/kg Group require less number of rescue analgesics as compared to Control Group.

In our study, the sedation score for 65% of patients in Group 1 was 0(score being 1 for 14 % and 2 for 17% of patients). The sedation score for 67% patients in Group 2 was 2 (score being 0 for 18% and 1 for 14% patients). The sedation score for 96% of patients in Group 3 was 0 (score being 1 for 4% of patients only). The above sedation scores were observed at immediate post operative period i.e. within 2 hours after surgery. Similar results were obtained in previous reports by Lee and Rubin who demonstrated a longer duration of post operative sedation following caudal bupivacaine with clonidine 2µg/kg [9]. They found that the mean duration of sedation in the immediate post operative period and before supplementary analgesia

was required were 5.8 hr and 9.1 hr for plain bupivacaine group and bupivacaine with clonidine (2μg/kg) group respectively. The longer duration of sedation in the clonidine group resulted partly from the sedative effect of clonidine and partly from longer duration of analgesia provided by clonidine. The sedative hypnotic effects of α_2- adrenergic agonists are related to the inhibition of neural firing in the locus coeruleus, a brainstem nucleus located in the dorsal part of the medulla [22]. This supraspinal effect is logical after systemic administration of clonidine. Ivani et al reported that sedation was present in all children who received a lumbar epidural injection of 2μg/kg clonidine and suggested that clonidine sedation is dose dependent [14]. Patients were evaluated for different side effects and none of the patients showed features of pruritis, headache, local hematoma and motor block post operatively. Nausea and vomiting was seen in three patients of Group 2. Similar results were reported by Joshi et al and Archna Koul et al [10], which were that since the patients who underwent Urethroplasty were cauterized, so urinary retention could not be assessed but overall there were two patients in Group 2 and one patient in group1 who showed signs of urinary retention.

No untoward effects in terms of motor weakness, hematoma, hypotension, or bradycardia were seen in any of the patients. Three patients developed urinary retention while two patients had nausea & vomiting.

Conclusion

To conclude, we recommend a dose of 1μg/kg clonidine as an adjuvant to 0.25% bupivacaine (0.75ml/kg) for infra-umbilical surgeries to significantly prolong post-operative analgesia without causing significant sedation. Increasing the dose of clonidine to 2μg/kg didn't significantly prolong postoperative analgesia but did produce significant sedation, which might interfere with discharge criteria for day care surgery.

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A Comparative Study of Intrathecal Midazolam and Intravenous Metoclopramide to Prevent Nausea and Vomiting During Elective Cesarean Delivery Under Spinal Anesthesia

Mukesh Somvanshi*, Abdul Alim Khan, Archana Tripathi***, Hemant Kumar******

Abstract

Background: The antiemetic efficacy of metoclopramide and midazolam was shown before. The aim of the present study was to compare the efficacy and safety using intravenous metoclopramide and intrathecal midazolam for the prevention of nausea-vomiting in parturient undergoing cesarean section under spinal anesthesia. *Methods:* This prospective and randomized double blind study was conducted in 100 parturient aged between 21 and 30 years, ASA physical status É, scheduled to undergo elective cesarean section under spinal anesthesia. Parturient presenting for cesarean section with standardized 0.5% hyperbaric bupivacaine 2 ml spinal anesthesia were randomized to intravenous metoclopramide 10 mg (group I) or intrathecal midazolam 2mg (group II). The incidence of nausea-vomiting and any other adverse effect were recorded during intraoperative and early postoperative period and compared between two groups by using chi-square test. *Results:* The incidence of nausea-vomiting was 36% with intravenous metoclopramide and 10% with intrathecal midazolam. No clinically adverse events caused by study agents were observed in either group. *Conclusion:* Intrathecal midazolam 2mg significantly reduces the incidence of nausea-vomiting when administered with 0.5% hyperbaric bupivacaine for cesarean section under spinal anesthesia.

Keywords: Nausea; Vomiting; Cesarean Section; Spinal Anesthesia; Metoclopramide; Intrathecal Midazolam.

Introduction

Perioperative nausea-vomiting is a frequent complains during spinal anesthesia for cesarean section and can occur in as many as 66% of cesarean section [1]. This can be distressing to patients and may increase the risk of gastric aspiration [2]. Various agents like droperidol, metoclopramide, ondansetron etc have been used to decrease this complain with variable results. However, their use has been discouraged because of their side effects such as intense sedation, restlessness, dystonic reactions and extrapyramidal symptoms [3-7] in addition to high cost [8].

Metoclopramide is in use as an antiemetic for many years. Intrathecal midazolam has been shown to reduce the incidence of nausea-vomiting in patients undergoing cesarean section [9, 10].

We designed this randomized, double blinded study to assess and compare efficacy of intravenous metoclopramide and intrathecal midazolam for the treatment of nausea-vomiting in parturient presenting for cesarean section under spinal anesthesia.

Methods

After obtaining approval from institutional ethical committee and written informed consent, 100 ASA physical status I, full term parturient aged 21 to 30 years, presenting for cesarean section under spinal anesthesia were included in the study. Pregnant patients with history of motion sickness, hyperemesis gravidarum, contraindication to regional anesthesia or sensitivity to any study drugs were excluded from the study.

Parturient were fasted overnight and received tab ranitidine 150 mg orally with sips of water as premedication 90-100 min before surgery. On arrival to operative room, peripheral intravenous access was secured with 18G cannula and patients were preloaded with ringer lactate solution at 20 ml/kg before spinal anesthesia. Routine monitoring

Author's Affiliation:
*Associate Professor, **Ex-Resident ***Professor, **** Postgraduate Student, Department of Anaesthesiology and Critical Care, Govt. Medical College and AG Hospitals, Kota (Rajasthan), India.

Corresponding Author:
Mukesh Somvanshi, 1- JHA-1, Vigyan Nagar, Kota–324005 (Rajasthan), India.
E-mail: mukeshsomvanshi81@gmail.com

devices were attached and baseline blood pressure, heart rate, ECG and pulse oximetry values were recorded. Spinal anesthesia was performed by using 25G whitacre needle at L_2-L_3 or L_3-L_4 interspace in left lateral decubitus position. The patients were randomly allocated into two groups of 50 each to receive one of the medications according to group.

Group I: Intravenous normal saline 2ml and intrathecal 2ml of hyperbaric bupivacaine 0.5% + 0.4 ml of midazolam + 0.1ml of normal saline.

Group II: Intravenous metoclopramide 2ml (10mg) and intrathecal 2ml of hyperbaric bupivacaine 0.5% + 0.5 ml saline.

Study drugs were prepared by an anesthesiologist not involved in this study. Immediately after intrathecal injection, patients were placed supine with left uterine displacement All patients received supplemental oxygen via facemask. NIBP, HR, SpO_2 were performed at 2 min interval for 10 min, then 5 min interval for rest of the procedure. The level of sensory blockade was recorded 10 min after intrathecal injection. Hypotension was treated with intravenous ephedrine (5-15mg). Vomiting or retching by patients in either study group was treated with 4mg of intravenous ondansetron. Intravenous fentanyl 50 µg was used to treat the pain. Intraoperative and postoperative nausea-vomiting were assessed by an observer blinded to treatment group allocated. Nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit; retching was defined as labored, spasmodic, rhythmic contraction of respiratory muscle without the expulsion of gastric content; vomiting was defined as forceful expulsion of gastric content from the mouth [3]. These were assessed according to the Belville´s score [11] (0= no nausea; 1= nausea; 2= retching and 3= vomiting). The neonates were evaluated using APGAR score. Data were reported as mean ± SD or percentage. The statistical analysis was done by Student …t test and Chi-square test. A $p < 0.05$ was considered as significant.

Results

Maternal demographics were not different between groups [Table-1]. The level of anesthesia was considered sufficient for the surgical procedure as an adequate sensory block up to T6 was documented in all patients. There were no significant differences in blood pressure and heart rate between two groups. Hypotension was noted in 9 (18%) patients in group II compared to 7 (14%) patients in group I as shown in Table-2. Hypotension was treated with intravenous fluids and injection ephedrine. No significant difference in ephedrine use amongst the study group was observed.

During perioperative period the incidence of emetic episodes was significantly lower in group I, where 5 (10%) parturient develop emesis compared to 18 (36%) parturient in group II who had emesis [Table- 3].

Neonatal outcome were similar in both groups [Table- 4].

Table 1: Maternal demographics

Parameters	Group I (n = 50)	Group II (n = 50)
Age (years)	24.18 ± 3.08	23.66 ± 3.13
Weight (kg)	60.41 ± 6.93	62.10 ± 7.63
Gestational age (week)	38 ± 0.60	38.± 1.77
Multiparous (n)	8	7
Baseline blood pressure (mm Hg)	125 ± 7.21	115 ± 11.18
Systole		
Diastole	80 ± 6.01	80 ± 8.16
Pulse rate / min.	85.5 ± 8.73	88.8 ± 12.03

Values are mean ± SD or number of patients.

Table 2: Operative management

Parameters	Group I (n = 50)	Group II (n = 50)
Duration of surgery (min)	54 ± 17.21	57.5 ± 15.10
Duration of exteriorization of uterus (min)	18.75 ± 5	17.5 ± 4.86
Hypotension	9 (18%)	7 (14%)
Apgar score	8 ± 0.64	8 ± 0.64
At 1 min		
At 5min	10	10

Values are mean ± SD or number of patients

Table 3: Incidence of emetic episodes

Emetic episodes	Group I (n = 50) n (%)	Group II (n = 50) n (%)
No Nausea	45 (90%)	32 (64%)
Nausea	3 (6%)	8 (16%)
Retching	1 (2%)	6 (12%)
Vomiting	1 (2%)	4 (8%)

n = number of patients

Discussion

Perioperative nausea-vomiting commonly occur during cesarean section under spinal anesthesia [1]. The etiology of perioperative nausea-vomiting is multifactorial and includes progesterone induced reduction in lower esophageal sphincter tone, increased intragastric pressure, hypotension, exteriorization of uterus and visceral stimulation. These problem may accompanied by visceral pain, that stimulate vagal afferents which occur despite apparently adequate dermatological sensory blockade [2]. Various drugs have been used to prevent perioperative nausea-vomiting, however, either undesirable effects or cost of agents limited their routine use. Metoclopramide is in use as an antiemetic for many years. Antiemetic effect of metoclopramide is well established to decrease intraoperative nausea-vomiting during cesarian section performed with spinal anesthesia; however it may produce extrapyramidal symptoms [7].

Metoclopramide has multiple site of action. It is a prokinetic drug that act by increasing the tone of lower esophageal sphincter. It also has an antidopaminergic action on chemoreceptor trigger zone and at higher dose has an antiserotonergic activity [12, 13].

The mechanism of antiemetic effect of midazolam has not been completely understood. It seems that reduction in anxiety and decrease in dopaminergic input to chemoreceptor trigger zone (CTZ) may be mechanism by which it act [14]. Midazolam may reduce the reuptake of adenosine, which lead to adenosine mediated reduction in the synthesis, release and postsynaptic action of dopamine at the CTZ. Also adenosine reduces dopaminergic neuronal activity and 5-HT_3 release by binding to the gama-amiobutyric acid (GABA) receptor [15].

Intrathecal midazolam have been reported to provide improved intra and postoperative analgesia and thereby decrease discomfort from intraoperative peritoneal manipulation which may initiate emetic episode [16].

In present study, we had compared the efficacy of intravenous metoclopramide and intrathecal midazolam to minimize the incidence of nausea-vomiting in cesarean section. The result of our study revealed that intrathecal midazolam 2mg significantly reduced the incidence of nausea-vomiting compared to intravenous metoclopramide in cesarean section under spinal anesthesia. The lesser incidence of nausea-vomiting in intrathecal midazolam group may be due to improved intraoperative analgesia produced by intrathecal midazolam and thus avoiding the initiation of nausea-vomiting by peritoneal traction, exteriorization of uterus and visceral pain [17].

Our results are in collaboration with Rudra P and Rudra A [18] who concluded that intrathecal midazolam significantly minimizing the incidence of nausea-vomiting during intraoperative and postoperative period in cesarean delivery.

In our study few patients had hypotension in both groups which was treated with intravenous ephedrine. There was no significant difference in ephedrine requirement amongst both groups. Neonatal outcome was similar in both groups. Therefore in this study, intrathecal midazolam had no adverse impact on neonatal condition.

Our results allow us to conclude that the co-administration of intrathecal midazolam 2mg with 0.5% hyperbaric bupivacaine in the spinal anesthesia significantly reduces the incidence of nausea-vomiting and superior to intravenous metoclopramide for the prevention of perioperative nausea-vomiting during cesarean section under spinal anesthesia. Moreover, as midazolam is cost effective, making it an attractive choice for routine use.

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A Study to Know the Effect of Intravenous Methyl Prednisolone Compared to Placebo on Hemodynamics in Patients with Long Bone Fracture of Lower Limb

Prashanth N.*, Neeta P.N.*

Abstract

Background: Fat embolism syndrome (FES) is a potentially lethal condition most commonly seen in polytrauma patients with multiple long-bone fractures. Treatment has centered on supportive care and early fracture fixation. Several small clinical trials have suggested corticosteroids benefit patients with FES, but this treatment remains controversial. Our objective was to determine the effect of corticosteroids on hemodynamic changes with respect to FES in patients with long-bone fractures. *Methods:* Forty four adults, who had sustained a tibia fracture, or a femoral fracture, were subjected to a double-blind randomized study to determine the effect of intra venous methylprednisolone in comparison with placebo on hemodynamic changes with respect to the development of the fat embolism syndrome. A Lindeque2 s criterion for the diagnosis of the fat embolism syndrome was used. *Results:* Post operatively there was significant decrease in the heart rate in methylprednisolone group of patients compared with placebo group. Other parameters like systolic blood pressure (SBP), diastolic blood pressure (DBP) did not show any significant results. *Conclusion:* Prophylactic corticosteroids can be used to prevent changes in vital parameters/ hemodynamic and to manage development of fat embolism syndrome.

Keywords: Fat embolism syndrome; Hemodynamics; Polytrauma .

Introduction

Fat embolism syndrome (FES) is an infrequent clinical consequence, arising from the systemic manifestations of fat emboli within the micro-circulation. Fat embolization is characterized by release of fat droplets into systemic circulation after a traumatic event, which cause direct tis-sue damage as well as induce a systemic inflammatory response resulting in pulmonary, cutaneous, neurological, and retinal symptoms. (1,2)

'Fat embolism syndrome' is a serious manifestation of fat embolism phenomenon characterized clinically by triad of dyspnoea, petechiae and mental confusion. In 1873, Bergmann was first to establish the clinical diagnosis of fat embolism syndrome. (3) Hypoxia is common after long bone fractures and may pass unnoticed.(4) There is no clinical or experimental study until now to demonstrate beneficial effect of any drug on the clinical course of the syndrome,(5) so that prevention, early diagnosis and adequate symptomatic treatment are the mainstays of treatment of this condition. Several pharmacological agents have been used as prophylactic treatment, such as hypertonic glucose,(6) aspirin,(7) dextrans(7) and corticosteroids with variable results.(8,9,10,11) In several clinical trials the use of corticosteroids in various pulmonary disorders and in FE was proven to be beneficial but their use remains controversial. None of the studies focused on the effect of corticosteroids with hemodynamic variables like heart rate and blood pressure in long bone fractures.

This present study was performed to determine the efficacy of methylprednisolone, in improving the hemodynamic parameters with long bone fractures, during development of FES and to improve prognosis.

Methodology

A randomized double blind placebo-controlled trial was

Author's Affiliation:
Assistant Professor, Vijayanagara Institute of Medical Sciences (VIMS), Ballari, Karnataka 583104

Corresponding Author:
Prashanth N., C-128, 5th Main, 3rd Cross, Opposite Vishnuvardhan Park, Cantonment, Ballari, Karnataka-583104
E-mail:
drprashanthnandibewur@gmail.com

performed on 44 patients with long bone fractures in a tertiary care hospital. Patients were diagnosed according Lindeque's criteria for fat embolism syndrome, considering inclusion and exclusion criteria and randomized into two groups. Group A as placebo group, receive placebo treatment with normal saline and Group B as study group, and receive methylprednisolone 30mg/kg over one hour.

The authors were blinded to this allocation of groups and drug administration. Institutional ethical clearance was obtained and written informed consent was taken from all the study subjects (No. HOSMAT/ ECM/ 248/ 2008-09).

Lindeques Criteria [8]

- A sustained PaO_2 of less than 8 k.Pa (60mm of Hg) with FiO_2 0.21.
- A sustained $PaCo_2$ of more than 7.3 k.Pa (55mm of Hg) or pH of less than 7.3
- A sustained respiratory rate of greater than 35breath/min. even after adequate sedation.
- Increased work of breathing judged by dyspnoea use of accessory muscles, tachycardia and anxiety.

Any patient with fracture femur and/or tibia showing one or more of these criteria was judged as having Fat Embolism Syndrome

A number of investigations were carried out on admission (baseline values), and again at 2nd, 3rd hour. Post operative temperature, pulse rate, blood pressure and respiratory rate were measured four-hourly for up-to 24 hours. The presence of any petechiae, and their sites was recorded.

Inclusion Criteria

Patients with closed fracture long bone in lower limb, ASA – I, Age- < 45 years.

Exclusion Criteria

Patients with polytrauma, Patients with head injury and sepsis, Patients associated with fracture ribs and lung contusion, Patients with ischemic heart disease, congenital heart disease, hypertension and valvular heart disease, Patients with blunt injury to thorax, abdomen, head and neck, Patients with cervical spine injury and faciomaxillary injuries, Patients with shock– hemorrhagic, septic, cardiogenic and neurogenic, Patients with vascular injuries, Associated with respiratory system and other medical illness like chronic obstructive airway disease, pneumonia (Aspiration) or lower respiratory tract infection.

Results and Discussion

Forty four patients were enrolled and completed the trial (36 men and 8 women). The age range of the patients was from 16 to 46 years (mean age: group A 26.95 ± 7.33 years and group B 28.78 ± 9.16 years). A study by M. K Mobarakeh et al [9] showed the age range of the patients was from 16 to 55 years (mean age: 27.38 ± 11.04 years). At the end of the study period, 23 patients were in the corticosteroid group and 21 patients to the placebo group. There were no statistically significant differences between the two groups regarding age, sex and fracture site. Similar results found in one study [9].

Table 1 shows measurements of hemodynamic parameters in two groups on admission. This shows that two groups received the patients in same condition and there was no disparity between groups about patient's general status.

The heart rate on admission were 92.90±12beats/ min in Group A patients and 90.96±9.23beats/min in Group B. 24 hours after surgery it has increased significantly in Group A patients i.e. 92.43±20.93 beats/min as compared to Group B (80.91±8.93 beats/ min).

Table 3 depicts that the systolic blood pressure was normal before the surgery. There was significant fall in B.P at 3rd hour of operation in Group A, but post operatively both groups maintained normal B.P for 24 hour.

The diastolic blood pressure does not show any variation between two groups in pre operative, intra operative or post operative period (Table 4).

There were no such studies to show the hemodynamic changes in the long bone fracture patients, who were given prophylactic methylprednisolone as preventing tachycardia or hypotension.

The protective effect of corticosteroids against FES and hemodynamic changes suggests that the two are different stages of the same condition [10, 11]. The clinical manifestations of FES frequently appear 24-48 h after the trauma. However, in the studies evalu-ated, prophylaxis with corticosteroids was initiated at hospital admission [10,11,12]. There is no evidence that, after a diagnosis of FES has been established, specific therapy provides any benefit. Therefore, the treatment is based on clinical support.

Administration of 6 mg/kg up to 90 mg/kg methylprednisolone, divided in six doses at 8 h intervals, initiated directly after patient admission, had reduced the incidence of posttraumatic hypoxaemia and has probably also reduced the incidence of FES. Repeated arterial blood gas analysis over the first 48 h in high-risk patients is extremely valuable in detecting and treating those patients with significant hypoxaemia and FES.

The effects of corticosteroids in all the studies have shown about arterial blood gas analysis and FES. None have focused on hemodynamics i.e heart rate, blood pressure.

Future studies are needed to better assess the hemodynamic as well as arterial blood gases for long-term effects of corticosteroid administration in this patient population.

After 3 hours of start of surgery there was fall in the mean systolic BP in Group A (control group) patients as compared to Group B (study group) patients, and it was statistically significant. This fall in systolic BP may be due to release of tourniquet at the end of surgery in some patients. This was not associated with any significant rise in heart rate.

But the reading at 24th hour after surgery showed a statistically significant rise in heart rate in Group A(Control group) patients as compared to that in Group B (Study group) patients. These changes at 24 hours after surgery in vital parameters suggests the development of Fat Embolism Syndrome in these patients due to fat emboli being released into the systemic circulation secondary to fracture manipulation and reaming of marrow cavity during surgery.

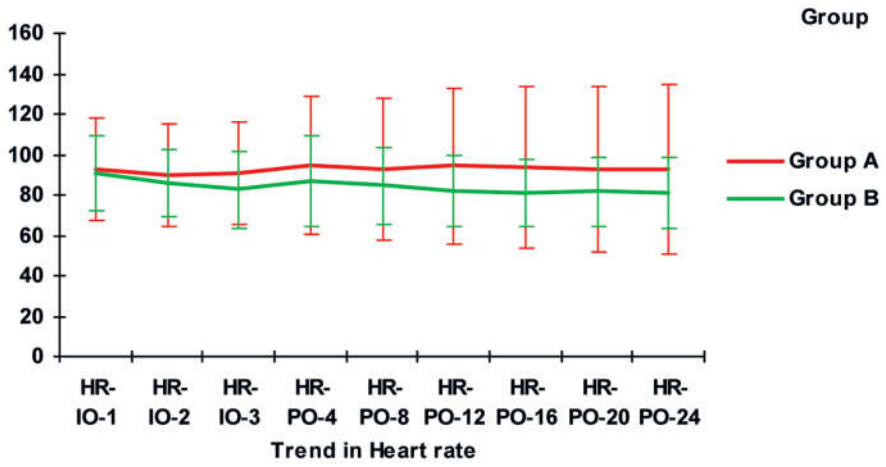
Limitation: The limitation of study is we could not

Table 1: Mean values of hemodynamic parameters on admission in both the groups

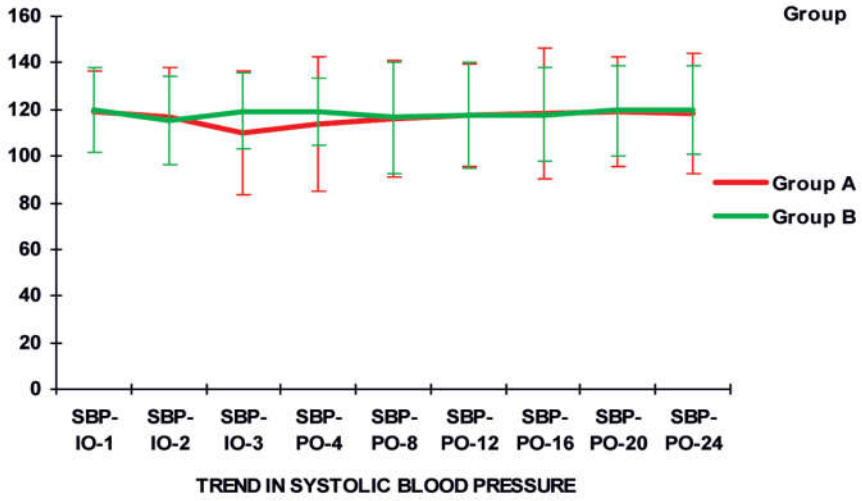
	Heart Rate	Systolic Blood pressure	Diastolic Blood pressure
Group A (n=21)	96.14±16.18	113.81±14.31	76.19±6.69
Group B (n=23)	96.13±13.87	116.96±12.59	76.09±6.56
t	0.002722	0.77143	0.051729
p-value	0.997842	0.444986	0.958995
Statistical significance	N.S.	N.S.	N.S.

Table 2: Mean readings of heart rate in patients at regular intervals

	Intraop 1st Hour	Intraop 2nd hour	Intraop 3rd hour	Postop 4th hour	Postop 8th hour	Postop 12th hour	Postop 16th hour	Postop 20th hour	Postop 24th hour
Group A (n=21)	92.90 ±12.57	89.71 ±12.72	90.71 ±12.80	94.33 ±17.07	92.95 ±17.59	94.19 ±19.10	93.95 ±19.93	92.62 ±20.69	92.43 ±20.93
Group B (n=23)	90.96 ±9.23	85.91 ±8.41	83.78 ±8.33	87.09 ±11.19	84.39 ±9.73	81.96 ±8.69	81.30 ±8.24	81.57 ±8.49	80.91 ±8.93
t	0.58	1.16	2.11	1.65	1.97	2.69	2.70	2.28	2.34
p-value	0.56	0.26	0.04	0.11	0.06	0.01	0.01	0.03	0.03
Statistical significance	N.S.	N.S.	S.	N.S.	N.S.	S.	S.	S.	S.



Graph 1: Trend in heart rate in patients of two groups



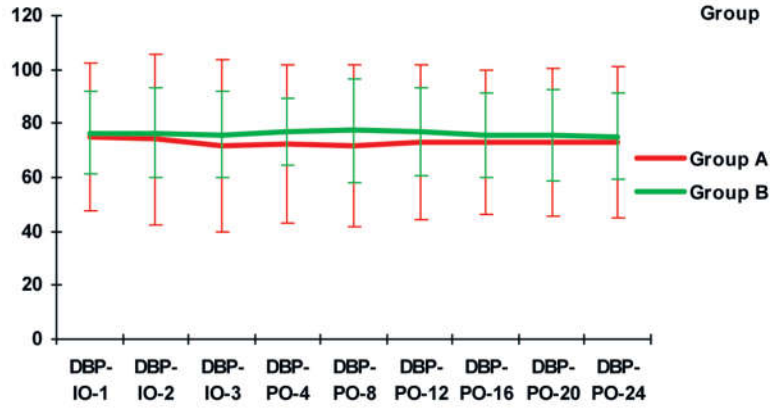
Graph 2: Trend in systolic blood pressure in patients of two groups

Table 3: Readings of systolic blood pressure in patients at regular intervals

	Intraop 1st hour	Intraop 2nd hour	Intraop 3rd hour	Postop 4th hour	Postop 8th hour	Postop 12th hour	Postop 16th hour	Postop 20th hour	Postop 24th hour
Group A (n=21)	119.05 ±8.89	117.14 ±10.56	110.00 ±13.42	115.00 ±13.57	115.71 ±12.48	117.62 ±10.91	118.10 ±14.01	119.05 ±11.79	118.10 ±12.89
Group B (n=23)	120.00 ±9.05	115.22 ±9.47	119.44 ±8.02	119.13 ±7.33	116.52 ±11.91	117.39 ±11.37	117.83 ±9.98	119.57 ±9.76	120.00 ±9.53
t	0.35	0.63	2.71	1.22	0.22	0.07	0.07	0.16	0.55
p-value	0.73	0.53	0.01	0.23	0.83	0.95	0.94	0.88	0.58
Statistical significance	N.S.	N.S.	S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.

Table 4: Readings of diastolic blood pressure in patients at regular intervals

	Intraop 1st hour	Intraop 2nd hour	Intraop 3rd hour	Postop 4th hour	Postop 8th hour	Postop 12th hour	Postop 16th hour	Postop 20th hour	Postop 24th hour
Group A (n=21)	77.14 ±7.84	76.67 ±11.11	74.29 ±12.07	74.76 ±9.81	74.48 ±10.52	75.81 ±9.10	75.71 ±7.46	75.71 ±8.11	75.71 ±8.70
Group B (n=23)	76.52 ±7.75	76.52 ±8.32	76.11 ±7.78	76.96 ±6.35	77.39 ±9.64	76.96 ±8.22	75.65 ±7.88	75.65 ±8.43	75.22 ±7.90
t	0.26	0.05	0.57	0.87	0.96	0.44	0.03	0.02	0.20
p-value	0.79	0.96	0.57	0.39	0.35	0.66	0.98	0.98	0.84
Statistical significance	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.



Graph 3: Trend in diastolic blood pressure in patients of two groups

get literatures to cite for the discussion as none of the studies focused on hemodynamics, instead they focused mainly on hypoxemia.

Conclusion

In summary, the current evidence suggests that cortico - steroids may prevent FES in patients with long-bone fractures as well as prevent changes in the hemodynamic parameters. We found no significant differences in the hemodynamic parameters except at the 3rd hour after start of surgery; there was peek fall in systolic pressure.

Based on our findings, which included mostly older and the studies which have not focused on mainly hemodynamic parameters, we would not currently recommend a change in practice. Our findings do, however, provide compelling rationale for the re-evaluation of corticosteroids use in long bone fractures to study effects on hemodynamic parameters. Ultimately, a large confirmatory randomized trial will provide the necessary evidence to guide patient care.

Usefulness

This study can guide us in using prophylactic corticosteroids to prevent changes in vital parameters/ hemodynamic and to manage development of fat embolism syndrome. And also we can find out the dosage of the corticosteroids to administer prophylactically during the long bone fractures patients while admission.

Conflicts of Interest

None

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Comparison of Efficacy of Caudal Clonidine in Two Different Dosages with Ropivacaine on Neuroendocrine Stress Response to Surgery in Children Undergoing Lower Abdominal and Urological Surgeries Under General Anaesthesia

Murthy Pooja R.*, Ahuja Sharmila, Choudary Sujata****

Abstract

Background: Neuroedocrine stress response(NESR) to surgery is manifested by increase in circulating catabolic hormones (cortisol) leading to protein catabolism. This can be modified by providing adequate postoperative analgesia in children in the form of caudal block using ropivacaine and non opioid adjuvants like clonidine.There is paucity of literature comparing effects of 3µg/kg and 1.5µg/kg of clonidine with 0.2% ropivacaine in terms of neuroendocrine stress response to surgery in caudal block. *Methods:* 45 children aged 1- 8 years, after premedication with oral midazolam and induction of anesthesia, caudal block was performed. Children were randomly allocated into 3 groups. Blood samples were obtained just after induction of anesthesia, 30 minutes after the start of surgery and 60 minutes after the end of surgery for measurement of serum levels of glucose and cortisol. *Results:* Mean blood glucose were within normal range and there was no statistically significant difference between the groups. There was a significant rise in serum cortisol levels from baseline values (T_0) in group R in the post operative period. There was statistically significant fall from baseline levels in cortisol values postoperatively in the clonidine 1.5 µg/kg group(RC1.5) and clonidine 3µg/kg group (RC3) and this fall in cortisol values was greater in the clonidine 3µg/kg group when compared to the clonidine 1.5 µg/kg group. *Conclusions:* There was blunting of NESR to surgery when clonidine was used as adjuvant to ropivacaine in caudal block and this was maximum with clonidine dosage of 3µg/kg.

Keywords: Neuroendocrine Stress Response; Clonidine; Ropivacaine; Caudal Block.

Introduction

Neuroendocrine stress response is a well established response to surgical and anaesthetic interventions manifested by increase in sympathetic tone, increase in circulating catecholamines and catabolic hormones (cortisol, ADH, ACTH, aldosterone, rennin angiotensin) [1]. This leads to increased oxygen consumption and protein catabolism which may impede recovery. Caudal anaesthesia provides satisfactory postoperative analgesia, reduces the amount of inhaled or intravenous anesthetic administration, facilitates a smooth and rapid recovery and attenuates stress responses to surgery [2,3].

In order to increase the success and overcome the unwanted side effects of local anaesthetics when used alone, different drug combinations in the form of adjuvants have been tried. These include opioids like morphine and fentanyl and non-opioids like α_2 adrenergic agonists clonidine, ketamine, epinephrine and neostigmine [4].

Clonidine among these, has in recent years emerged as a popular adjuvant has lesser side effects like respiratory depression, nausea and vomiting when compared to opioids. It has been used in dosages of 1.5 and 2 µg/kg [5]. Ivani et al [6] used 2 µg/kg of clonidine with caudal ropivacaine and reported it to be efficacious without causing adverse haemodynamic changes and sedation. A higher dosage of 5 µg/kg has been shown to be associated with adverse effects of sedation and bradycardia by Motsch et al [7]. There is paucity of literature to show comparison of effects of 3µg/kg and 1.5µg/kg on neuroendocrine stress response to surgery.

Thus, this study was designed with the aim to assess and

Author's Affiliation:
*Senior Resident, **Professor, Dept. of Anaesthesiology and Critical Care, University College of Medical Sciences, Delhi, Delhi University.

Corresponding Author:
Pooja R. Murthy, Senior Resident, Department Anaesthesiology and Critical Care, University College of Medical Sciences, Dilshad Garden, New Delhi, Delhi 110095, India.
E-mail: murthypooja@ymail.com

compare efficacy of two different dosages of clonidine (1.5μg/kg and 3μg/kg) when used as adjuvant with 0.2% ropivacaine in single shot caudal epidural block in children on neuroendocrine stress response to surgery.

Methods

The study was conducted in the Department of Anaesthesiology and Critical Care at University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi after approval from institutional review board. The procedure of the study including blood sampling for stress response measurement was explained to the parents / guardians and to the children (who could understand). Informed written consent was obtained from the parents of children included in the study.

Study Design

The study design was prospective, controlled, randomized and double blind. Randomization was performed by computer generated randomization code and delivered in sealed, opaque, sequentially numbered envelopes. The number of patients required in each group was determined according to data obtained from previous studies. According to this hypothesis, a sample size of 15 patients in each group was adequate with alpha risk of 0.05 and a power of 0.8.

Patient Selection

Three groups of children of age group 1-8 years undergoing elective lower abdominal and urological surgeries with average duration of 90 minutes belonging to ASA grade I and II were randomized to receive caudal block after induction of general anaesthesia as follows:

- Group R: Ropivacaine 0.2% (1 ml/kg) + 0.9% normal saline (0.1 ml/kg) (weight related volume) to ensure that volume of solution injected remains same in all the study groups
- Group RC1.5: Ropivacaine 0.2% (1 ml/kg) + clonidine 1.5 μg/kg
- Group RC3: Ropivacaine 0.2% (1 ml/kg) + clonidine 3.0 μg/kg

It was ensured that the upper limit of dose of ropivacaine, which is 2 mg/kg, is not exceeded in any of the subjects. Drugs were prepared by an anaesthesiologist before induction of anaesthesia, leaving the observer unaware of the group assigned.

Exclusion Criteria

- History of allergy to local anaesthetics or clonidine.
- History of coagulation abnormalities.
- History of aspirin ingestion in the preceding week.
- History of pre-existing neurological or spinal disease.
- Patients with known endocrine abnormalities.
- Patients with conditions which are likely to alter stress hormones such as hypovolemia and preexisting pain.
- History of ingestion of any drug which has depressant effects on central nervous system or cardiovascular system.

Anaesthesia Technique

A standard anaesthesia technique was followed in all children included in the study. Routine preoperative evaluation was performed on all children. After conducting a thorough pre-operative check up to ensure adherence to our exclusion criteria, children were premedicated with oral midazolam syrup(0.4 mg/kg) 30 minutes prior to induction of anaesthesia. After receiving the patient in the operation theatre, routine monitoring was established and anaesthesia was induced with 6-8% sevoflurane in oxygen using a face mask.

After the child was adequately anaesthetized, intravenous access with appropriate size IV cannula was obtained. An appropriate sized laryngeal mask airway was placed. The patient was allowed to breath spontaneously via an Ayre's T piece (with Jackson Rees modification) breathing system. Anaesthesia was maintained with a mixture of 40% oxygen in nitrous oxide and isoflurane 0.5-1.0%. The child was then positioned in lateral position and caudal block was performed by a skilled anaesthetist or resident under the supervision of consultant anaesthesiologist using aseptic technique and a short bevelled 22-23G needle. After negative aspiration of blood and CSF, the study drug was injected according to the group assigned as per the randomization code. The anaesthesiologist involved in the study was blinded to the contents of the syringes containing the study medications.

Standard monitoring included non-invasive blood pressure (by oscillometry), ECG, heart rate, pulse

oximetry, end tidal carbon dioxide, respiratory rate and temperature. These parameters were monitored at the time of induction and at 5 minute intervals thereafter. An intraoperative rise in baseline arterial pressure or heart rate of >10% after surgical incision was taken as an indicator to insufficient anaesthetic depth and concentration of inhalational agent was increased. If there was persistent rise in heart rate and blood pressure for more than 10 minutes, then failure of caudal block was presumed and rescue analgesia in the form of opioids (fentanyl 1 µg/kg IV) was injected and the patient was excluded from the study.

At the end of surgery, the laryngeal mask airway was removed and the child was shifted to post-anaesthesia care unit (PACU). All children had at least one parent / guardian in attendance during recovery. One blinded observer recorded all the data in PACU.

1. Blood samples were taken :
   a) Just after induction as baseline value before giving caudal block
   b) 30 minutes after start of surgery
   c) 60 minutes after end of surgery

Samples were Analysed for

- Measurement of blood glucose by glucometer.
- Serum cortisol levels measured by radio-immunoassay (through commercially available kits).

Approximately 5-6 ml of blood was drawn from a dedicated vein cannulated with 22 G IV cannula.

2. All children were observed for side effects of drugs used and complications till the end of the study. This included observations for sedation, respiratory depression, nausea and vomiting, urinary retention, hypotension and bradycardia. The sedation in the postoperative period was assessed by a scoring system as follows:

Sedation Score [15]

0 Awake and alert

1 Asleep, arousable by verbal contact

2 Asleep, arousable by physical contact

3 Asleep, not arousable

Statistical Analysis

Data was analysed using SPSS version 17 computer software. Student's t-test was used for significance and $p<0.05$ was taken as significant. The comparison of sedation scores between the 3 groups was done using non parametric tests - Mann Whitney test and Kruskal Wallis test Inter group comparisons for blood glucose and serum cortisol levels was done using multivariate tests.

Results

Neuroendocrine Stress Response (NESR)

NESR was assessed by measurement of blood glucose and serum cortisol at T_0 (baseline), T_{30} (thirty minutes after surgical incision) and T_{60} (sixty minutes post operatively)

Blood glucose (mg/dl)

Mean blood glucose at T_0 (baseline) was 89.93 ± 13.776 in group R, 91.07 ± 16.62 in group RC1.5 and 92.53 ± 13.23 in group RC3. These values were within normal range and there was no statistically significant difference between the groups ($p>0.05$).

The mean blood glucose levels in groups R increased above baseline values(89.93) at T_{30} - thirty minutes after surgical incision (95.6)and a fall in blood glucose levels was noticed postoperatively – T_{60} (91.73) when compared to introperative values, but this difference was not statistically significant.

The blood glucose values in group RC1.5 increased above baseline levels(91.07) both intraoperatively (T_{30} – 95.67) and post operatively.(T_{60} – 96.33). The post operative values were higher than intraoperative blood glucose levels but this was not significant statistically.

In group RC3, an increase in blood glucose levels was noted introperatively - T_{30} (94.27) when compared to baseline levels.(94.27). the blood glucose values decreased postoperatively – T_{60} (89.6) when compared to intraoperativ and baseline values. This was also not significant statistically.

Thus, although the blood glucose values at T_{30} and T_{60} were highest in group R and lowest in group RC3, this difference was not statistically significant.The trend in the blood glucose levels at T_{30} and T_{60} were lowest in RC3 group.

Serum Cortisol (µg/dl)

The mean serum cortisol at T_0 was 10.36 ± 6.13 in group R, 7.60 ± 3.96 in group RC1.5 and 10.53 ± 4.54 in group RC3. All the groups had comparable serum

cortisol levels at baseline and this was within the normal range in all the groups.

T_{30}

30 minutes after surgical incision (T_{30}) groups R and RC3 showed a fall in serum cortisol levels which were 7.2 ± 3.99 and 6.25± 3.71 respectively. The values in RC1.5 (7.74 ± 3.66) were similar to baseline cortisol levels.The change of serum cortisol levels in groups R and RC3 was statistically significant when compared baseline (T_0) values. However all the values were within normal range for the age group studied.

T_{60}

At T_{60} -- the serum cortisol levels in group R(17.5 ± 5.78) increased significantly when compared to baseline and intraoperative levels. In group RC1.5, the postoperative values(6.85 ± 3.37) decreased when compared to intraoperative and baseline levels. In group RC3, no further fall was noticed postoperatively and the values were similar to intraoperative values, however this value was significantly less when compared to baseline

Thus, there was a significant rise in serum cortisol levels from baseline values (T_0) in group R in the post operative period. There was statistically significant fall from baseline levels in cortisol values postoperatively in RC1.5 and RC3 group and this fall in cortisol values was greater in the clonidine 3µg/kg group when compared to the clonidine 1.5µg/kg group.

Side Effect Profile

Sedation Score

The patients in group RC3 and RC1.5 were significantly more sedated when compared to group R in the immediate post operative period, but were arousable within 30 minutes postoperatively. There was no significant difference in sedation between group RC 1.5 and RC3 till 1hour post operatively.

All children who received only ropivacaine were awake and alert within 30 minutes after completion of surgery. Sedation persisted till 2 hours postoperatively in children who received clonidine with ropivacaine, but all children were awake and alert by 4 hours. postoperatively. The difference in sedation between children who received 1.5µg/kg and 3µg/kg of clonidine was not significant statistically and clinically.

Table 1: Demographic profile

Group	R	RC 1.5	RC 3
Age (years) (mean ± SD)	5.9 ± 1.94	5.7 ± 2.37	5.9 ± 1.94
Surgical duration (minutes) (mean ± SD)	46.06± 13.50	47.66 ± 12.79	46.26 ± 11.51
Males/ Females	14/1	14/1	14/1

Table 2: Mean blood glucose levels in all groups at different time intervals (mg/dl)

Time	Group R	Group RC1.5	Group RC3
T_0	89.93 ± 13.77	91.07 ± 16.62	92.53 ±13.23
T_{30}	95.60 ± 12.40	95.67 ± 13.069	94.27 ± 16.224
T_{60}	91.73 ± 10.38	96.33 ± 11.22	89.60 ± 14.94

Table 3: Serum cortisol levels in all three groups at various time intervals (µg/dl)

Time	Group R	GROUP RC1.5	GROUP RC3
T_0	10.36 ± 6.13	7.60 ± 3.96	10.53 ± 4.54
T_{30}	7.2 ± 3.99	7.74 ± 3.66	6.25± 3.71
T_{60}	17.5± 5.78	6.85 ± 3.37	6.75 ± 4.35

Table 4: Sedation Score in all 3 groups at various time intervals

Postoperative Time (hrs)	Group R	Group RC1.5	Group RC3
0	1.8 ± 0.56	3 ± 0.0	2.86 ± 0.35**,
0.5	0.6 ± 0.63	2.33 ± 0.48*	2.4 ± 0.82**,
1	0.0 ± 0.0	1.53 ± 0.63*	1.26 ± 0.79**,
2	0.00 ± 0.00	0.3 ± 0.49	0.58 ± 0.79**,
4	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00

*Significant difference between group R & RC1.5 (P value ≤ 0.05);
** Significant difference between group R &RC 3(P value ≤ 0.05);

Discussion

Neuroendocrine Stress Response (Nesr)

Attenuation of NESR by various drugs and techniques has been a recent area of research interest. The most frequent markers used to assess NESR are serum cortisol and blood glucose levels.

Although many drugs have been extensively reviewed to modulate NESR, very few studies are available to study the effect of caudal clonidine with ropivacaine for the same in the paediatric age group. M Akbas et al [8] studied the effect of clonidine on NESR in a dose of 1µg/kg with ropivacaine in caudal block, and compared it to ketamine as adjuvant to ropivacaine. These authors reported a blunting of NESR as depicted by a decrease in blood glucose and serum cortisol levels and an increase in insulin levels. We compared 1.5 µg/kg and 3 µg/kg clonidine with ropivacaine in caudal block.

We did not take blood samples preoperatively for hormonal levels because changes in these are likely to occur in emotionally stimulated children preoperatively, especially in older ones who feared operation or had separation anxiety. Hence a baseline sample was taken immediately after induction but before administering caudal block.

The baseline values (T_0) for all the markers were within the normal ranges for children in this age group (cortisol 3.3 – 20.8 µg/dL, glucose 65 – 125 mg/dL).There were no differences amongst the three groups in the cortisol and glucose values measured before the start of surgery.

Blood Glucose

Normally, a rise in blood glucose levels is observed peroperatively and may be explained by hepatic glycogenolysis, gluconeogenesis and insulin resistance at cellular level that takes place perioperatively. Thus normal regulation of glucose homeostasis is ineffective perioperatively and hyperglycemia is inevitable.

In our study too, a rise in blood glucose levels perioperatively was found to occur in all the study groups although the values remained within normal range for that subset of population.

Earlier studies comparing caudal block with General Anaesthesia(GA) alone group have reported a reduction in the NESR in caudal group as opposed to GA alone [9].

Tuncer et al measured glucose concentration in children who received either caudal with GA or GA alone. In both groups glucose concentration increased above baseline values, however this increase was lower in caudal group when compared to in control group (G A alone) [9] .

M Akbas et al reported a suppression of NESR with ropivacaine [10]. In another study, a greater blunting of stress response was noted by the same authors when clonidine in a dose of 1µg/kg was used as adjuvant. They compared the suppression of NESR by clonidine with that of ketamine when used as adjuvant to ropivacaine. The findings of this study indicated a greater blunting of NESR with clonidine as depicted by decrease in glucose and cortisol levels and increase in insulin levels [8].

Although we did not have a control group comprising only GA group (without any caudal block), the fact that all blood glucose values were within normal range may indicate a blunting of NESR in all the three groups. This beneficial effect was found to be maximum with clonidine 3µg/kg group (children in clonidine 3µg/kg group had lowest blood glucose levels in the post operative period).

Serum Cortisol

The baseline cortisol values were comparable in all the 3 groups and the mean value ranged between 7.6 and 10.53µg/dl. The values at 30min following surgical incision were similar to baseline values in ropivacaine only group and ropivacaine with clonidine 1.5µg/kg group, but a significant decrease in cortisol levels at 30 minutes was noticed in children receiving clonidine 3µg/kg with ropivacaine.

The trends in children who received ropivacaine with clonidine 1.5µg/kg group showed a slight rise intraoperatively as against a fall in cortisol levels with the other two groups. We are unable to provide a suitable explanation for the same. A larger study group is probably required to seek further information in this regard.

There was a modest fall in the serum cortisol values postoperatively in clonidine1.5µg/kg group and a significant fall in clonidine 3µg/kg group as against a significant rise in serum cortisol levels in ropivacaine only group (albeit within normal range). These trends signify significant blunting of NESR with clonidine.

According to Nicholson G et al, serum cortisol levels begin to rise within minutes of surgical incision and reach maximum values upto 4 – 6 hours postoperatively [11].

Solak et al [12] assessed the effects of caudal analgesia with 0.25% bupivacaine in addition to general anesthesia on plasma cortisol and prolactin concentrations during the early postoperative period in children who underwent abdominal and genitourinary surgery. They found low-pain scores and lower hormone concentrations in the general anesthesia plus caudal analgesia group than general anesthesia alone.

A review article by Desborough et al [13] have shown that clonidine reduces the stress response to surgery. The results of our study correlates well with the above mention facts and suppression of NESR is seen to be significant with clonidine in a dosage of 3µg/kg.

Murat and co workers[14]demonstrated that epidural anaesthesia reduces the cortisol response to surgery in children 1 to 8 year old during the first 24 hours after lower abdominal or perineal surgery. Cortisol values decreased significantly at the end of surgery in caudal epidural group while the patients who received GA alone had increased cortisol values. Throughout the study all cortisol values remained at a significantly lower level in the caudal group than in the control group. This finding is in agreement with our study where cortisol levels remained at lower values in the postoperative period. This is explained by the fact that the decrease in stress response is due to complete blockade of afferent neurogenic impulses from the site of surgery.

Our findings, therefore, clearly indicate a modulation of NESR with caudal clonidine and a significant reduction of stress response with clonidine in a dosage of 3µg/kg.

Conclusions

Both dosages of clonidine (1.5 and 3µg/kg) were effective in blunting NESR. The effect was significantly higher with clonidine 3µg/kg.

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Original Article

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A Comparative Study of Ketamine and Propofol Versus Fentanyl and Propofol in Total Intravenous Anaesthesia for Short Surgical Procudures

Ramakrishna Reddy Mudiganti*, Aditya Pradeep Reddy B., Dasta Giri Reddy P.*****

Abstract

Background: Total Intravenous Anaesthesia using various drug combinations to produce adequate sedation and analgesia with rapid recovery for short surgical procedures is known for more than two decades. *AIM:* To compare the haemodynamic responses intra operatively and time to recovery in patients receiving Propofol-Ketamine and Propofol-Fentanyl in short surgical procedures. **Design:** Randomised controlled study. **Material and Method:** The study included 100 patients randomly selected into 2 Groups of 50 each.

Group 1: received Propofol 1.5mg/kg and Ketamine 1mg/kg (PK group)

Group 2: received Propofol 1.5mg/kg and Fentanyl 1 mcg/kg (PF group). **Statistical Analysis:** Using Chi-Square Test, Student t-test (paired and unpaired). **Results and Coclusion:** From the present study we concluded that both Propofol-Ketmine and Propofol-Fentanyl are equally safe and effective in Total Intra Venous Anaesthesia for patients undergoing short surgical procedures. Propofol-Ketamine combination has better haemodynamic stability than Propofol-Fentanyl combination.

Keywords: Not Provided

Introduction

Total Intra venous Anaesthesia is a technique of General Anaesthesia using a combination of agents given solely by IV route in the absence of all inhalational agents and Nitrous Oxide.

Propofol (2-6 di-isopropyl phenol) is a newer IV anaesthetic agent. It has already achieved considerable popularity for induction and maintenance of anaesthesia for short duration surgeries. *Propofol* has got favourable pharmacokinetic profile. It is suitable for infusion because of rapid decline in blood concentration. The decline in *Propofol* concentration following a bolus dose or following termination of an infusion can be described by 3 compartmenta open model. The first phase is rapid distribution (t1/2 alpha 2-8min) followed by rapid elimination (t1/2 beta 30-70min) and terminal long and slow elimination half life (4 to 23.5 hrs). *Propofol* is 96-99% protein bound. It has high clearance rate 1.5-2.2L/min. *Propofol* is rapidly metabolized in the liver by conjugation. *Propofol* rapid metabolism and high clearance rate explains the faster and clearheaded recovery after its use and makes it an ideal drug for use in day case surgery.

Propofol effect on Central Nervous System includes dose dependant sedation and hypnosis. It decreases cerebral blood flow by 26-51% due to cerebral vasoconstriction. It also reduces CMRO2 (Cerebral Metabolic requirement for oxygen) by 30% and reduces Intra Cranial Pressure by 30%. *Propofol* is associated with various neuroexcitatory events including convulsions, myoclonus and tremors, involuntary movements and dystonic posturing during induction of anaesthesia.

Propofol effect on Cardio Vascular system includes: decrease in mean arterial pressure, cardiac output and systemic vascular resistance. *Propofol* depresses the baroreceptor reflex control of heart rate. *Propofol* is a respiratory depressant, reduces both tidal volume and respiratory rate. Airway reflexes are depressed making it more advantageous to insert laryngeal mask. Apart form these major effects, it has anti-emetic effect and antipruritic effect, anti oxident effect.

Ketamine is a water soluble IV anaesthetic agent belongs to Phencyclidine group. It is the only

Author's Affiliation:
*Associate Professor, ** Senior Resident, *** Professor, Dept. of Anaesthesia, Mediciti Institute of Medical Sciences, Ghanpur, RR District, Telangana.

Corresponding Author:
Ramakrishna Reddy Mudiganti, Associate Professor, Dept. of Anaesthesia, Mediciti Institute of Medical Sciences, Ghanpur, Rr District, Telangana 501401.
E-mail: drrk_2003@yahoo.com

IV anaesthetic agent which has hypnotic, analgesic and amnestic properties and cheaper. *Ketamine* has high lipid solubility and low protein binding and extensive distribution. It has short elimination half-life of 2-3 hours due to high clearance (mean 1.4L/min). *Ketamine* is metabolized by hepatic microsomal enzymes.

Ketamine effect on Central Nervous system includes: Dissociative anaesthesia (disassociates the thalamus from the limbic cortex). It resembles a cataleptic state in which eyes remain open with a slow nystagmic gaze, but patient is not oriented to surroundings. *Ketamine* produces amnesia and intense analgesia. *Ketamine* increases cerebral oxygen consumption, cerebral blood flow and intracranial pressure. It is known to produce emergence reactions.

Ketamine increases arterial blood pressure, heart rate and cardiac output due to central stimulation of sympathetic nervous system. Respiration is not depressed by ketamine except in large doses and usually mildly stimulated. It increases salivary and tracheobronchial secretions.

Neither *Propofol* nor *Ketamine* are suitable as sole anaesthetic agents. The most common adjuvant is opiod analgesic to provide complete anaesthesia.

Fentanyl is used extensively nowadays in TIVA. It is hundred times more potent than morphine and as a part of balanced anaesthesia. It relieves pain, reduces somatic, autonomic response to airway manipulation, and provides haemodynamic stability with less respiratory depression.

Hence this study of two drug regimens were compared.

AIM

To compare the haemodynamic responses intra operatively and time to recovery in patients receiving *Propofol-Ketamine* and *Propofol-Fentanyl* in short surgical procedures.

Objectives

To Compare

- Haemodynamic stability
- Respiratory depression
- Emergence Phenomenon
- Time for spontaneous Eye Opening
- Post Operative Nausea and Vomiting

Patients and Methods

This prospective randomised study was conducted in Mediciti Institute of Medical Sciences, Ghanpur after approval by ethics committee from December 2012 to June 2014.

Inclusion Criteria

Age between 18-60years

ASA Grade 1 & 2

Short surgical procedures like:

Dilatation and Curettage

Suction and Evacuation

Incision & Drainage

Wound debridement

Circumcision

Closed reduction in Orthopaedic procedures.

Exclusion Criteria

Patient refusal

Allergy and Known Hypersensitivity to drugs

Contraindication to either *Propofol* or *Ketamine*

ASA physical status 3 and above

Age <18yrs and >60years

Anticipated difficult intubation

Pregnant and Lactating mothers

The Patients are randomly selected into 2 Groups of 50 each.

Group 1: *Propofol* 1.5mg/kg and *Ketamine* 1mg/kg (PK group)

Group 2: *Propofol* 1.5mg/kg and *Fentanyl* 1 mcg/kg (PF group)

Intermittent bolus doses were given when there was patient movement to surgical stimulus.

These are *Prpofol* 0.5mg/kg and *Ketamine* 0.5mg/kg in PK group, Propofol 0.5mg/kg and Fentanyl 0.5mcg/kg in PF group.

All patients were premedicated with Inj. Midazolam 1mg and Glycopyrrolate 0.2mg and Ranitidine 50mg IV before shifting to operating theatre. Standard Monitors like Pulse Oximeter, NIBP, ECG were attached to the paient.

Oxygen 5Lt/min was given throughout the procedure. Blood pressure, Heart Rate, Oxygen saturation were recorded at base level, at the time of induction and every 3 minutes thereafter.

Time for spontaneous eye opening, response of the patient to commands after surgery were recorded. Need for rescue analgesics was noted. Other parameters observed were nausea and vomiting, emergence reactions like hallucinations. Ramsay sedation score was also compared between the two groups. A total of 100 patients of either sex were participated in the study. Statistical data was analysed with stata 13.1 using: Chi-Square Test, Student t-test (paired and unpaired), P value of <0.05 was taken as significant and >0.055 was taken as not significant.

Table 1: Ramsay scale for the assessment of the level of sedation

Level of Activity	Points
Patient anxious, agitated or restless	1
Patient cooperative, oriented and tranquil	2
Patient responding only to verbal commands	3
Patient with brisk response to light glabella tap or loud auditory stimulus	4
Patient with sluggish response to light glabella tap or loud auditory stimulus	5
Patient with no response to light glabella tap or loud auditory stimulus	6

Table 1: Age distribution of the patients

Age (in yrs)	No. of patients	
	Group -PK(N=50)	Group PF (N=50)
18-30	20(40%)	17(34%)
31-40	21(42%)	18(36%)
41-50	8(16%)	14(28)
51-60	1(2%)	1(2)

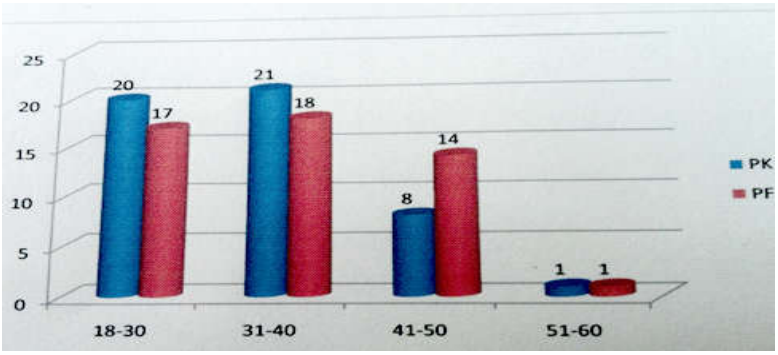

Fig. 1: Age wise distribution of patients

Age wise distribution was similar in two groups. Majority of the patients belonged to the age group 31-40 years.

Table 2: Sex distribution of patients

No. of patients	Female	Male
Group PK (N=50)	42(84%)	8(16%)
Group PF (N=50)	39(78%)	11(22%)

Gender Wise Distribution

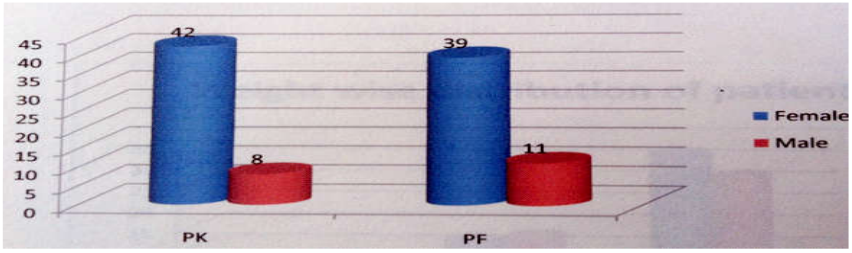

Fig. 2:

The majority of the patients were females 84% (PK group) and 78%(PF group) because most of the surgeries were gynaecological procedures.

Table 3: Weight wise distribution of patients

Weight in kgs	Group		P value
	Group PK (N=50)	Group PF (N=50)	
Mean(SD)	57.94±5.57	60.26±11.59	0.2051

The mean weight of both the groups was comparable.

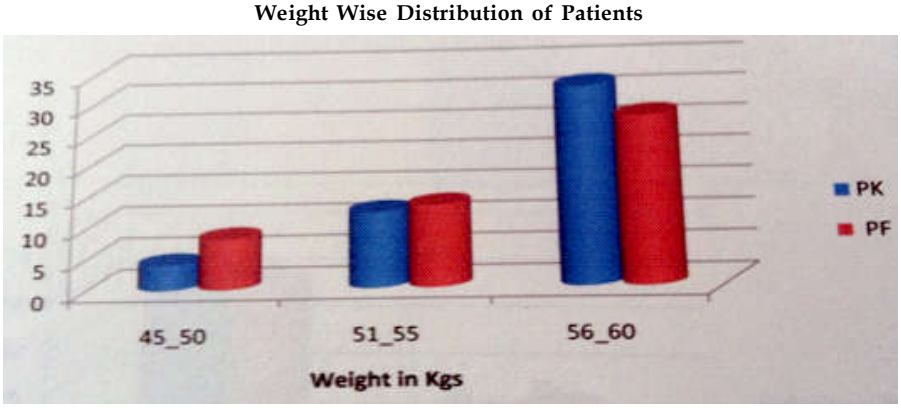

Fig. 3: Weight wise distribution of patients

Table 4: Comparison of mean age and weight between the groups

	Group – PK (n=50)		Group – PF (n=50)		*p* value	Result
	Mean	Std. deviation	Mean	Std. deviation		
Weight (KGS)	57.94	5.57	60.26	11.59	0.2051	Not sig.
Age (years)	33	8.92	35	9.41	0.2781	Not sig.

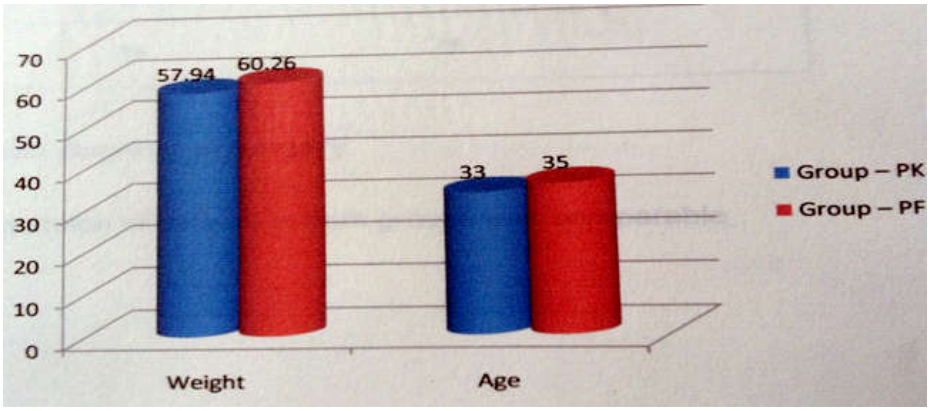

Fig. 4: Comparison of mean age and weight

'p' value: <0.05 – significant. The mean age and weight values in both groups were comparable each other statistically('p' value >0.05).

Table 5: Mean duration of surgery

Group	Mean duration of surgery	P value
PK	25.84 ± 1.76 min	0.4782
PF	26.1 ± 1.89 min	

Mean duration of surgery in both the groups was comparable.

Table 6: Comparision of Heart Rate between the two groups

Group	PK		PF		P value
	AVG	SD	AVG	SD	PK VS PF
Before induction	86.38	8.10	84.98	9.60	0.432
After induction	89.08	8.30	81.72	9.74	0.000
3 min	93.86	7.96	77.38	9.47	0.000
6 min	97.1	5.57	70.14	7.70	0.000
9 min	95.42	7.36	67.86	11.93	0.000
12 min	89.42	4.87	73.5	6.74	0.000
15 min	85.96	3.57	76.86	7.36	0.000
18 min	82.64	3.14	80.98	6.42	0.104
21 min	82.1	4.56	81.52	7.58	0.644
24 min	81.42	4.81	81.04	6.91	0.750
27 min	82.1	4.72	81.52	7.55	0.646
30 min	81.42	4.58	81.16	6.95	0.826

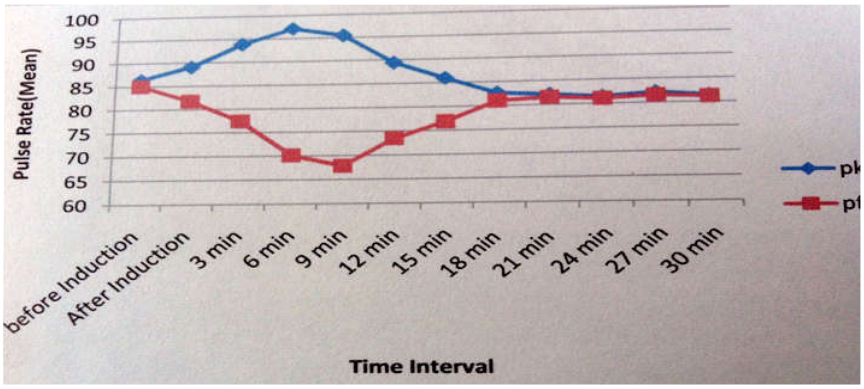

Fig. 5: Comparison of heart rate between the two groups

There was an increase in Heart rate after induction in PK group, whereas heart rate decreased after induction in PFgroup. At 30 min heart rate in both the groups was comparable.

Table 7: Comparision of Systolic Blood Pressure between the two groups

Group	SBP in mmHg				
	PK group		PF group		P value
	AVG	SD	AVG	SD	PK vs PF
Before induction	126.48	5.40	123.52	9.20	0.053
After induction	128.52	5.58	121.88	9.21	0.000
3 min	130.02	4.52	114.24	9.72	0.000
6 min	134.52	4.26	106.76	8.48	0.000
9 min	135.76	5.67	107.2	9.84	0.000
12 min	133.22	7.44	113.38	9.46	0.000
15 min	130.12	6.33	117.1	9.06	0.000
18 min	125.82	5.89	123.02	8.94	0.067
21 min	125.56	5.93	122.7	9.41	0.072
24 min	123.3	5.84	122.36	8.30	0.514
27 min	125.62	5.50	122.62	9.34	0.053
30 min	122.98	5.62	121.64	8.80	0.366

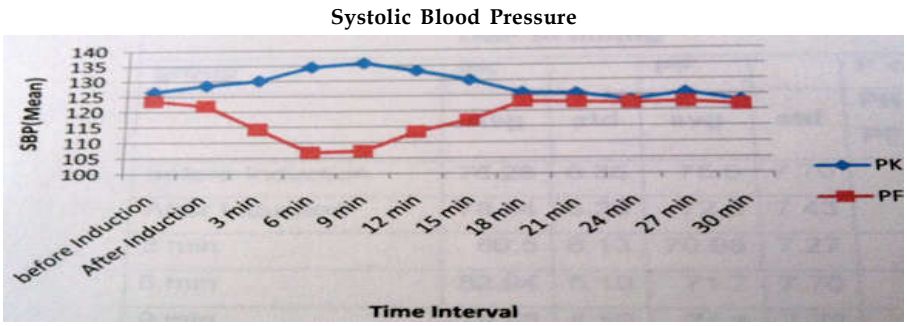

Fig. 6: Comparison of systolic blood pressure between two groups

There is statistically significant difference in systolic blood pressure between the two groups. In PK group there was an increase in SBP 3 min after induction, whereas in PF group SBP decreased.

Table 8: Comparision of diastolic blood pressure between the two groups

Group	Diastolic Blood Pressure in mmHg PK AVG	PK STD	PF AVG	PF STD	P value PK VS PF
Before induction	76.28	6.35	75.6	7.70	0.631
After induction	78.84	6.29	72.9	7.43	0.000
3 min	80.5	6.13	70.98	7.27	0.000
6 min	82.94	5.10	71.7	7.70	0.000
9 min	79.58	6.52	74.4	7.72	0.000
12 min	77.16	6.49	74.56	7.84	0.074
15 min	76.18	6.52	74.78	7.78	0.332
18 min	76.02	6.47	74.5	8.12	0.303
21 min	75.1	5.83	74.58	7.90	0.709
24 min	76.14	6.53	74.76	8.00	0.347
27 min	75.86	6.47	74.94	7.64	0.517
30 min	76.1	6.54	75.52	7.87	0.689

There is statistically significant difference between the two groups.

Diastolic Blood Pressure

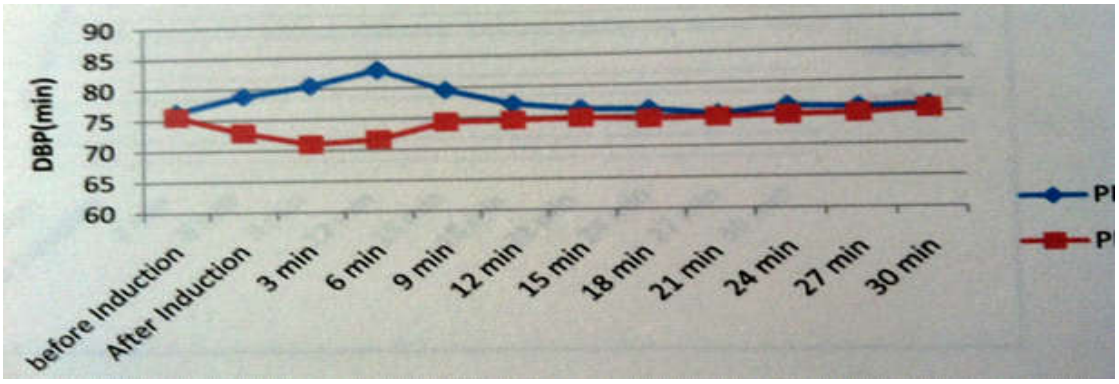

Fig. 7: Comparison of Diastolic blood pressure between two groups

In PK group DBP increased 3 min after induction. In PF group DBP decreased 3 min after induction.

Table 9: Comparison of Oxygen saturation between the two groups

Group	Oxygen saturation in % PK Avg	PK Std	PF Avg	PF Std	P value PK vs PF
Before induction	97.56	1.417	97.66	0.94	0.678
After induction	99.28	0.454	99.34	0.48	0.521
3 min	99.28	0.454	99.32	0.47	0.666
6 min	99.44	0.501	99.32	0.47	0.220
9 min	99.34	0.479	99.32	0.47	0.834
12 min	99.34	0.479	99.36	0.48	0.836
15 min	99.4	0.495	99.34	0.48	0.539
18 min	99.44	0.501	99.46	0.50	0.843
21 min	99.28	0.454	99.32	0.47	0.666
24 min	99.26	0.443	99.3	0.46	0.660
27 min	99.3	0.463	99.32	0.47	0.831
30 min	99.28	0.454	99.34	0.48	0.521

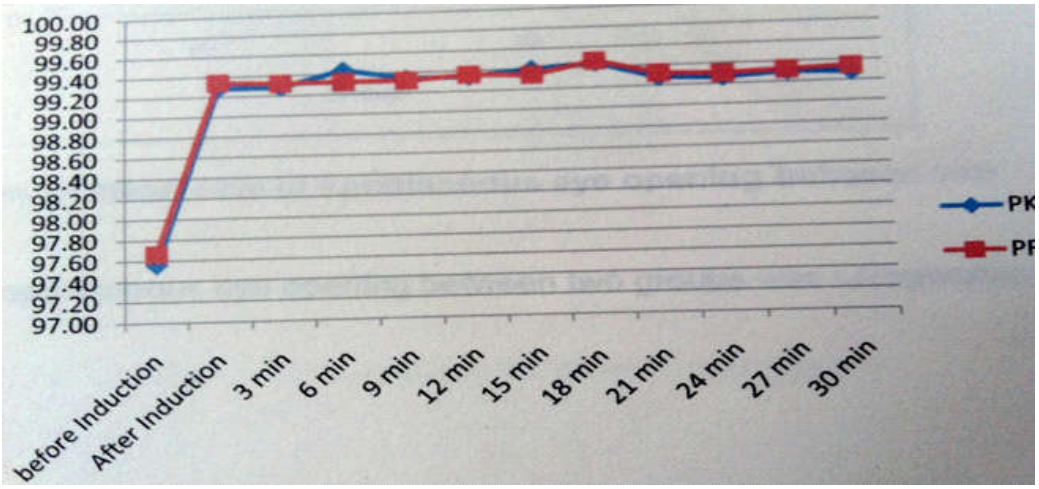

Fig. 8: comparison of oxygen saturation between two groups

Time for Spontaneous Eye Opening

Group	Mean time of Eye opening	P value
PK	6.42 ±1.3 min	<0.01
PF	3.64±1.2 min	

At the end of the surgery time for spontaneous eye opening is more in PK group. P value is significant.

Duration of Drowsiness

Group	Mean duration of drowsiness	P value
PK	12.72±1.61 min	>0.01
PF	7.42±1.32 min	

There is statistically significant difference in duration of drowsiness between the two groups.

Nausea and Vomiting

Group	No. of patients	P value
PK	6	0.74
PF	5	

The was slightly less incidence of post operative nausea and vomiting in PF group.

Emergence Reactions (Postop Delirium)

Group	No. of patients	P value
PK	3	>0.05
PF	0	

Postoprative delirium was noted in PK group.(in 3 cases)

Discussion

Total Intra Venous Anaesthesia has been a subject of interest for all the anaesthesiologists, as it avoids operating theatre pollution.

The availability of rapid and short acting sedatives, hypnotics,analgesics, muscle relaxants has refocused the attention on complete anaesthesia by IV route.The advent of continuous infusion system has made TIVA more popular and convenient.

In this study comparison was done between *Propofol* and *Ketamine* Vs *Propofol* and *Fentanyl* in terms of haemodynamic stability and postoperative recovery.

Patient Demographics

Weight: The mean weight of patients in PK group and PF group were 57.94+/-5.57 and 60.26+/-11.59. The two groups were statistically comparable.

(p>0.05) The mean weight of the patients in two groups of the present study correlates with that of study done by R Mahajan et al. Gender: In present study majority of patients were females as most of surgeries done were dilatation and curettage and suction curettage. Age: The mean age of the patients in two groups of the present study (PK group33+/-8.92, PF group 35+/-9.41) correlates with that of study done by R Mahajan et al.

Haemodynamic Parameters

Changes in Heart Rate

In the PK group there was an increase in the heart rate after induction in the present study and study by R Mahajan et al [1] , whereas there was no increase in the heart rate after induction in the study by Ranju Singh et al [2]. There was decrease in heart rate in PF group after induction in all the three studies. At 30 minutes all the three studies showed heart rate comparable to that of baseline value. Propofol does not change heart rate significantly. Ketamine increases heart rate due to increase in central sympathetic tone. Whereas Fentanyl can cause dose dependant decrease in heart rate. Bradycardia may occur due to central vagal nucleus stimulation.

Changes in Blood Pressure

The baseline systolic and diastolic blood pressure in both groups PK and PF in the present study and studies by R Mahajan et al, Ranju Singh et al were comparable. 3 minutes after induction in PK group there was significant rise in systolic blood pressure in Ranju Singh study, whereas in the present study only slight increase was observed. In PF group 3 minutes after induction significant decrease in systolic blood pressure in present study which is comparable to study by Ranju Singh et al. At 30 minutes systolic blood pressure was comparable in both groups in all three studies.

In the present study, diastolic blood pressure 3 minutes after induction in PK group slightly increased, in PF group a slightly decreased. However at 30 minutes diastolic blood pressure comparable in both the groups in all the studies.

The reason for the rise in Systolic and Diastolic blood pressure in PK group is Ketamine associated stimulation of cardiovascular system. In PFgroup fall in BP observed as Propofol decreases mean arterial pressure and cardiac index.

Nalini KB et al [3], Riham Hasaneun, Wael-El-Syed [4] studies have shown that Propofol-Ketamine combination is superior to Propofol-Fentanyl in terms of haemodynamic stability and respiratory depression.

Ritu Goyal et al [5] concluded that Ketamine being a cardio stimulant drug is better than Fentanyl with respect to haemodynamic stability. The incidence of apnea and respiratory depression are less with Ketamine, but Fentanyl showed faster recovery. Studies by *Guit JB et al [6], Meyer and co-workers [7]* showed stable haemodynamics in both the groups.

Hernandez et al [8] compared 3 combinations in TIVA: Propofol-Ketamine, Propofol-Fentanyl, Midazolam-Ketamine. They concluded that PK group was haemodynamically stable with less respiratory depression. Propofol induced fall in blood pressure was noted in the study by *Berlic et al [9]* .

Sameer kumar Khutia et al [10] Erdenl A , Panuk AG [11] conducted studies in paediatric patients for short surgical procedures. They concluded that Propofol-Ketamine combination provides better sedation and analgesia and reduces the incidence of hypotension when compared to Propofol-Fentanyl.

Oxygen Saturation

Oxygen saturation of both groups before induction were 97.34+/-1.55 and 97.66+/-0.94 which were comparable.

Post Operative Parameters

Time for Spontaneous Eye Opening

In the present study there was significant difference in both PK and PF groups at the end of surgery which were 6.42+/-1.3 min and 3.64+/-1.2 min respectively, p value<0.001 which is significant. In study done R Mahajan et al both groups did not differ significantly in relation to spontaneous eye opening.

Duration of Drowsiness

In present study duration of drowsiness in both PK and PF groups were 12.72+/-1.61 min and 7.42+/-1.32 min, p value is <0.01 which is statistically significant. **S**ukhminder Singh and Sukhminder Bajwa [12] compared Propofol-Ketamine Vs Propofol-Fentanyl, and found recovery was better in Propofol-Fentanyl group. This correlates with our present study.

Ramsay Sedation Score

The mean Ramsay sedation score in PK group is lower than PF group during the procedure.

Mortero et al [13] Sincignano et al [14] found adequate sedation and anaesthesia with fewer side effects with Propofol-Ketamine combination.

Post Operative Nausea and Vomiting

In present study 5patients in PK group and 6 patients in PF group complained of nausea and vomiting, p value 0.74. Similar results were reported by R Mahajan et al. In study by Ranju Singh et al nausea and vomiting higher in PK group when compared to PF group where p value was significant(0.04).

Vallejo et al [15] compared Propofol-Ketamine and Propofol-Fentanyl for laparoscopic tubal ligation. They concluded nausea and vomiting are not less in PK group when compared to PF group.

Emergence Reactions (Postop Delirium)

In present study 3 patients had emergence ractions like postop delirium in PK group whereas none in PF group. In study by R Mahajan et al incidence of emergence reaction in PK group were high.

Benzodiazepines have proved more effective in preventing this phenomenon, Midazolam being more superior than Diazepam. (Cart Wright and Pingel 1984). Inclusion Thiopentone may decrease the incidence whereas Atropine or Droperidol may increase the emergence delirium.

Summary

The present clinical study '*A Comparative Study of Ketamine and Propofol Versus Fentanyl and Propofol in Total Intravenous Anaesthesia for Short Surgical Procudures*' was undertaken in Mediciti Institute of Medical Sciences, Ghanpur, RR District, Telangana.

Total of 100 patients of either sex aged between 18-65 years and ASA grade I & II undergoing short surgical procedures of less than half an hour were allocated into two groups of 50 each.

Group 1: *Propofol* 1.5mg/kg and *Ketamine 1*mg/kg (PK group)

Group 2: *Propofol* 1.5mg/kg and *Fentanyl* 1 mcg/kg (PF group)

Observations Made in this Study

Heart rate is statistically significant in both PK and PF groups upto 15 minutes. In PK group it returned to base line level at 15th minute.

Systolic blood pressure in both PK and PF group show significant difference upto 15min. At 18th minute systolic blood pressure in both groups returned to base line level.

Diastolic blood pressure in both PK and PF group showed significant difference statistically upto 9 min. In both groups it returned to base line level at 12 min.

There was no incidence of apnea or desaturation in both the groups.

Incidence of Post operative nausea and vomiting is more in PF group, although insignificant when compare to PK group.

Emergence reactions observed in PK group only. (3 patients).

Conclusion

From the present study we concluded that both *Propofol-Ketmine* and *Propofol-Fentanyl* are equally safe and effective in Total Intra Venous Anaesthesia for patients undergoing short surgical procedures.

Though there was statistically significant difference in haemodynamic parameters when both groups compared, clinically there was not much difference. *Propofol-Ketamine* appears to be slightly better haemodynamic stability compared to *Propofol-Fentanyl*. Postoperative recovery was superior in *Propofol-Fentanyl* group. Postoperative nausea and vomiting was more in Propofol-Fentanyl group.

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Original Article

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A Comparison of A Crystalloid Co-Load, with or without A Phenylephrine Infusion, for Prevention of Hypotension Following Subarachnoid Block for Caesarean Section

Elizabeth Joseph*, Sunilkumar T.S., K.K. Mubarak***, Anto Paul******

Abstract

Hypotension produced by the sympathetic blockade associated with spinal anesthesia has maternal and foetal adverse effects. Intravenous fluid expansion and vasopressors are used to prevent this hypotension. In this study we compared the effect of a combination of crystalloid co-load of lactated Ringer's solution and a prophylactic phenylephrine infusion versus crystalloid co-load alone in preventing pre-delivery hypotension in the mother following subarachnoid block for lower segment caesarean section. 100 ASA I or II term parturients posted for caesarean delivery were enrolled. They were randomly divided in to two groups: Group 1) a co-load of lactated Ringer's solution at a volume of 15ml/kg body weight given over 10 minutes and a prophylactic phenylephrine infusion at rate of 50mcg/min. Group 2) a co-load of lactated Ringer's solution at a volume of 15ml/kg body weight given over 10 minutes alone. Subarachanoid block was performed with 2 ml hyperbaric 0.5% bupivacaine (10 mg) at L3-4 interspace. Immediately after the injection of the intrathecal medication, the co-load with or without infusion of phenylephrine was started depending on the group allocated. NIBP, heart rate and SpO_2 were recorded every 1 minute until delivery, and thereafter every 3 minutes until the end of study. The incidence of pre-delivery hypotension was 2 % and 68 % respectively in group 1 and group 2. The lower incidence of pre-delivery hypotension in the group 1 was found to be statistically significant with a p value less than 0.01. The side effect profile of the two regimens was also comparable. In conclusion we found that prophylactic phenylephrine infusion at rate of 50mcg/min with a co-load of lactated Ringer's solution at a volume of 15ml/kg body over 10 minutes significantly lowered pre-delivery hypotension in the mother.

Keywords: Ringer Lactate Co-Load; Phenyephrine Infusion; Sub-Arachnoid Block; Hypotension.

Introduction

Caesarean deliveries have increased in incidence over the past several decades and have become a commonly performed surgical procedure [1]. Providing anaesthesia for caesarean delivery is a challenging task for the anaesthesiologist

The most commonly used anaesthetic technique for caesarean delivery is spinal anesthesia [2,3]. This simple and reliable technique provides rapid onset of dense neuroblockade. The risk of systemic local anaesthetic toxicity is negligible with spinal anaesthesia. The transfer of drug to the foetus is minimal. The danger of aspiration and neonatal depression associated with general anaesthesia is also avoided.

Hypotension produced by the sympathetic blockade associated with this technique is a concern as it has maternal and foetal adverse effects. Anaesthesiologists should aim to actively prevent hypotension. Among several ways to prevent hypotension are intravenous fluid expansion and use of vasopressors.

Phenylephrine infusion is a safe and effective way to reduce incidence and frequency of hypotension during subarachnoid block for caesarean delivery [4]. A rapid administration of crystalloid after the induction of spinal anaesthesia (co-load) rather than before (preload) has been shown to be of advantage in preventing maternal hypotension prior to delivery [5]. However, the optimal administration regimen is undetermined.

Author's Affiliation:
*Associate Professor, **Assistant Professor, ***Professor and Head ****Senior Resident, Department of Anaesthesiology, Govt. Medical College Thrissur.

Corresponding Author:
Elizabeth Joseph, Associate Professor, Department of Anaesthesiology, Govt. Medical College, Thrissur, 680596, Kerala.
E-mail: lizcibu@yahoo.co.in

Hypotension was virtually eliminated by use of high-dose prophylactic phenylephrine infusion at a rate of 100mcg/min and rapid crystalloid co-load up to two litres. However, incidence of reactive hypertension was up to 47% [6]. This is of concern in patients in whom increase of blood pressure might be detrimental, like in the presence chronic hypertension or a compromised uteroplacental blood flow. Phenylephrine 25 and 50 mcg/min administered as a prophylactic fixed rate infusion provided greater maternal hemodynamic stability than phenylephrine 75 and 100 μg/min [7].

There is a paucity of studies comparing crystalloid co-loading versus phenylephrine infusion with crystalloid co-loading in parturients undergoing caesarean section under spinal anaesthesia. This study compared incidence of hypotension in mothers who received a co-load of lactated Ringers solution at a volume of 15ml/kg body weight over ten minutes, with or without a phenylephrine infusion at the rate of 50mcg/min.

Objectives

To compare the effect of a combination of crystalloid co-load of lactated Ringer's solution at a volume of 15ml/kg body weight given over 10 minutes and a prophylactic phenylephrine infusion at rate of 50mcg/min versus crystalloid co-load alone in preventing pre-delivery hypotension in the mother following subarachnoid block for lower segment caesarean section.

Materials and Methods

The study was a prospective cohort study conducted over a period of 18 months after obtaining approval of Institutional Technical Committee and Human Ethical Committee of Government Medical College, Thrissur. Based on similar studies in the past a total sample size of 100 in two groups of 50 each was found sufficient for a two sided confidence level (1-alpha) of 95% and power (1-beta) of 80 %.

Inclusion Criteria

1. ASA physical status 1 and 2 pregnant women posted for caesarean delivery under spinal anaesthesia.
2. Singleton gestation at a gestational age of > 36 weeks

Exclusion Criteria

1. ASA physical status 3 or more,
2. Age < 20yrs or >40yrs
3. Height <145 cm or >165 cm,
4. Body weight <45 kg or >75 kg
5. Presence of foetal distress

Patients were assessed for eligibility for the study during pre-anaesthetic evaluation. A total of 100 patients who were found eligible and were willing to be part of the study, were enrolled after obtaining informed written consent in the patients mother tongue.

Group 1 consisted of 50 patients who received a co-load of lactated Ringer's solution at a volume of 15ml/kg body weight given over 10 minutes and a prophylactic phenylephrine infusion at a rate of 50mcg/min.

Group 2 consisted of 50 patients who received a co-load of lactated Ringer's solution at a volume of 15ml/kg body weight given over 10 minutes.

All patients were premedicated with intravenous ranitidine 50 mg; on the night before and on the morning of day of the surgery and intravenous metoclopramide 10 mg on the morning of day of the surgery. Baseline systolic blood pressure and heart rate (mean of 3 consecutive measurements taken 5 minutes apart with patient left undisturbed in supine position with left uterine displacement) was recorded. Phenylephrine infusion with concentration of 50mcg/ml in measured volume infusion devices was prepared. Rescue syringes of Phenylephrine (50mcg/ml), and atropine (0.6mg/ml) were also prepared and labelled. Patient was transferred on to a levelled operating table and pulse-oximetry , electrocardiography, and non-invasive blood pressure monitoring established. Oxygen at a rate of 5 L/min was given by a facemask. Intravenous cannulas of 16G and 18G were inserted on the forearm and connected to a bottle of warmed lactated Ringer's solution and a measured volume infusion device respectively. 2 ml hyperbaric 0.5% bupivacaine (10 mg) was given intrathecally with a 25-gauge Quincke's spinal needle at L3–L4 vertebral interspace by aseptic technique with the patient in right lateral position. Immediately after the injection of the intrathecal medication, the co-load of Ringer Lactate 15ml/kg was started. Infusion from the measured volume infusion device was started at a rate of 60ml/h, group 1 patients were given phenlyephrine 50mcg/min. Patients were returned to the supine position with a 15-degree wedge under

the right hip. The upper dermatomes blocked to light touch and cold sensation was recorded. NIBP, heart rate and SpO_2 were recorded every 1 minute until delivery, and thereafter every 3 minutes until the end of study. Systolic blood pressure was maintained above the lower limit of acceptable range with phenylephrine 50mcg boluses when needed

After delivery oxytocin 10 IU was administered intravenously as an infusion, phenylephrine infusion if administered was stopped . On completion of the co load, lactated Ringer's solution was administered at a maintenance rate. Completion of surgery marked the end of the study. All patients were subsequently followed up until they were discharged from the hospital.

The primary outcome was the incidence of pre-delivery hypotension in the mother. Secondary outcomes were the total number of episodes of hypotension during the study period, maternal bradycardia, the incidence of nausea and vomiting, the total dose of phenylephrine used, Apgar scores at 1 and 5 minutes Side effects were defined as following

1. Hypotension - Systolic BP < 20% of baseline, or <100 mm of Hg whichever is higher.
2. Hypertension- Systolic BP> 20% of baseline.
3. Bradycardia- Heart rate < 50 beats per minute.

The side effects were managed as mentioned below.

Hypotension- 50 mcg intravenous boluses of phenylephrine

Hypertension - Stopping of infusions. Infusion was restarted only when SBP decreases to below the upper limit of the target range.

Bradycardia - Stopping of drug infusion and, if associated with hypotension intravenous Atropine 0.6 mg.

Intraoperative nausea or vomiting was treated with Ondansetron 4 mg IV.

Observations and Results

The observations made were tabulated and analysed using computer software, Statistical Package for Social Sciences. The mean and standard deviation for various parameters were calculated. Independent t-test, Chi-square tests, and Mann-Whitney U test were used to compare variables

Table 1: Comparison of maternal characteristics

Variable	Group 1 Mean ± SD, (range)	Group 2 Mean ± SD, (range)	p value
Age (years)	27.2 ± 4.2, (20-39)	27.8 ± 4.7, (20-38)	0.501
Height (cms)	152.0 ± 5.2, (145-165)	154.0± 5.3, (145-165)	0.050
Weight (kg)	63.0 ± 8.2, (49-75)	65.5 ± 7.4, (49-75)	0.109
BMI	27.2 ± 2.5, (21.7-30)	27.5 ± 2.8, (21.7-30.4)	0.45
Gestational age (days)	270.3 ± 5.8, (254-283)	269.8 ± 6.7, (253-285)	0.727

The patients in both groups were comparable with respect to their age, height, weight, body mass index, and period of gestation.

Table 5.2: Comparison of parity

Gravidity	Group 1		Group 2		χ^2	P
	Count	Percent	Count	Percent		
Nullipara	12	24.0	7	14	2.3	0.129
Multipara	38	76.0	43	86		

The differences between the groups were not statistically significant.

Table 5.3: Comparison of baseline hemodynamic parameters

	Group 1 Mean ± SD, (range)	Group 2 Mean ± SD (range)	p value
Baseline Heart rate	84.3 ± 6.7, (75-95)	83.1 ± 6.1, (76 -95)	0.376
Baseline Systolic BP	119.6 ± 10.3, (100 -132)	119.5 ± 8.4, (103-132)	0.966

The patients in both groups were comparable with respect to their baseline heart rate and systolic blood pressure.

Table 5.4: Comparison of sensory block level at beginning of surgery

Sensory block level at beginning of surgery	Group 1		Group 2		χ^2	P
	Count	Percent	Count	Percent		
T5	2	4.0	21	42.0	27.7**	0.000
T6	22	44.0	22	44.0		
T7	21	42.0	7	14.0		
T8	5	10.0	0	0.0		

** Significant at 0.01 level

The level of sensory blockade at the beginning of surgery was analysed using the Chi-Square test. There was a significant difference between the two groups with respect to the level of sensory blockade at the beginning of surgery with a p value of < 0.01.

Table 5.5: Comparison of operative data

Variable	Group 1 Mean ± SD, (range)	Group 2 Mean ± SD, (range)	p value
Spinal induction – Delivery interval (minutes)	14.3 ± 1.6, (11-18)	14.3 ± 1.9, (11- 18)	0.955
Skin incision – Delivery interval (minutes)	10.3 ± 1.4, (8- 13)	10.3 ± 1.6, (8- 13)	0.842
Uterine incision – Delivery interval (minutes)	1.4 ± 0.5, (1-2)	1.6 ± 0.5, (1-2)	0.073
Duration of surgery (minutes)	43.2 ± 2.9, (37- 49)	43.3 ± 2.9, (38- 49)	0.863
Volume of RL (ml)	1006.8 ± 127.9, (800 - 1200)	1046.0 ± 115.9, (780 - 1220)	0.112
Intraoperative Blood loss (ml)	412.8 ± 62.3, (250 - 540)	391.8 ± 67.4, (270 - 550)	0.109

The two groups were comparable with respect to operative data like Spinal induction – Delivery interval, Skin incision – Delivery interval, Uterine incision – Delivery interval, Duration of surgery, Volume of Ringer Lactate infused, and Intraoperative Blood loss

Table 5.6: Comparison of incidence of pre delivery hypotension

Pre delivery hypotension	Group 1		Group 2		χ^2	P
	Count	Percent	Count	Percent		
No	49	98.0	16	32.0	47.87**	0.000
Yes	1	2.0	34	68.0		

** Significant at 0.01 level

The difference in incidence of pre delivery hypotension was found to be of statistical significance with a p value <0.01.

Table 5.7: Comparison of number of episodes of pre delivery hypotension

Number of episodes of pre delivery hypotension	Group 1		Group 2		Z#	P
	Count	Percent	Count	Percent		
0	49	98.0	16	32.0	6.82**	0.000
1	1	2.0	5	10.0		
2	0	0.0	14	28.0		
3	0	0.0	12	24.0		
4	0	0.0	3	6.0		

Mann-Whitney U Test
** Significant at 0.01 level

A comparison of number of episodes of hypotension using the Mann-Whitney U Test showed a statistically significant difference between the groups with a p value < 0.01.

Table 5.8: Comparison of total dose of phenylephrine used based on group

	Group1	Group 2
Mean	718.0	92.0
SD	81.9	82.9
Median	725.0	100.0
Minimum	550	0
Maximum	900	300

The difference in mean of total dose of phenylephrine between the groups was statistically significant with a p value < 0.01.

Table 5.9: comparison of number of physician intervention based on group

	Group1	Group 2
Mean	0.1	1.8
SD	0.2	1.7
Median	0.0	2.0
Minimum	0	0
Maximum	1	6

t = 7.51**, p = 0.000
The difference in mean number of physician interventions between the groups was statistically significant with a p value < 0.01.

Table 5.10: Distribution of APGAR scores of new borns

APGAR score		Group 1		Group 2	
		Count	Percentage	Count	Percentage
1 minute	9	50	100.0	50	100
5 minutes	9	50	100.0	50	100

All new-borns born to mothers in both groups had APGAR scores of nine at one and five minutes after delivery.

There were no episodes of maternal bradycardia, nausea, vomiting, or any other side effects in either group.

Discussion

Single-shot spinal anaesthesia has emerged as the technique of choice for routine scheduled caesarean delivery. It is a simple, fast, reliable, and cost-effective technique. Hypotension following subarachnoid blockade for caesarean delivery remains a common clinical problem with a reported incidence of up to 85 %.

Pregnant patients at term are more prone to develop hypotension due to the occurrence of aortocaval compression and due to the higher level of sympathectomy owing to increased spread of local anaesthetic in the cerebrospinal fluid. Hypotension is hazardous to the mother and foetus and is associated with morbidity for both the mother (nausea and vomiting) and the foetus (foetal acidosis). The aim of anaesthesiologists should be to actively prevent maternal hypotension and to treat it quickly and efficaciously.

Hypotension has been variously defined as a reduction in arterial pressure of 30 mm of Hg, a reduction to less than 100 mm of Hg or as a reduction of 20% below baseline pressure. For the purpose of this study, hypotension was defined as a reduction of systolic blood pressure to less than 100 mm of Hg or to 20% of the baseline pressure whichever was higher.

Strategies that have been used to minimize hypotension include maternal left tilt, leg wrappings, sympathomimetic drugs, and intravenous fluid loading before or with induction of spinal anaesthesia. The combination of vasopressors with a rapid crystalloid loading at the time of spinal injection is an interesting strategy. Recent work suggests that prophylactic continuous infusion of the alpha-adrenergic agonist phenylephrine is superior to ephedrine in prevention of spinal anaesthesia induced hypotension. Although some studies showed that phenylephrine was not associated with maternal or foetal morbidity, the high incidence of maternal bradycardia is of concern.

This study aimed to compare the effect of a combination of crystalloid co-load of lactated Ringer's solution at a volume of 15ml/kg body weight given over 10 minutes and a prophylactic phenylephrine infusion at rate of 50mcg/min versus crystalloid co-load alone in preventing pre-delivery hypotension in the mother following subarachnoid block for lower segment caesarean section. In this study 100 term parturients posted for caesarean delivery were allocated to two groups.

Group 1 consisted of 50 patients who received a co-load of lactated Ringer's solution at a volume of 15ml/kg body weight given over 10 minutes and a prophylactic phenylephrine infusion at rate of 50mcg/min

Group 2 consisted of 50 patients who received a co-load of lactated Ringer's solution at a volume of 15ml/kg body weight given over 10 minutes The two groups were comparable with respect to age, height, weight, body mass index, and period of gestation and parity. The baseline heart rate and systolic blood pressure were also comparable between the groups

In this study, there was a statistically significant difference between the groups with respect to the level

of sensory blockade at the beginning of the surgery.

2 patients (4%) in group 1 had T5 sensory blockade, while 22 patients (42%) in group 2 had T5 sensory blockade at the beginning of the surgery. 22 patients (44%) in both groups had a T6 sensory blockade, 21 patients (42%) in group 1 and 7 patients (14%) in group 2 had a T7 sensory blockade. 5 patients (10%) in group 1 had a T8 sensory blockade; while none of patients in group 2 had a T8 sensory blockade at the beginning of the surgery. Thus the level of sensory blockade was found to be significantly lower in the group 1 (Chi-square test, $p < 0.01$).

Cooper et al [8] in 2004 reported that intravenous administration of phenylephrine, to prevent maternal hypotension during combined spinal epidural anaesthesia for caesarean section decreases the rostral spread of spinal anaesthesia. A possible mechanism is by reduction of epidural pressure as a result of epidural vein constriction produced by phenylephrine.

The two groups were comparable with respect to operative data like Spinal induction – Delivery interval, Skin incision – Delivery interval, Uterine incision – Delivery interval, Duration of surgery, Volume of Ringer Lactate infused, and Intra operative blood loss

The primary outcome studied was the incidence of pre-delivery hypotension in the mother. Only 1 patient (2%) in group 1 developed pre-delivery hypotension while 34 patients (68%) had pre-delivery hypotension in group 2. The lower incidence of pre-delivery hypotension in the group of patients who received a co-load of lactated Ringer's solution at a volume of 15ml/kg body weight given over 10 minutes and a prophylactic phenylephrine infusion at rate of 50mcg/min was found to be of statistical significance with a p value less than 0.01

Secondary outcomes studied were the total number of episodes of pre-delivery hypotension, maternal bradycardia, incidence of nausea and vomiting, total dose of phenylephrine used, number of physician interventions, Apgar scores at 1 and 5 minutes

There was only one episode of pre-delivery hypotension among all of the group 1 patients, while among group 2 patients, 5, 14, 12 and 3 patients had 1,2,3,4 episodes of pre-delivery hypotension. The lower number of episodes of pre-delivery hypotension in the group 1 was found to be of statistical significance (Mann-Whitney U test, $p < 0.01$)

There were no episodes of maternal bradycardia, nausea, vomiting, or other side effects in both groups.

The mean of total dose of phenylephrine used in group 1 and group 2 were 718 and 92 micrograms respectively. The higher total dose of phenylephrine in group 1 was found to be of statistical significance with a p value less than 0.01. However, this higher dose did not produce any side effects in those patients.

There was a statistically significant decrease in the number of physician interventions in the group 1 (p value less than 0.01).

All new-borns born to mothers in both groups had Apgar scores of nine at one and five minutes. Thus in this study there was no difference in neonatal outcomes as assessed clinically by using Apgar score.

Conclusion

According to the results of this study prophylactic phenylephrine infusion at rate of 50mcg/min with a co-load of lactated Ringer's solution at a volume of 15ml/kg body over 10 minutes significantly lowered pre-delivery hypotension in the mother. This prophylactic phenylephrine infusion also reduced the number of physician interventions needed to maintain hemodynamic stability during caesarean section under subarachnoid block. However, in this study, the prophylactic phenylephrine infusion resulted in a significantly higher total dose of phenylephrine when compared to a lone co-load of lactated Ringer's solution at a volume of 15ml/kg body over 10 minutes. But this higher dose did not produce any side effects in those patients. No significant difference in neonatal outcomes clinically assessed by Apgar score was however evident between the groups. The side effect profile of the two regimens was also comparable in this study.

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Indian Journal of Anatomy	3	8000	800
Indian Journal of Ancient Medicine and Yoga	4	7500	750
Indian Journal of Anesthesia and Analgesia	3	7000	700
Indian Journal of Anthropology	2	12000	1200
Indian Journal of Biology	2	4000	400
Indian Journal of Cancer Education and Research	2	8500	850
Indian Journal of Communicable Diseases	2	8000	800
Indian Journal of Dental Education	4	4500	450
Indian Journal of Forensic Medicine and Pathology	4	15500	1550
Indian Journal of Forensic Odontology	2	4500	450
Indian Journal of Genetics and Molecular Research	2	6500	650
Indian Journal of Law and Human Behavior	2	5500	550
Indian Journal of Library and Information Science	3	9000	900
Indian Journal of Maternal-Fetal & Neonatal Medicine	2	9000	900
Indian Journal of Medical & Health Sciences	2	6500	650
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International Journal of Practical Nursing	3	5000	500
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Journal of Forensic Chemistry and Toxicology	2	9000	900
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Post Dural Puncture Headache in LSCS: A Comparison of 25g Whitacre with 25g and 27g Quincke Spinal Needle

Sharma Lata*, Somvanshi Mukesh, Khangaroot Singh Sharad***, Yadav Amit******

Abstract

The object of this study was to evaluate the effect ofgauze and type of spinal needle in causing post dural puncture headache (PDPH) in parturient undergoing LSCS. Seventy five parturient ASA grade I and grade II , age 20-35year with singleton uncomplicated pregnancy, who were randomized into three group I, II, and III received spinal anaesthesia using 25G quincke, 27G quincke and 25G whitacre needle respectively. Patients were interviewed on first, second, third and fourthday , after surgery, and were questioned with regard to incidence of headache, its severity, location, character, duration and associated symptoms like nausea, vomiting, auditory, ocular symptoms, and backache.The observations were analyzed by chi square and student t test. Statistical significance was assumed when p was <0.05. Incidence of PDPH was 20% in group I, 12% in group II and 4% in group III, which was not statistically significant. Among patients who developed headache, majority of patient had mild generalized headache. Most of patients develop PDPH on first postoperative day. Although the incidence of headache was statically similar among three groups, but clinically the headache was lesser in patients who received subarachnoid block with 25G whitacre spinal needle is compared to 25G quincke and 27G quincke spinal needle. 25G whitacre spinal needle is appropriate to minimize post dural puncture headache in cases of caesarean section.

Keyword: PDPH; Spinal Anaesthesia; LSCS.

Introdution

Spinal anaesthesia is more widely practice anaesthetic technique in caesarean section. The main advantages of this technique are it is simple to institute, rapid in onset, require minimum apparatus and small volume of drug, patient remain conscious during surgery, maintain airway, reduces risk of aspiration pneumonitis, and require minimum post-operative care & post-operative analgesia. It also avoids foetal as well as maternal risk of general anaesthesia. Since the introduction of spinal anesthesia, headache is remained a well recognizediatrogenic complication. So we had undertaken this study to evaluate the effect of type and gauze of the spinal needle on PDPH in parturient undergoing LSCS under spinal anaesthesia.

Method

After approval from hospital ethical committee, this study was carried out on 75 parturient ASA grade I and grade II aged 20-35years with singleton uncomplicated pregnancy who were undergoing LSCS under spinal anaesthesia.

Written consent was taken from each patient. Patients were randomly divided into three groups of 25patients each.Group I patients received SAB with 25G quincke spinal needle, Group II patients received SAB with 27G quincke spinal needle,and Group III patients received SAB with 25G whitacre spinal needle.

Patient, those having more than one attempt to achieve CSF flow, history of convulsion and bleeding disorder, previous history of headache, backache, toxaemia of pregnancy, CVS/CNS disorder, neuromuscular disorder (myopathies, neuropathies) patient on anticoagulant therapy and vertebral anomalies were excluded from the study .

All the patient were screened preoperatively. On arrival of the patients in the operation theater, venous line was secured with 18G cannula and patients were kept in supine position with wedge under right hip to maintained left uterine

Author's Affiliation:
*Medical Officer, **Associate Prof.essor ***Profesoor **** Senier Resident, Dept. of Anaesthesiology, Govt. Medical College, Kota.

Corresponding Author:
Lata Sharma, 255: Ka, Back Ajay Ahuja School, Rangpur Road 4, Dadwara, Kota 324002.
E-mail: drmps_singh@yahoo.co.in

displacement. Then ECG three leads, noninvasive BP & pulse oximeter attached through multipara meter monitor. Patients were preloaded with 500c.c Ringer lactate solution prior to administration of spinal anaesthesia. Under all aseptic precaution, spinal anaesthesia was given in sitting position at L2-3 or L3-4 inter space,with disposable spinal needle according to group allocated.Quincke needle was introduced with bevel direction parallel to sagittal plane of the dural fibers. When free flow of CSF was started 2.25 - 2.5ml of 0.5% heavy bupivacaine was introduced into the intrathecal space, and betadine dressing was applied at the puncture site. Then patient was turned to her back with left uterine displacement with wedge under right hip.

Soon after performing central neuraxial block intraoperative BP and Pulse were recorded. Level of sensory block was assessed by pin prick method. Motor blockade was assessed by modified Bromage motor scaleColloid and blood was transfused according to the blood loss. Complications like hypotension, bradycardia, nausea, vomiting and respiratory depression were treated accordingly. Hypotension and bradycardia were denoted in this study, when BP and pulse were decreased 20% of the base line value. Vitals were recorded every one minute during first 10min.,after that every 5 min. till completion of surgery.

Patients were interviewed on first, second, third and fourth postoperative day about the incidence of headache, its severity, location, character, and duration, associated symptoms like nausea, vomiting, auditory, ocular symptoms, and backache. For blinding patients were interviewed by another anaesthesiologist who were unaware about the type and size of needle used.

The headache that occur after mobilization, mostly localized in occipital, frontal or generalized, aggravated by erect or sitting position and coughing, sneezing or straining and relieved by lying flat is considered as PDPH.

Severity of headache was assessedaccording to Crocker's 4point scale

1. Mildheadaches which permitted long period of sitting/erect position and no other symptoms.
2. Moderate headache, which made it difficult for the patient to stay up right for more than half an hour,occasionally accompanied by nausea, vomiting, auditory and ocular symptoms.
3. Intense headache which immediately occur upon getting up from bed, alleviated while lying horizontal in bed often accompanied by nausea, vomiting, ocular and auditory symptoms ,and
4. Severeheadache that occurred even while lying horizontal in bed and greatly aggravated immediately upon standing up, eating is impossible because of nausea and vomiting.

Statistical analysis was done using chi square tests and student t test and p was <0.05 was considered as significant.

Patient, who developed PDPH treated with bed rest, inj. Diclofenac 75mg IM and adequate hydration.

Result

The groups were comparable in with respect to age, weight and height (Table 1).

The incidence of PDPH in all the three groups was statistically insignificant (Table 2). Onset of headache was varies from first to third postoperative day in all three groups (Table 3). Majority of patients develop generalized headache, while two patient in group I developed frontal headache (Table 4). All patients in three groups who developed headache had grade I (mild) headache, none of them had moderate to severe headache (Table 5). Headache was subsided within 24hours in most of the patient but it was lasted upto 48hours in 3 patients in group I (Table 6). Patient who had headache were treated with analgesic and hydration. None of the patient required epidural blood patch.

Table 1: Demographic data

	Group I (n=25)		Group II (n=25)		Group III (n=25)	
Age (yr)	23.0	± 3.31	23.6	± 3.17	23.4	± 3.67
Height (cm)	156	± 3.7	157	± 4.05	155	± 4.28
Weight (kg)	59.2	± 4.66	60.8	± 4.61	60.28	± 5.15

Values are mean ±SD

Table 2: Incidence of post dural puncture headache

Duration	Group I (n=25)		Group II (n=25)		Group III (n=25)	
No headache	20	(80%)	23	(88%)	24	(96%)
Headache	5	(20%)	2	(12%)	1	(04%)

Table 3: Onset of headache

Post OP. Day	Group I (n=25)		Group II (n=25)		Group III (n=25)	
1st Day	1	(4%)	2	(8%)	0	-
2nd Day	2	(8%)	0	-	1	(4%)
3rd Day	2	(8%)	0	-	0	-
4th Day	0	-	0	-	0	-

Table 4: Location of headache

Location	Group I (n=25)		Group II (n=25)		Group III (n=25)	
Frontal	2	(8%)	0	-	0	-
Occipital	3	(12%)	2	(8%)	1	(4%)
Generalized	0	-	0	-	0	-

Table 5: Severity of headache

Serverity	Group I (n=25)		Group II (n=25)		Group III (n=25)	
Mild	5	(20%)	2	(8%)	1	(4%)
Moderate	0	0	0	0	0	0
Intense	0	0	0	0	0	0
Severe	0	0	0	0	0	0

Table 6: Duration of headache

Hours	Group I (n=25)		Group II (n=25)		Group III (n=25)	
<24 Hrs.	2	(8%)	2	(8%)	1	(4%)
25 - 48 Hrs.	3	(12%)	0	0	0	0
> 48 Hrs.	0	0	0	0	0	0

Discussion

General anaesthesia for performing caesarean section is associated with increase chance, of complications. Therefore, the spinal anaesthesia is the method of choice for caesarean section.But the PDPH is an iatrogenic complication of spinal anaesthesia. Postdural puncture headache is defined as a headache that occurs after dural puncture and has a significant effect on the patient's postoperative well-being. The headache is postural and continuous for more than 24 hours at any level of severity or intensity and unable the patients to maintain upright posture.

The overall incidence of this distressing complication of post dural puncture headache has varied from 0.00% to25.00%, as reported by various authors. If the PDPH is taken lightly and not treated properly, maternal morbidity and mortality may occur. Therefore anaesthesiologist should know about this complication and its preventive methods.

The most important factor contributing to the higher incidence of PDPH was the gauge and type of needles used. Higher the gauge or thicker the needle, more traumatic type of (cutting type) needle, more the incidence of post spinal headache [1,2].

There is considerable evidence that the PDPH is due to low CSF pressure consequent upon seepage of CSF through the dural puncture hole and choroid plexus is unable to secrete sufficient fluid to maintain the CSF pressure [3]. Moreover the negative pressure in the epidural space may draw CSF from subarachnoid space. The magnitude and rapidity of CSF is lost and the rate at which it is reformed governs the incidence, rapidity of onset and severity of headache.

Cerebrospinal fluid leaking from the duralhole produces low CSF pressure that leads to intra cranial venous dilatation resulting in an increase in brain volume . Venous dilation and compensatory increase in brain volume will result in brain sag which in turn will exert traction and stimulate pain sensitive anchoring structures like dural vessels, basal dura and tentorium cerebella, causing post spinal headache [4].

Larger the hole in dura mater more will be the leakage of CSF and longer the time required for repair. The numbers of holes are also made a difference in the loss of CSF. It takes about two weeks or more for the holes to seal.

Parturients are particularly more prone to PDPH than other female patients because of the younger age less than 40 year and reduction of both the intra-abdominal and epidural pressure after delivery. Thereby promoting extraleakage of the CSF than usual. Other factors for increased incidence of headache are hormonal changes,stress of labour and dehydration.

Design of needle tip is most important factor.The tip of the pencil point needle separates the longitudinal dural fibers and arachnoid without producing serious injury. When the needle is withdrawn the fibers return to a state of close approximation. The cutting needle tip cuts out longitudinal fibers of dura even when the bevel is parallel to the fibers [5].

Reina M.A. et al. observed that when the needle was inserted with its bevel parallel to the axis of the dural sac in fresh cadavers the size of the dura-arachnoid lesion was 0.032 mm^2 in the epidural surface and 0.037 mm^2 in the subarachnoid surface of the dural sac. When the needle's bevel was perpendicular to the axis the measurement of the lesion size was 0.042 mm^2 for the external surface and 0.033mm^2 for the internal.

In a meta-analysis byRichman JM et al. indicates that with use of a cutting needle, insertion in a parallel fashion may significantly reduce the incidence of PDPH.

In the present study, bevel of the needle was inserted parallel to the longitudinal dural fibers in all the patients where quincke needle was used. So that narrow opening is obtained without much damaging the dural fibers, thereby decreasing the CSF

leakage.

Adequate hydration is recommended before applying the spinal block by various authors states that dehydration increased the severity of the PDPH, whereas the incidence was unaffected [6]. However in present study all patients were preloaded and adequately hydrated, so this factor did not contributed in headache development.

In our study, once the patient had headache, they were instructed to take complete bed rest. All patients who had PDPH received Inj. Diclofenac sodium IM (75 mg) 8 hrly and hydration therapy with 5% dextrose 500 cc. as additional fluid with in a period of one hour. All the patients responded with this treatment and did not complain of headache after 24 hrs, except three patientswho required a similar pattern of treatment for another 24 hrs. None of the patients required epidural blood patch.

Although the difference was statistically insignificant, the 25G Whitacre (pencil point) spinal needle caused a lower incidence of PDPH than the 27G Quincke (cutting type) spinal needle.

Thus we concluded that 25G Whitacre (pencil point) needle is appropriate spinal needle to minimize Post Dural Puncture Headache in cases of cesarean section.

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Efficacy of Combination Therapy with Reduced Volume of Crystalloid Preloading and Reduced Dose of Vasoconstrictor as an Effective Prophylaxis Against Spinal Hypotension

Balaraju Thayappa C.*, G. Amarappa*, Kiran Kumar K.S., Naveed Abrar****

Abstract

Background: Various methods have been devised to prevent hypotension, a very common complication of subarachnoid block(SAB). This study was conducted to evaluate the efficacy of combined use of crystalloid preloading and vasoconstrictor for prevention of hypotension due to SAB, when compared to crystalloid preloading. *Methods:* 100 adult patients of physical status ASA I and II scheduled to undergo elective surgical procedure on lower abdomen under SAB were divided into two groups of 50 each. *Crystalloid group:* Preloaded with Ringer's lactate: 15 ml/KBW over 20 min before SAB. *Combination group:* Preloaded with 7.5 ml/KBW of Ringer's lactate over 10 min preceding SAB, followed by IV bolus of 2.5 mg of ephedrine in the first and second minute and 0.5mg ephedrine at the end of each minute for next 18 minutes after SAB. In each patient, pulse rate and systolic blood pressure were recorded. Subsequently, the recordings were done at 5th, 10th, 15th, 20th, 25th and 30th minute after SAB. *Results:* The incidence and severity of hypotension was maximum (18%) in the crystalloid group and less (2%) in the combination group. The difference in incidence of hypotension among two groups was statistically significant(P<0.05). The incidence of reactive hypertension was more in combination group (4%) than the crystalloid group (2%) and was statistically significant (P<0.05). The incidence of nausea (4 %) and vomiting (2%) was seen in combination group whereas there were no incidence of the same in crystalloid group. *Conclusion:* Combination therapy with the reduced volume of crystalloid preloading and reduced dose of vasoconstrictor is an effective preventive measure against hypotension due to SAB and provides better haemodynamic stability when compared to the use of preloading alone.

Keywords: Subarachnoid Block; Hypotension; Crystalloid Preloading; Vasoconstrictor; Ephedrine.

Introduction

Spinal anaesthesia was introduced into clinical practice by a general surgeon Karl August Bier in 1898 [1]. More than a century has passed and even today, it is one of the most popular techniques for both elective and emergency surgical procedures particularly Caesarean Sections, lower abdominal surgeries, lower limb and urological surgeries just to name a few [2].

The most common serious problem associated with spinal anaesthesia still remains the rapid onset of profound hypotension and it can cause significant mortality and morbidity. Various studies indicate an incidence of hypotension varying from 20% to 92% [1,3].

Spinal induced hypotension is undesirable in obstetrics because it may adversely affect both maternal and neonatal outcome owing to a significant fall in uteroplacental blood flow. Even a mild drop in blood pressure must be avoided in high risk patients such as the elderly and in those with underlying organ dysfunction in whom the autoregulatory mechanism may be abnormal [4].

Considering all this, the prevention of hypotension during subarachnoid block is an important subject and there is no perfect method to prevent it. The corner stones of prevention of hypotension due to SAB for caesarean section are the use of a left lateral tilt and volume pre-loading [5]. Mechanical methods like left lateral tilt, use of sluder, leg wrapping with esmarch bandages and thrombo-embolic stockings, volume pre loading and vasopressors have been tried from time to time with variable results

Author's Affiliation:
*Associate Professor, **Post Graduate, Department of Anesthesiology, Navodaya Medical College, Raichur.

Corresponding Author:
Naveed Abrar, Post Graduate, Department of Anesthesiology, Navodaya Medical College, Raichur-584 103 Karnataka.
E-mail: drnad007@gmail.com

[4]. Several studies have shown that an adequate preload of at least 1 L of crystalloid before spinal anaesthesia reduces the incidence of hypotension to some extent [3,6]. The ideal fluid for co-prehydration is still a matter of debate. Colloid pre-loading is more reliable. At the same time, colloid co-loading appears equally effective if infused rapidly at the time of identification of cerebrospinal fluid. It needs repeated mention that both modalities are inefficient as single interventions and should be combined with timely and judicious use of vasopressors. Ephedrine has been the drug of choice for more than 30 years in the treatment of maternal hypotension in obstetric anaesthesia when conservative measures fail. Ephedrine with its long duration of action still has a role in obstetric anaesthesia in preventing or treating spinal induced hypotension when given in an appropriate dose. Other studies have shown that an infusion of Ephedrine may be an effective alternative for preblock crystalloid administration for prevention of hypotension due to SAB. Prophylactic infusion of ephedrine not only may be more effective against hypotensive episodes, but may also reduce the volume requirements of colloid [7].

Keeping all this in mind, the present study was undertaken to clinically evaluate the efficacy of pre-loading (with Ringer's Lactate) and vasoconstrictor (Ephedrine) as a combined prophylaxis for hypotension during sub arachnoid block.

Methodology

Adult patients of physical status ASA I and II scheduled to undergo elective surgical procedures on lower abdomen under subarachroid block at Tertiary care centre.

Method of Collection of Data

The patients were randomly allocated to two groups of n=50 each.

Group I: n=50 Study: **(**crystalloid group): preloaded with Ringer's Lactate only.

Group II: n=50 Study: (combination group): received pre-loading with Ringer's Lactate as well as ephedrine intravenously.

Selection of Patients

Inclusion Criteria

1. ASA grade I &II
2. 18 to *55* years of age.
3. Who gave informed, written and valid consent.
4. Those patients scheduled to undergo elective surgical procedures on the lower abdomen under sub arachnoid block.

Exclusion Criteria

1. Significant cardiovascular or renal or hepatic or respiratory disorders.
2. History of hypertension or patients on medication which have direct cardiac effects such as beta-blockers.
3. History of mental dysfunction.
4. History of diabetes mellitus
5. Patient with hemoglobin concentration less than 10rng%.
6. Morbid obesity
7. Pregnancy and Caesarean sections.
8. History of known allergy to study drugs.
9. Patients with contraindications to subrachnoid block.
10. Those patients refusing to give consent.

Methods

The patients were randomly allocated into three groups of 50 each.

Group I (Crystalloid Group)

Patients received preloading with 15 ml Kg1 of

Ringer's Lactate over 20 minutes period preceding the subarachnoid block.

Group - 11 (Combination Group)

Patients received pre loading with 7.5 ml/Kbw of Ringers Lactate over 10 minutes period preceding the subarachnoid block followed by intravenous bolus of 2.5 mg Ephedrine in the first and second minute and 0.5mg Ephedrine at the end of each minute for the next 18 minutes after the subarachnoid block.

Results

There was no statistically significant difference in

the age group of patients included in the two groups.

There was a significant increase in meanpulse rate compared to the base line at 5th and 10th minute incrystalloid group and was not significant in rest of the period. Whereas in combination group it was highly significant at 5th min, significant at 10th and 15th minute while it was not significant at 20th, 25th and 30th minute.

There was a significant fall in mean systolic pressure compared to the base line at 10th and 20th minute and highly significant fall at 25th and 30th minute incrystalloid group.While there was no significant fall in mean systolic pressure throughout the study period in combination group when compared to baseline.

Table 1: Age distribution

Age in yrs	Crystalloid Group(n=50)	Combination Group(n=50)	p-value	Remarks
Mean±SD	33.28±7.21	33.48±7.54	0.892	NS

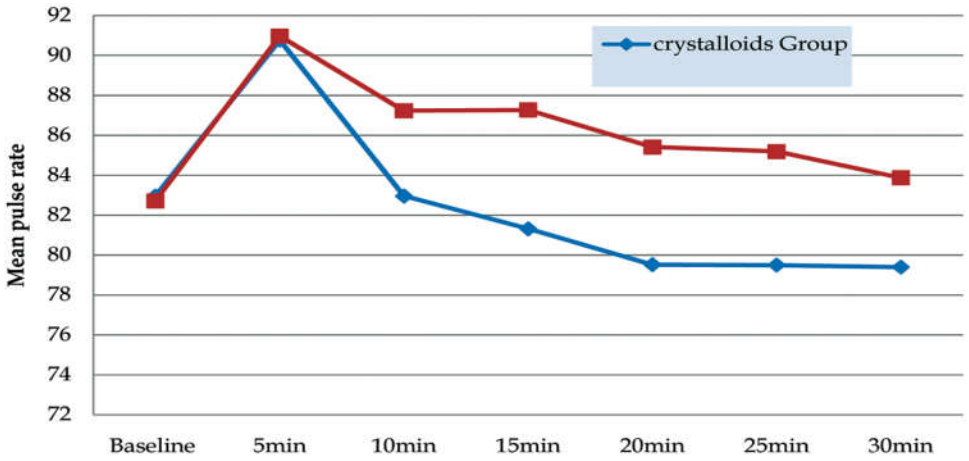

Fig. 1: Mean pulse rate

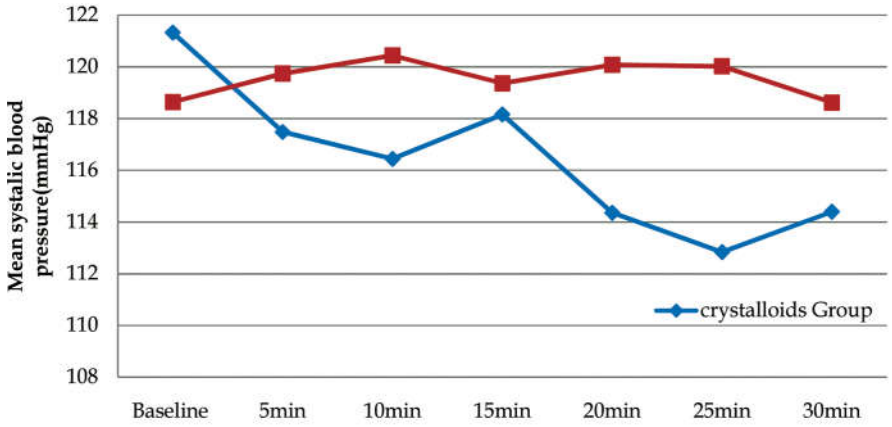

Fig. 2: Mean systolic blood pressure

Table 2: Mean Systolic blood pressure inter group comparison and their statistical significance

Time	Groups	t-value	p-value	Result
Baseline	I&II	1.596	0.91	NS
5min	I&II	0.886	0.939	NS
10min	I&II	1.523	<0.001	HS
15min	I&II	0.51	0.032	Sig
20min	I&II	2.11	0.037	Sig
25min	I&II	2.764	0.007	Sig
30min	I&II	1.968	0.052	Sig

Table 3: Hypotension and management

	Crystalloid Group	Combination Group	p-value
No.of Hypotensive patients	9	1	<0.05
No.of Episodes of Hypotension	11	1	<0.05
%of patients managed by IVF	9(81.82%)	1(100%)	--
No.of boluses of IVF	13	1	--
%patients required 6mg of Ephedrine	2(18.18%)	0	--
No.of boluses of 6mg Ephedrine given	2	0	--

Table 4: Incidence of hypertension,nausea &vomiting

	Crystalloid Group	Combination Group	p-value
Hypertension	1(2%)	2(4%)	<0.05
Nausea	0(0%)	2(4%)	--
Vomiting	0(0%)	1(2%)	--

Intergroup comparisonamong two groups reveal that the difference in mean systolic pressure at baseline and 5th minute was not significant, was highly significant at 10thminute. While it was significant throughout the rest of the study period.

Nine(18%) patients in crystalloid group and one (2%) patient in combination group had hypotension following SAB.And the difference among the groups were statistically significant. While 7 patients in crystalloid group were managed with IV fluids alone, 2 of them required Inj ephedrine boluses. In combination group the lone hypotensive patient was managed with IV fluids alone and didn't require Inj ephedrine.

One (2%) patient in crystalloid group and two (4%) patients in combination group had hypertension and these were statstically significant.

While no patient had nausea and vomiting in crystalloid group. There were two(4%) patients who had nausea and one(2%) patient had vomiting in combination group.

Discussion

Hypotension during subarachnoid block is common and can cause significant morbidity and mortality. Pre-block crystalloid administration has been recommended by some to reduce the incidence of hypotension. The use of Ephedrine may be an alternative approach [3]. The present study is based with an ideato take the advantage of both preloading and vasoconstrictor in preventing spinal hypotension, & at the same time avoiding their undesirable effects by using reduced volume & dose when compared to preloading alone.

As shown in the above table, in 1969, Marx et al [16], conducted a study on 34 parturients and found that there was a statistically significant difference in incidence of hypotension between crystalloid preloaded group and control group.

In 1976, Clark et a1 [3], conducted a study on 103 pregnant ewes who underwent elective caesarean delivery and found that, there was a statistically significant difference in the incidence of hypotension between crystalloid preloaded and control group, thus showing that crystalloid preloading reduces the incidence of post spinal hypotension. But in the present study the incidence of hypotension in crystalloid preloaded group was significantly present throughout.

In 1993, Gajrajet al [9], conducted a study on 54 females undergoing postpartum tubal ligation under spinal anaesthesia. In their study, there was a statistically significant difference in the incidence of hypotension between crystalliod and Ephedrine group. Thus showing that Ephedne infusion reduces the incidence of hypotension after spinal anaesthesia. But in the present study Ephedrine was used with reduced volume of preloading which showed the incidence of hypotension in the combination group was less when compared to the crystalloid group.

In 1993, another study was conducted by Rout et al [10] on 140 women undergoing elective Caesarean section under SAB. They found that, there was a statistically significant difference in the incidence of hypotension between crystalloid preloaded group and control group. In the present study, however the incidence of hypotension in the crystalloid group was not less.

Rielyet a1 [6], in 1995, conducted a study on 40 women undergoing elective Caesarean section under SAB. They compared crystalloid (RL) preload with colloid (6% HES) preload and found that colloid preload was better the crystalloid preload in the

Table 5: Crystalloids and incidence of hypotension due to SAB

No	References	Fluid volume (ml) crystalloid/colloid preload		Hypotension (%)		Definition of hypotension	Comments
		Ex	Co	Ex	Co		
1	Marx et al4'.,(1969)	1000 D5RL	0	0	100	Any decrease in BP	Statistically significant difference in incidence of hypotension
2	Clark et al[3]., (1976) (Elective C/D)	1000 D5RL	0	57	92	sBP<100mm Hg	Statistically significant difference in incidence of hypotension
3	Clark et al[3]., (1976) (C/D) following labour)	1000 D5RL	0	46	50	sBP<100mm Hg	No statistically significant difference in incidence of hypotension
4	Kangas et al[8], 1990	20ml/kg RL	15ml/kg RL	50	50	>10% decrease in sBP	No statistically significant difference in incidence of hypotension
5	Rout et al[5], 1992	1790 ml PL (20min)	1725 ml PL (10min)	70	60	>10% decrease in sBP	No statistically significant difference in incidence of hypotension
6	Gajraj et al[9], 1993	15ml/kg RL	Ephedrine with infusion	56	22	sBP<80% of the baseline	statistically significant difference in incidence of hypotension
7	Rout et al[10], 1993	1413 PL	0	55	71	sBP<100mmHg andsBP<80% of baseline	statistically significant difference in incidence of hypotension
8	Jackson et al[11], 1995	997 H	204 H	30	30	>30% decrease in sBP from baseline or a sBP<90mmHg	No statistically significant difference in incidence of hypotension
9	Karinen et al[12,] 1995	1000 RL	500 6% HES	62	38	sBP<90mmHg and sBP<80% baseline	No statistically significant difference in incidence of hypotension
10	Riley at al[13], 1995	1000 RL	500 6% HES	85	45	sBP<100mmHg and sBP<80% baseline	statistically significant difference in incidence of hypotension
11	Husaini et al[14], 1998	1000 RL	0	19	37	>30% decrease in sBP from baseline	No statistically significant difference in incidence of hypotension
12	Bhagath et al[4], 2004	15ml/kg RL	Ephedrine 28mg	13	5	>30% decrease in sBPfrom baseline or a sBP<90mmHg	No statistically significant difference in incidence of hypotension
13	M. Goel et al[15], 2009	15ml/kg RL	Ephedrine 25mg	30	10	>30% decrease in sBPfrom baseline or a sBP<90mmHg	Statistically significant difference in incidence of hypotension

prevention spinal hypotension. In the present study colloid was not used.

Clark et al [3], (1976) conducted a study on 57 pregnant women undergoing Caesarean delivery following labour under spinal anesthesia and found that there was no statistically significant difference in the incidence of hypotension between the crystalloid preloaded group and non-preloaded group, thus showing that crystalloid preload is not effective in the prevention of spinal hypotension. This is similar to findings of the present study that crystalloid preload is not effective in the prevention of spinal hypotension as shown in Table 6, 8 and Figure 8 where the incidence of hypotension is 18% in crystalloid group and 2% in combination group.

Kangaset a1 [8], in 1990 did a study of crystalloid preloading on 16 women undergoing Caesarean section under SAB. They found that both - a preload of 20mlkg' RL or a preload of 15m1 kg1 were equally effective in preventing spinal hypotension.

Conclusion

The combined use of both crystalloid preloading and vasoconstrictor (Ephedrine) is effectivein reducing the incidence, severity and duration of hypotension due to SAB.

The combination of decreased volume of preload with crystalloid and reduced dose of vasoconstrictor provides better haemodynamic stability when compared to preloading alone.

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Original Article

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Prevention of Post-Anaesthetic Shivering After General Anaesthesia, Ondansetron Verses Butorphanol, A Randomized Double-Blinded, Placebo-Controlled Study

Sujeet Rai*, Sandeep Sahu, Apurva Agarwal***, Chitra****, Anil Verma***, H.D. Pandey******

Abstract

Background: Post-anesthetic shivering (PAS) is distressing for patients and may induce a variety of complications. The neurotransmitter pathways involved in the mechanism of post-anesthetic shivering are complex and poorly understood. We compared the effect of ondansetron (5-HT_3 antagonist) and butorphanol (agonist at "Kappa"-receptors and mixed agonist antagonist at mu opioid receptors) on intraoperative core and peripheral temperatures and PAS. *Methods:* After approval from institutional ethics committee and written informed consent 90 patients of age 18–60 years, ASA I-II, undergoing orthopedic, general or urological surgery were randomized into three groups. In this double-blinded, placebo-controlled, study: Group A (n = 30) received ondansetron 8 mg, Group B (n = 30) received Butorphanol, 25 µ gm / kg and Group C (n = 30) received saline 4 ml intravenous (IV) immediately before the anesthetic induction. Heart rate (HR), mean arterial pressure (MAP), oxygen saturation (SPO_2), core (nasopharynx) and fingertip temperature (dorsum of middle finger) was recorded. Balanced general anaesthesia was induced by propofol 2.5 mg/kg and intubation was done with Vecuronium 0.1mg/kg. Anaesthesia was maintained with 70% N_2O in O_2 and propofol infusion. PAS was documented by persons blinded to the study and included trainees in anesthesiology who were unaware of the group assignment. *Results:* PAS occurred in 19 of 30 (63.3%) patients in Group C (saline), compared with 6 of 30 (20%) in ondansetron group (P = 0.002) and 7 of 30 (23.3%) in butorphanol group (P = 0.004). Within each group, core temperature decreased and peripheral temperature increased significantly, but there were no significant differences among the groups A and B at any time interval. *Conclusion:* We conclude that both, ondansetron (8 mg) and butorphanol (25 µ gm / kg) IV given during the induction of anesthesia prevents PAS equally without affecting the core-to-peripheral redistribution of heat during general anesthesia.

Keywords: Ondansetron; Butorphanol; Post-Anesthetic Shivering; General Anesthesia; Hypothermia.

Introduction

Incident hypothermia in homoeothermic human in intraoperative as well as early postoperative period leads to post anesthetic shivering (PAS). PAS is defined as an involuntary movement of one or several muscle groups, occurring in the early recovery phase due to general or regional anesthesia. The incidences are in between 5 to 65% and vary with age, sex, choice of drugs for induction and maintenance of anesthesia, and duration of surgery [1,2]. Besides the discomfort experienced by patients in the recovery period, shivering may increase tissue oxygen consumption (by 100–600%), cardiac output, carbon dioxide production, and circulating catecholamines, and furthermore significantly decrease the mixed venous oxygen saturation.

Although there is general agreement that it is a thermoregulatory phenomenon, a physiological response to anesthesia-induced core hypothermia leads central hypothermic and peripheral

Author's Affiliation:
*Assistant Professor, Department of Anesthesiology, Mahamaya Rajkiya Allopathic Medical college, Ambedkar Nagar. **Additional Professor, Department of Anesthesiology & Emergency Medicine, Sanjay Gandhi Postgraduate Institute of Medical Sciences Lucknow, UP. ***Associate Professor, ****Professor, Department of Anesthesiology, G.S.V.M. Medical College, Kanpur, UP, India.

Corresponding Author:
Sandeep Sahu, Additional Professor, Department of Anesthesiology & Emergency Medicine, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, UP, 226014,India.
E-mail: drsandeepsahu@yahoo.co.in

vasoconstriction that may have some non-thermoregulatory component [3]. The neurotransmitter pathways conveying signals from hypothalamus to skeletal muscle are not clearly understood. But probably it involves multiple levels of information integration and numerous neurotransmitters [4,5]. There are several reports that IV administration of pharmacological agents like the opioids (meperidine, alfentanil, tramadol, nalbuphine) [6,9], clonidine [10], doxapram [11], physostigmine [12], ketanserine [13], ondansetron [14], granistron [15], dolansetron [16], ramosetron [17], ketamin [18] and dexmetomidine [19] have all reduced the incidence of shivering or suppressed established shivering. Besides pharmacological agents the non-pharmacological methods also decreases incidence of shivering [20,21].

5-HT impacts thermoregulatory responses through its action on different sites in the hypothalamus, medulla and midbrain. Buspirone, $5HT_1A$ partial agonist, acts synergistically with meperidine in reducing the threshold of shivering. In animal models, direct intra-ventricular injections of 5-HT influence body temperature and shivering [22]. All these observations suggest that the serotonergic system has a role in the control of post- anesthetic shivering. Ondansetron is a specific $5\text{-}HT_3$ antagonist has a role in neurotransmission may affect perioperative thermoregulation and PAS [14,22]. Butorphanol, an opioid agonist at 'Kappa' receptors and mixed agonist-antagonist at 'mu' opioid receptors may affect perioperative thermoregulation and PAS. Till now on reviewing literature, no study had compared ondansetron and butorphanol. Therefore, we compare the effectiveness of ondansetron and butorphanol premedication on the typical core-to-peripheral temperature redistribution evoked by general anesthesia and on the incidence of PAS, in this randomized, placebo-controlled, double-blinded study.

Material and Methods

After approval from institutional ethics committee and written informed consent 90 patients (ASA physical status I or II), scheduled for elective general, urological, orthopedic, otorhinolaryngeal and gynecological surgery were taken into the study. Exclusion criteria were allergy to ondansetron or butorphanol, surgery > 2 hr (surgeries duration more than two hrs excluded because keeping of similarities in subjects to avoid any chance of hypothermia), age <18 or > 60 yr, use of vasoconstrictors or vasodilators and pyrexial illness. All the Patients were randomly allocated by computerized randomization table into three groups (each 30 patients). Group A received ondansetron (8 mg), Group B received butorphanol (25 μ gm / kg) and Group C received IV saline, all the patients received total 4ml volume of drug or saline. These trial preparations were prepared fresh and by persons blinded to the study. The injection of trial medication was given immediately after placement of IV cannula and 5 min before induction of anaesthesia. Core temperature was recorded by using temperature probe by placing it in nasopharynx under aseptic condition and peripheral temperature was recorded by temperature probe on the dorsum of the middle finger of the hand opposite to IV infusion line. The fluid used perioperatively in all three groups was having temperature of 37^0C. Base line heart rate (HR), mean arterial pressure (MBP) and oxygen saturation were also recorded. These parameters were recorded every 10 min during surgery and postoperatively up to 1 hr. All patients were draped routinely and were not actively heated.

Analgesia was provided with injection Ketorolac 30 mg IM 1 hr before induction and after induction and injection diclofenac 75mg in 100 ml normal saline infusion run over 30 min in all three groups 30 min prior to skin closure. General anesthesia was induced with propofol 2.5 mg/kg and intubation was facilitated with vecuronium 0.1mg/kg. Anesthesia was maintained with nitrous in O_2 (70%), propofol infusion and vecuronium. PAS was documented by persons blinded to the study and included trainees in anesthesia. It was defined as readily detectable fasciculation or tremor of the face, trunk, or limb of 15 seconds duration. In the post anesthetic care unit (PACU) all the patients oxygen saturation were monitored by pulse oximetry and equipment for oxygen supplementation were kept ready bedside . All the patients who have surgeries lasting more than 2 hrs and having PAS in the post-operative period were oxygenated by nasal prongs at 3 l/min (surgeries duration more than two hrs excluded because keeping of similarities in subjects to avoid chance of hypothermia).The previous studies had found an incidence of PAS up to 40%–65%. We anticipated an incidence of 45% in the control group and took a difference of 40% in incidence of shivering between control and treated groups as being clinically meaningful. Hence, we prospectively calculated that 29 patients were required in each group for a Type I error of 0.05 and a Type II error of 0.2. One-way analysis of variance was used to analyze differences between the groups. Incidence of shivering was

analyzed by using Chi Square Test with Yates' correction and was expressed as mean ± SD, with $P < 0.05$, is considered significant.

Results

Demographic data (Table 1) and duration of anesthesia were comparable with in the groups.PAS was significantly reduced in patients receiving ondansetron compared with saline control (20% vs. 63.3% respectively, p = 0.002), and also in patients receiving butorphanol compared with saline control (23.3% vs. 63.3% respectively, p = 0.004). But there is no significant difference in the incidence of PAS between ondansetron group and butorphanol group (p = 0.754) (Table 2). Hemodynamic values, oxygen saturation (SpO2), are shown in figure 3, 4 and 5. There were no significant differences among the groups intraoperatively but MAP and HR values at recovery and in postoperative room show significant increase in control group as compared to ondansetron group or butorphanol group (p < 0.05). While oxygen saturation values in postoperative room shows significant decrease in saline group (control) as compared to ondansetron group or butorphanol group (p < 0.05), because as saline group having more incidence of PAS, so requirement of oxygen increased in this group (Figure 5). Because there is no incidence of warning hypoxia to any patient, but we continuously monitored by pulse oximetry and kept prepare the equipment for possibility of bedside oxygenation and supplementation, when saturation falls below 92% in any groups as per protocol in PACU. Core and fingertip temperature changes with the duration shown in Figures 1 and 2. Although core temperature decreased and fingertip temperature increased significantly in all groups with respect to baseline, but there were no significant temperature differences at any time among the groups.

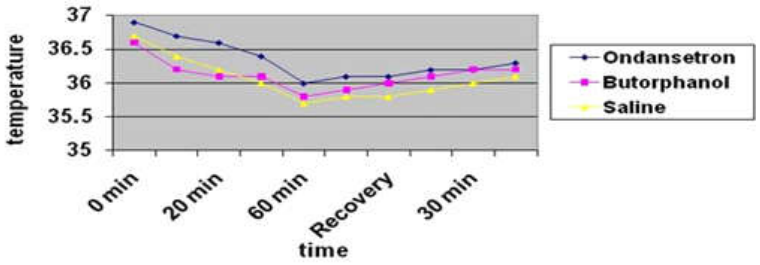

Fig. 1: Changes in core temperature: Data are expressed as mean with SD error bars. Temperature in all groups decreased significantly from baseline, but no significant differences among groups.

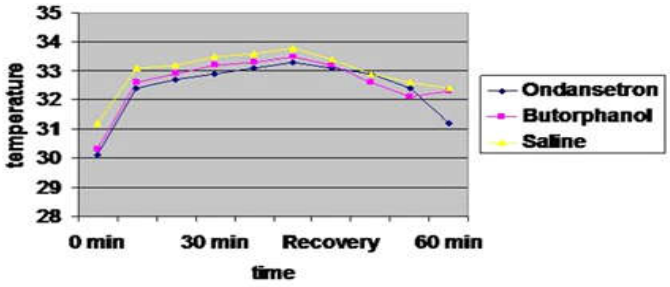

Fig. 2: Changes in peripheral temperature: Temperature in all groups increased significantly from baseline, but no significant differences among groups(mean with SD)

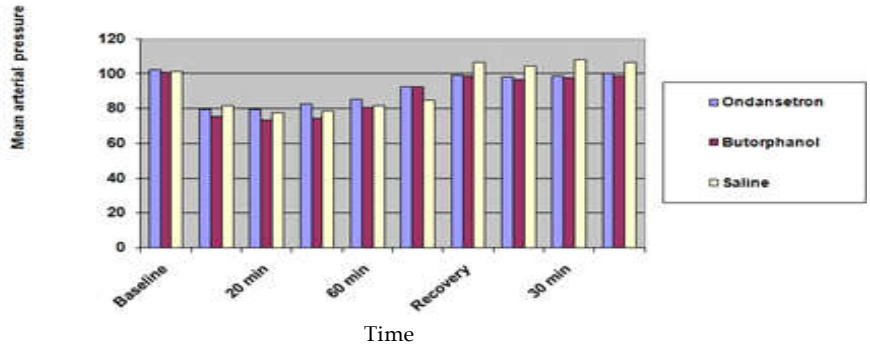

Fig. 3: Comparison of MAP in three groups

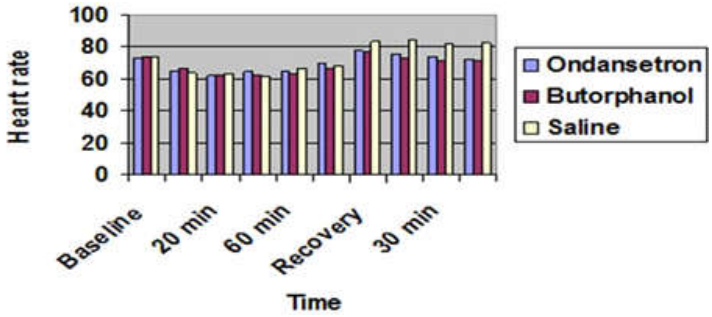

Fig. 4: Comparison of Heart Rate in three groups

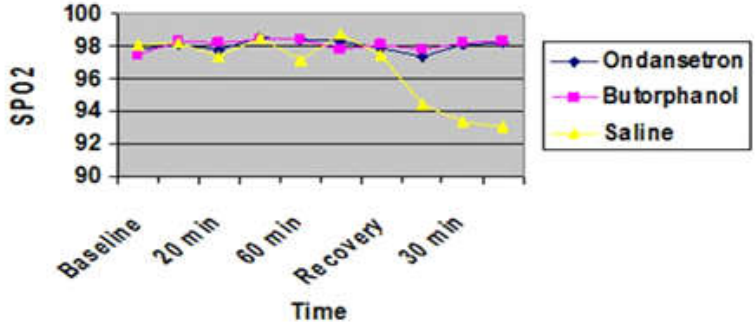

Fig. 5: Comparison of Oxygen saturation (SPo2) in all three groups

Table 1: Patients characteristics in three groups

	Ondansetron	Butorphanol	Saline
SEX(M:F)	22:8	23:7	20:10
AGE(Yrs.)	35.4±5.52	32.7±7.64	33.5±6.38
WEIGHT (Kg)	61.3±12.24	64.6±11.61	65.4±10.32

Data are mean ± SD, No group showed any significant differences in demo graphic profile among them.

Table 2: Incidence of shivering in three groups

	Ondansetron n=30	Butrophanol n=30	Saline n=30
Shivered	6(20.0%)	7(23.33%)	19(63.33%)
Did not shivered	24	23	11

p value = 0.002, control vs. ondansetron that is very significant
p value = 0.004, control vs. butorphanol that is very significant
p value = 0.754, ondansetron vs. butorphanol that is not significant

PAS was significantly reduced in patients receiving ondansetron and butorphanol as compared to saline control.

Discussion

Anesthesia induced thermoregulatory impairment and exposure to a cool environment makes most surgical patient hypothermic. Inadvertent hypothermia is associated with numerous adverse outcome PAS, is one of them in postoperative period [24,25]. We found the incidence of PAS was 63.3% in the saline group compared with 20% in the ondansetron (8 mg) group and 23.3% in the butorphanol (25 μgm / kg) group. We found that distinguishing between "mild," "moderate," and "severe" shivering on the basis of clinical observation alone will be highly subjective and of limited relevance [22].

Specific inhibition of the 5-HT_3 system by ondansetron produced statistically significant reduction in shivering. Perhaps 5-HT_3 inhibition has a specific antishivering effect, but given the variety of neurotransmitter systems known to be also involved in regulating shivering, an inhibitory effect at the 5-HT_3 receptor probably results from a generalized thermoregulatory inhibition at the level of the hypothalamus, where the bulk of thermoregulatory

control occurs [14,22].

Opoids also effects change in body temperature by acting on preoptic anterior hypothalamus,dorsal raphe nucleus,raphe magnus and locus coeruleus by increase formation of cyclic AMP, that increases thermosestivity in neuron [26]. At the same time butorphanol an agonist at 'Kappa'-receptors like meperidine and mixed agonist- antagonist at 'mu' opioid receptors like morphine (agonist) regulates its anti-shivering effect. This has been studied that for anti-PAS effect 'kappa' receptors are more important than 'mu' receptors [11]. It has a high affinity for 'kappa' -opioid receptors in the central nervous system, this was supported by the fact that meperidine also prevents shivering via kappa-opioid receptors because the anti-shivering effect of meperidine is also minimally impaired by small-dose naloxone, which blocks most μ-receptors and is diminished by large-dose naloxone, which blocks both ' mu' and 'kappa' receptors. Data suggests it may be more effective than fentanyl, morphine or even meperidine although it has not been studied in great detail [27].

These explanations are supported by our data on perioperative temperature. The anticipated core-to-peripheral redistribution of body temperature after the administration of general anesthesia is characterized by an approximate 1°C decrease in core temperature within the first 20–30 minutes after the induction, followed by an increase in fingertip temperature, measured at the skin [28]. This was unchanged in our patients who received ondansetron or butorphanol. Thus, the PAS effect of ondansetron or butorphanol is independent of intraoperative core hypothermia, suggesting that they inhibit thermoregulatory responses by a central mechanism. The extent of core hypothermia seems to be related to the degree of vasodilatation induced during anesthesia administration [28]. Ondansetron and butorphanol, both are notable for its lack of hemodynamic side effects [29] hence; their lack of effect on redistribution hypothermia is unsurprising. Ondansetron and butorphanol did not alter the hemodynamic profile of either group while it was significantly changed in control group in post-op period due to more incidence of shivering.

In contrast to some other drugs used to treat PAS like tramadol, doxapram, physostigmine, clonidine, ketamin and dexmetomidine all have unwanted cardiovascular effect. These are also commonly associated with postoperative nausea and vomiting. In contrast, ondansetron effectively relieves postoperative nausea and vomiting. Meperidine may potentially cause respiratory depression, which did not occur with butorphanol because it shows a ceiling effect on respiratory depression. So ondansetron and butorphanol, both could very plausibly be an attractive and alternative preventive treatment for PAS, especially as ondansetron has powerful antiemetic effects and a favourable cardio-respiratory profile and butorphanol has powerful analgesic effects [30].

The limitation of our study is that there are small numbers of patients in each arm.

However, the present study shows usefulness of ondansetron and butorphanol in prevention of PAS.

We have demonstrated that ondansetron 8mg and butorphanol 25μ gm / kg given before induction of anaesthesia effectively reduces the incidence of PAS equally in without effecting the core-to-peripheral redistribution of temperature that is normally observed during the administration of general anesthesia. PAS effect of ondansetron or butorphanol is independent of intraoperative core hypothermia, suggesting that they inhibit thermoregulatory responses by a central mechanism. Further studies are recommended to confirm our findings.

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Original Article

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Recovery Profile after Subarachnoid Block in Elderly Versus Young Adult Patients

Vinayak Sirsat*, Satish Deshpande**

Abstract

Routinely, Subarachnoid block is practiced for performing operative procedures under general surgery, orthopaedic and obstetrics and gynecology below umbilicus. 100 patients ASA grade I - II of either sex were divided into 2 equal groups of 50 each pout which Group I were young adults (20-40 years age) and Group II were elderly patients above 60 years age. All patients were preoperatively evaluated for fitness of anaesthesia. In group I mean age was 32.42 ± 3.44 and in group II mean age was 66.40 ± 3.91 years. After intravenous access, preloading was done with 7 ml / kg Ringer lactate solution. The mean duration of operation in group I was 77.6 ± 14.6 mints and in group II was 81.0 ± 14.6 mints, there was no statistical significant difference. Mean preoperative pulse rate in group I was 87.12 ± 7.17 per min and 84.92 ± 14.6 min in group II patients. Mean arterial pressure was 90.0 ± 5.17 in group I and 91.2 ± 5.45 in group II patients with no significant difference. The maximum height of sensory blockade was significantly higher in elderly patients as compared to adult patients. Intraoperative fluid requirement was same in both groups. Intraoperative hypotension was noted in 22% of patients in group I and 34% of patients in group II and average number of patients requiring vasopressor was 2 patients in group I and 6 patients in group II. Thus incidence of intraoperative hypotension requiring immediate correction was more in elderly group as compared to adult patients.

In recovery room, highest level of sensory blockade was more in group II as compared to adult group. In recovery room after application of orthostatic challenge, the changes mean pulse rate and MAP were noted at 0, 30, 60 and 90 minutes. At all time intervals percentage rise in mean pulse rate and percent fall in MAP was more significant in elderly (group II) patients at all time intervals as compared to group I patients and it was more significant at 0 and 30 minutes and even upto 90 minutes in elderly patients. The sensory level was higher and regression was slower in elderly patients as compared to adult patients. Thus orthostatic challenge test can be safely applied in elderly patients to assess its efficacy for discharging patients from recover to wards without harm to patients.

Keywords: Spinal Anaesthesia; Differential Spread of Blockade; Higher Sensory Block In Elderly; Delayed Regression of Block; Orthostatic Challenge; Efficacy; Criteria for Early Shifting of Patients from Recovery to Wards; Curtails Load on Recovery Room.

Introduction

Subarachnoid block has upmost potential being a uniquely safe technique of anaesthesia due to the combination of profound analgesia, muscle relaxation, less sympathetic and metabolic disturbances. It also preserves airway, decreases intraoperative blood loss and provides residual postoperative analgesia. Despite these various advantages anaesthesiologist has to face confusion about balancing risks and benefits of spinal ananesthesia.

Now a days, geriatric operative procedures are increasing day by day due increase in life expectancy and evolutions in medical fraternity. Currently about one quarter of all operations are being performed on elderly patients above 60 years age. The elderly patients appears to be at greater risk due to underlying concomitant medical disorders and normal physiological changes of various systems which are aught to be present in these patients.

Author's Affiliation:
*Associate Professor, **Professor, Department of Anaesthesiology, Government Medical College, Latur (Maharashtra).

Corresponding Author:
Satish Deshpande, Professor, Department of Anaesthesiology, Government Medical College, Latur Maharashtra 413512.
E-mail: satdeshpande@rediffmail.com

As far as spinal anaesthesia is concerned, empirical discharge criteria from recovery room desires regression of sensory level by 2 dermatomes, return of motor function (toe movement) and stable cardiovascular parameters. There is no guarantee of return of autonomic function and may lead to haemodynamic instability when subjected to autonomic stress in ward.

Recent discharge criteria are based on checking return of autonomic function by subjecting the patients to orthostatic challenges in recovery room. There is no correlation between orthostatic decrease in Mean arterial pressure (MAP) and concurrent sensory level. It is also safe hemodynamically to review discharge criteria even though sensory level is above T_{10} dermatome. The present study was undertaken to compare and evaluate efficacy of discharge criteria in elderly and young adult patients after subarachnoid block.

Material and Method of Study

100 patients of either sex were randomly divided in 2 groups as Group I and Group II of 50 patients each. Group I comprised of 50 adult patients between 20-40 years and Group II had 50 elderly patients above 60 years of age. The patients with cardiovascular diseases, respiratory disorders, peripheral and autonomic neuropathy, severe systemic diseases and patients where spinal anaesthesia is contraindicated were excluded from study. All patients were preoperatively evaluated for fitness of anaesthesia, and usual preoperative preparation with informed consent was advised.

After arrangement of all monitors and emergency drugs anaesthesia trolly was prepared. After Intravenous access all patients were preloaded with 7 ml/kg of Ringer lactate solution. Under all aseptic precautions, lumbar puncture was performed in left lateral position with 23G LP needle at L_3-L_4 or L_4-L_5 interspace in all patients. 3 ml of 0.5% hyperbaric Bupivacaine hydrochloride was injected in subarachnoid space after obtaining clear CSF flow. Intraoperatively all patients were monitored for changes in pulse rate, blood pressure, ECG, level of analgesia, respiratory rate, Oxygen saturation with suitable monitors attached.

The blood pressure was maintained at ±20% of baseline reading with adequate intravenous fluids and with Vasopressors Inj. Mephenterimine 6mg bolus as when required. Total dose requirement of vasopressor, total fluids infused intraoperatively, highest level of analgesia and total duration of operative procedure were noted in all patients.

In the recovery room, highest level of sensory block, presence of toe movement, pulse rate, mean arterial pressure (MAP) were noted at 0, 30, 60 and 90 minutes postoperatively 2 minutes following orthostatic challenge. Orthostatic challenge was performed by giving 60^0 head up tilt for 2 minutes and after that the changes in pulse rate and blood pressure were noted. During the procedure, these patients were asked for dizziness or chest pain and having in those then immediately given supine or head low position, oxygenation with mask and were settled. All patients were shifted to respective wards after 90 minutes of recovery observation. All observations were statistically evaluated with Paired T test, two sample t test or Z test.

Observations or Results

100 patients were divided into 2 equal groups of 50 patients each according to the age. Age distribution in Group I (Adults) and Group II (Geriatric) was as shown in Table 1.

Mean age range in Group I was 32.42 ± 3.44 (t = 46.15)

Mean age range in Group II was 66.4 ± 3.91 (p -< 0.001)

In group I maximum number of patients were in age range of 26 to 35 years and in group II 60 – 70 years.

Sex distribution was as shown in Table 2.

There was no significant difference as far as sex distribution was concerned in both groups.

Weight distribution was as shown in Table 3.

Mean weight range in Group I was 59.24 ± 8.51 kg

Mean weight range in Group II was 57.30 ± 7.28 kg

There was no significant difference in weight range in 2 groups.

There were maximum number of patients with weight range of 51 – 60 kg and 61-70 kg in both groups.

Height distribution in both groups was as shown in Table 4.

Mean height in group I was 158.5 ± 16.5 cm

Mean height in Group II was 157.3 ± 15.1 cm

There was no significant difference in height distribution in both groups. Maximum number of

patients was having height in range of 151-160 and 161-170 cm.

During preoperative evaluation, all patients were divided into ASA grading in both groups as shown in Table 5.

There was no significant difference in ASA grading distribution was concerned in both groups.

The distribution of operative procedures performed in both groups was as shown in Table 6.

Distribution of operative procedures performed was identical in both groups.

Mean preoperative pulse rate was 81.72 ± 7.17 in group I and 84.92 ± 5.91 in group II patients.

Mean preoperative systolic blood pressure was 90.0 ± 5.17 in group I and 91.2 ± 5.42 in group II patients. There was no statistical significant difference in mean pulse rate and mean blood pressure in both groups.

All patients were monitored for maximum height of sensory block at about 10 minutes after the administration of intrathecal drug by pin prick method. Maximum level of sensory blocked noted in both groups was as shown in Table 7.

There were more number of patients in group II having sensory level T_5 and T_6 as compared to group I . It was observed that the level of analgesia was higher in more number of patients of group II when compared to group I patients. Intraoperatively the toe movements were absent in both group patients indicating complete muscle relaxation.

Total duration of operative procedure was noted in both groups as shown in Table 8.

In group I – mean total duration of operation was 77.6 ± 15.5 mints

In group II – mean total duration of operation was 81.0 ± 14.6 mints.

There was no significant difference as far as total duration of operation was concerned in both groups.

Intraoperatively fluid requirement or total IV fluids infused were noted in both groups including preoperative loading fluids as shown in Table 9.

In group I – Total IV fluids infused mean : 1201 ± 141 ml.

In group II – Total IV fluids infused Mean – 1225 ± 155 ml.

The fluid requirement was insignificantly more in group II patients as compared to group I patients.

All patients were monitored for incidence of intraoperative complications as shown in Table 10.

The incidence of dreadful intraoperative complication was very less in both groups. Only hypotension and bradycardia were noted in more number of patients of group II as compared to group I patients. For correction hypotension and bradycardia 1-2 doses of inj.Mephenterimine 6mg and inj. Atropine .6mg were required to normalize the parameters in group II patients only.

Postoperatively in recovery room, sensory level was noted at 0, 30, 60 and 90 minutes in both groups as shown in Table 11.

At 0 minutes – mean level was T_{10} In 04 ± 0.9 in group I patients and T_9 in 48 ± 1.01 in group II patients. At 30 minutes, mean level was T_{11} 86 ± 1.05 patients in group I and T_{11} 02 ± 1.06 in group II patients. At 60 minutes, mean level was L_1 in 76 ± 1.08 in group I patients and $T_{12\text{ in }58}$ ± 1.07 in group II patients. At 90 minutes, mean level was L_4 in 081 in group I patients and L_2 in 76 ± 1.08 in group II patients.

It was observed that immediately in recovery room (0 minutes) sensory level was $T_9 - T_{11}$ was noted in maximum number of patients of group I and $T_9 - T_{10}$ in maximum number patients of group II but there was no significant difference.

At 30 minutes, the maximum number of patients of group I had sensory level at T_{12} to L_1 but in group II maximum number of patients were having $T_{10} - T_{11}$ level. Thus statistically significant higher level of analgesia was noted I maximum number of patients of group II as compared to group I.

At 60 minutes, in group I maximum number of patients sensory regression $L_2 - L_3$ but in group II maximum number of patients had sensory level at $T_{10} - L_1$ and was significantly higher in group II as compared to group I patients.

At 90 minutes, in group I there was almost complete regression of sensor level below L_5 in all patients but in group II level of analgesia was upto $L_2 - L_4$ in maximum number of patients. Thus the regression of sensory level as delayed in more number of patients of group II as compared to group I.

At about 90 minutes, there was complete regaining of motor functions in both groups, somewhat more faster in group I as compared to group II patients.

The changes in pulse rate were noted before and after orthostatic challenge at various time intervals as shown in Table 12.

It was noted that at all time intervals, % change in mean pulse rate was more significant in group II patients as compared to group I patients. It signifies

that, group II patients are at more risk for orthostatic challenges as compared to group I patients.

The changes I mean arterial pressure before and after orthostatic challenge in both groups at various time intervals was as shown in 13.

The percentage (%) change in mean arterial pressure after orthostatic challenge was more significant in group II patients at all time intervals as compared to group I patients. These group II patients are at more risk of orthostatic challenge for mean arterial pressure immediately in recovery room and also upto I hour. As the tim passes the risk of changes after orthostatic challenges decreases and remains very less after 90 minutes onwards.

Table 1: Age wise distribution of patients group I

Age in years	Group I No. of Patients	Percentage	Age in Years	Group II No. of Patients	Percentage
20-25	1	2	60-65	24	48
26-30	15	30	66-70	17	34
31-35	22	44	71-75	8	16
36-40	12	24	76-80	1	2
Total	50	100	Total	50	100

Table 2: Gender wise distribution of patients

Gender	Group I No. of patients	Percentage	Group II	Percentage
Male	33	66	32	64
Female	17	34	18	36
Total	50	100	50	100

Table 3: Weight wise distribution

Weight in Kg	Group I No. of patients	Percentage	Group II No. of patients	Percentage
41-50	7	14	9	18
51-60	24	48	28	56
61-70	13	26	10	20
71-80	6	12	3	6
Total	50	100	50	100

Table 4: Showing height distribution

Height in Cm	Group I No. of patients	Percentage	Group II No. of patients	Percentage
141-150	8	16	7	14
151-160	17	34	22	44
161-170	20	40	20	40
171 & above	5	10	1	2
Total	50	100	50	100

Table 5: Showing ASA grading

ASA grade	Group I No. of patients	Percentage	Group II No. of patients	Percentage
I	36	72	31	62
II	14	28	19	38
Total	50	100	50	100

Table 6: Showing operative procedures performed

Operative procedures	Group I No. of patients	Group II No. of patients
Hernia repair	26	24
Vaginal Hysterectomy	12	13
Abdominal hysterectomy	5	5
Hydrocele	7	8
Total	50	50

Table 7: Showing Maximum Height of Sensory Blockade

Dermatome Level	Group I No. of patients	Group II No. of patients
T_5	1	3
T_6	5	7
T_7	10	20
T_8	24	12
T_9	6	6
T_{10}	4	2
Total	50	50

Table 8: Showing Total duration of operative procedure

Group I	Mean duration of operative procedure	77.6 ± 15.5 mints
Group II	Mean duration of operative procedure	81.0 ± 14.6 mints

Table 9: Intraoperative Total IV fluid requirement

Group I	Total IV fluids Mean	1201 ± 141 ml
Group II	Total IV fluids Mean	1225 ± 155 ml

Table 10: Showing Intraoperative complications

Intraoperative Complications	Group I No. of patients	Group II No. of patients
Hypotension	11	17
Bradycardia	2	4
Shivering	4	8
Nausea	1	1
Vomiting	0	0
Respiratory Inadequacy	0	0
Higher level of block	0	0

Table 11: Showing Sensory Level in Recovery room at various Time Intervals

Dermatome level	Time Interval							
	0 minutes		30 minutes		60 minutes		90 minutes	
	Gr. I	Gr. II	Gr. I	Gr. II	Gr. I	Gr. II	Gr. I	Gr. II
T_7	0	2						
T_8	3	6						
T_9	7	14	1	4				
T_{10}	28	23	5	10	0	2		
T_{11}	9	4	8	22	1	6		
T_{12}	3	1	24	9	6	12	0	1
L_1	-	-	10	5	10	21	0	5
L_2	-	-	2	4	22	7	2	13
L_3	-	-	-	-	9	2	9	19
L_4	-	-	-	-	2	0	27	10
L_5	-	-	-	-			12	2

Table 12: Showing changes in mean pulse rate After Orthostatic Challenge

Group	Time Interval in mints	Mean Pulse rate Before orthostatic challenge	Mean Pulse rate After Orthostatic Challenge	% change
I	0	79.64 ± 4.10	85.28 ± 4.37	7.38%
	30	79.42 ± 4.18	81.0 ± 4.31	1.99%
	60	78.98 ± 4.60	80.32 ± 4.56	1.99%
	90	80.30 ± 4.10	80.98 ± 4.0	0.77%
II	0	77.6 ± 3.84	84.94 ± 4.10	9.46%
	30	78.72 ± 4.06	84.30 ± 4.07	7.09%
	60	80.42 ± 3.82	85.16 ± 3.72	5.89%
	90	80.44 ± 3.90	82.64 ± 3.96	2.70

Table 13: Showing MAP changes After Orthostatic challenge

Group	Time Interval in mints	Mean Pulse rate		
		Before orthostatic challenge	After Orthostatic Challenge	% change
I	0	87.34 ± 3.58	82.40 ± 4.0	5.66%
	30	87.32 ± 3.76	86.38 ± 3.69	1.08%
	60	89.40 ± 3.48	88.68 ± 3.72	0.81%
	90	91.16 ± 3.27	90.02 ± 4.01	1.25%
II	0	88.94 ± 3.27	82.62 ± 3.52	7.11%
	30	89.44 ± 3.06	84.42 ± 3.26	5.61%
	60	89.92 ± 3.0	85.94 ± 3.22	4.43%
	90	90.18 ± 2.45	87.78 ± 2.79	2.66%

Discussion

Subarachnoid block after its introduction by J.L. Corning and August Bier has its own place in the practice of anaesthesia. Now a days it is most accepted technique of anaesthesia by administering anaesthesiologist, operating surgeon and many times by the patients also. As far as anaesthesiologists are concerned it is somewhat safe, do not require any sophisticated instruments and equipments for monitoring, easily administered by less trained or junior anaesthesist. But it should be given with all monitoring devices and resuscitative measures to avoid dreadful complications. The technique has got its own merits and demerits and limitations that should be known before administration. Again with introduction of epidural block and combined spinal+ epidural, the safety has been much more increased even in complicated patients where conventional general anaesthesia is contraindicated. As far as surgeons are concerned, there is complete analgesia, muscle relaxation and operative satisfaction but limited to regional surgeries. Here the patient is not completely anaesthetized, aware and there is postoperative pain relief.

Despite of various advantages, anaesthesiologist continue to face confusion about balancing risk and benefits of spinal anaesthesia because of autonomic complications as unpredictable level of block, bradycardia and hypotension. So it is necessary to monitor these patients intraoperatively and also in postoperative recovery room. The empirical discharge criteria are patient in supine position, haemodynamic stability, regression of sensory level below T_{10} dermatome and return of motor activity (toe movement) In busy operative schedules, the recovery room is over crowded and delays the discharge of patients from recovery room to wards.

Modifying discharge criteria based on checking recovery of autonomic functions by subjecting the patients to orthostatic challenges in recovery room (Alexander CM 1989, Zaidi MN 2008) this innovation is coming up in the practice.

M Pitkanon (1984), J P Racle (1987), B T Veering (1987) and many others, have noted that there is differential spread of blockade as far as sensory and motor functions are concerned after subarachnoid block. They observed that, sensory level to be significantly higher in elderly patients as compared to young adults. Our observations coincides with above authors. The peripheral motor and sensory conduction velocities slowed progressively and onset latencies of F-waves and somatomotor evoked potentials increased gradually with advancing age.

B T Veering (1991), M N Zaidi (2008), Leslie J, observed more number of patients having hypotension and bradycardia after spinal anaesthesia intraoperatively in elderly patients as compared to young patients. In their opinion, it may be due to associated cardiovascular instability, autonomic imbalance which is common in elderly patients. As age advances, these are bound to be there due to physiological changes in geriatric patients. The incidence of hypotension and requirement of vasopressor is considerable higher in elderly patients as compared to adult patients.

In the recovery room, sensory level was comparatively higher and regression of sensory block was slower in elderly group than adults. The observations were statistically significant at 0 minutes and highly significant at 30, 60 and 90 minutes time intervals. Same were observations of M Pitkanan etal (1984), B T Veering (1987, 1991) and M N Zaidi etal (2004). Motor recovery was identical in both groups at 0, 30, 60, and 90 minutes in recovery room.

Orthostatic challenge comprises 60^0 head up tilt for 2 minutes after subarachnoid block in the recovery room. It mainly assess the recovery of autonomic nervous system after subarachnoid block. Normal pulse rate and blood pressure response to orthostatic challenge is modest tachycardia with increase by 3-10 beats per minute. Systolic blood pressure does not fall significantly. Diastolic blood pressure and mean arterial pressure increases there by decreasing mean

arterial pressure. These modest changes of tachycardia and vasoconstriction are due to increased sympathetic activity due to rapid translocation of blood to lower extremity which is a normal response. These autonomic reflexes are less effective in elderly patients.

In the present study, after orthostatic challenge, the changes in pulse rate at various time intervals were statistically insignificant in young adult patients of group I. In group II, the changes in mean pulse rate at 0 and 90 minutes were insignificant and significant at 30 and 60 minutes time interval in elderly patients.

In the present study, MAP after orthostatic challenge was statistically significant at 0 minutes in group I patients and no change at 30, 60 and 90 minutes time interval. In group II, fall in mean arterial pressure (MAP) after orthostatic challenge was highly significant at all time intervals in the recovery room.

Same were Findings of M N Zaidi Etal (2008)

The autonomic recovery was found to be slower in elderly patients as compared to adult patients. As age advances it is associated with alteration in vascular reactivity manifested clinically as exaggerated changes in blood pressure like hypotension and orthostatic hypotension. Orthostatic hypotension is quite common (about 20%) in the elderly due to diminished baroreceptor responsiveness in spite of increased norepinephrine levels.

Alexendar etal (1989), D V Koneri etl, M N Zaidi etal were of opinion that, application of orthostatic challenge is good alternative test for discharge criteria for patients from recovery room to wards after spinal anaesthesia. A E Pfhy etal (1978), Roe & kim etal quotes that sympathetic nervous system recovers earlier than sensory and motor functions. Thus orthostatic haemodynamic stability (< 10% decrease in MAP) in presence of high levels of sensory and motor blockade could have resulted either from early return of sympathetic functions or fro local vasomotor factors. This can be safely applied as discharge criteria following subarachnoid block even in presence of higher sensory or motor block without compromising patients' safety.

Conclusions

In elderly patients intraoperative hypotension and bradycardia is more common as compared to adult patients after subarachnoid block. Overall, the level of sensory block is higher in elderly patients as compared to adults and also the recovery from the subarachnoid block is slower in elderly. Orthostatic challenge test application in recovery room in patients receiving subarachnoid block, with less than 10% decrease in MAP is safe in all patients for discharging patient from recovery room to respective wards. It is of help to decrease over crowding in the recovery room. It is safe as it does not hampers patients safety.

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Original Article

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A Study on Efficacy of Clonidine and Dexmedetomidineas Adjuvants with 0.5% Levobupivacaine in Ultrasound Guided Axillary Brachial Plexus Block for Upper Limb Orthopedic Surgeries

G. Amarappa*, Balaraju Thayappa C.*, Hanni Vinay, Naveed Abrar****

Abstract

Introduction: Clonidine, the older drug is a selective α-2 adrenergic agonist with some α-1 agonist property. In clinical studies, the addition of clonidine to local anesthetic solutions has shown produce anti-nociception and enhance the effect of local anaesthetics. *Methodology:* This study was conducted on 80 patients undergoing upper limb surgeries aged between 20 to 60 years under ultrasound guided axillary brachial plexus block at Medical College Hospital. Informed written consent was taken. *Results:* Statistical analysis of sedation score by Chi-square test showed that the difference in sedation score was significant (P <0.05) at 30 and 60 min. The difference in sedation score at 15 min is not statistically significant though few subjects in both the groups were sedated (P >0.05). *Conclusion:* In conclusion, when compared to clonidine (1μg/kg), dexmedetomidine (1μg/kg) has a superior clinical profile as adjuvant to levobupivacaine (0.5%) in axillary brachial plexus block.

Keywords: Clonidine; Dexmedetomidine; Levobupivacaine.

Introduction

"For all the happiness mankind can gain is not in pleasure but in rest from pain"- John Dryden. Regional anaesthetic techniques are as successful as general anaesthesia in alleviating pain during various surgical procedures. There are many advantages of a single shot PNB (Peripheral Nerve Block) like rapid onset, predictable and dense anaesthesia, a relatively simpler technique, good muscle relaxation, adequate postoperative analgesia and sympathetic block. The sympathetic block decreases postoperative pain, vasospasm and oedema. It also means early ambulation, early oral intake, avoiding intubation and its complications with lesser systemic side effects and fewer postoperative effects.

Among the various PNB, Brachial Plexus Block (BPB) is one of the most commonly practiced blocks. The various local anaesthetics used in axillary block are quite effective but the duration of analgesia is a major limiting factor. There has always been a search for adjuvants which can be added to the local anaesthetics in peripheral nerve block to improve the duration and quality of analgesia but without producing any major adverse effects. Various studies have investigated several adjuncts, including opioid, neostigmine, hyaluronidase, dexamethasone etc [1-3].

Since their synthesis, α-2 adrenergic receptor agonists have been used intrathecally, epidurally or as part of peripheral nerve blocks either alone or in conjunction with local anaesthetics in an attempt to prolong the duration of analgesia and to improve the quality of the block.

Clonidine, the older drug is a selective α-2 adrenergic agonist with some α-1 agonist property. In clinical studies, the addition of clonidine to local anesthetic solutions has shown produce anti-nociception and enhance the effect of local anaesthetics. Clonidine produces this effect by reduction in the onset time of the block and a more efficient peripheral nerve block with longer post operative analgesia. Dexmedetomidine, the newer drug, is a potent α-2 adrenoceptor agonist, and about eight-times more selective towards the α-2 adrenoceptor than clonidine. In previous clinical studies, administration of intravenous dexmedetomidine has shown to produce significant opioid sparing effects as well as a decrease in inhalational anaesthetic requirements. In humans, it has been used in various strengths as an adjunct to local anaesthetics to prolong the duration of block and postoperative analgesia in various peripheral blocks [4].

Author's Affiliation:
*Associate Professor, **Post Graduate, Department of Anesthesiology, Navodaya Medical College, Raichur.

Corresponding Author:
Naveed Abrar, Post Graduate, Department of Anesthesiology, Navodaya Medical College, Raichur-584 103 Karnataka.
E-mail: drnad007@gmail.com

Very few studies have compared dexmedetomidine with clonidine with respect to duration of block and postoperative analgesia especially as an adjuvant to levobupivacaine 0.5%. Keeping their pharmacologic interactions and other beneficial properties, we planned a double blind prospective randomized clinical study at our institute with an aim to evaluate and compare the onset and duration of sensory and motor blockade, duration of analgesia and sedation score by both these drugs when used in axillary brachial plexus block as adjuvants to levobupivacaine in patients undergoing upper limb orthopedic surgeries.

The Brachial plexus blocks provide a useful alternative to general anaesthesia for upper limb surgeries. They achieve near ideal operating conditions by producing complete muscular relaxation, maintaining stable intraoperative haemodynamic condition and sympathetic block.

The application of ultrasound technique for exact localization of nerves has revolutionized the regional anaesthesia field and is becoming increasingly popular as it increases success rates, shortens block onset time and reduces the number of needle insertions and complications [5].

Levobupivacaine is a long acting local anaesthetic, S(-)– enantiomer of racemic bupivacaine. When compared with bupivocaine it produces less vasodilation, so less hypotensive episodes, less CNS toxicity, less negative inotropic effect and less prolongation of QTc interval and hence higher toxic threshold

Methodology

This study was conducted on 80 patients undergoing upper limb surgeries aged between 20 to 60 years under ultrasound guided axillary brachial plexus block at Medical College Hospital.

Informed written consent was taken. Result values were recorded using presetproforma.

Inclusion Criteria

- ASA Class I and II
- Age between 20 to 60 years
- SBP - 100-140 mm of Hg
- DBP - 60-90 mm of Hg

Exclusion Criteria

- ASA Class III and IV
- Patients with medical complications like severe anemia, severe hypovolumia, shock, septicemia
- Abnormal CT, BT or anticoagulant therapy
- Local infection at the site of proposed puncture for axillary block
- History of drug allery to local anaethetics, clonidine, or dexmedetomidine
- Patient refusal

The procedure of the technique and the development of sensory and motor block were explained to the patient to ensure good co-operation

Technique

The technique, ultrasound guided axillary brachial plexus, was conducted in the major operation theatre.

Group LC: (n=40) receive 25ml of 0.5 % of levobupivacaine +1 µg/kg of clonidine , the whole solution made 30 ml by adding sterile water for injection

Group LD: (n=40) receive 25ml of 0.5 % of levobupivacaine + 1µg/kg of dexmedetomidine, the whole solution made 30 ml by adding sterile water for injection.

Sedation score was assessed using 5 point sedation scale. The scoring was recorded as follows:

1= Awake and alert.

2= Sedated but responding to verbal stimulus.

3= Sedated, responding to mild physical stimulus

4= Sedated, responding to moderate or strong physical stimulus

5= Not arousable

Intramuscular injection of diclofenac sodium 75mg was given as rescue analgesic when patient complains of pain.

Sample size calculation was based on pilot study of 10 patients and was selected to detect a projected difference of 20% in duration of analgesia between the groups, with a type I error of 0.05 and power of 0.8.

All the collected data was entered in microsoft excel sheet. It was then transferred to SPSS (Statistical Package for Social Science) ver. 17software for statistical analysis.

• Quantitative data were analyzed by student's 't' test .

• Qualitative data were analyzed by Chi-square test.

• P value <0.05 was considered statistically significant.

Results

Eighty ASA class I and II patients of either sex, aged between 20-60 years, posted for upper limb surgeries under ultrasound guided axillary brachial plexus block were selected for the study. The study was undertaken to evaluate and compare the efficacies of dexmedetomidine with that of clonidine as adjuvants to newer local anaesthetic levobupivacaine in brachial plexus block by ultrasound guided axillary approach.

The minimum age of the patient was 20 years and maximum age was 60 years. The mean of the patients in group LC was 39.90 ±11.41 years and in group LD was 39.60 ±11.03 years. Age incidences between two groups were comparable, i.e., there is no statistically significant difference in age incidences between groups as P value is more than 0.05.

Table 1: Age distribution of study groups

Study groups	Mean ± SD (Years)	t* Value	P Value	Significance
Group LC	39.90±11.41	0.120	0.90	**NS**
Group LD	39.60±11.03			

Student's unpaired 't' test, NS – Nothing Significant

Table 2: Patient distribution based on ASA grade

Study groups	ASA Class I	ASA Class II	Total	X^2 Value	P Value	Significance
Group LC	25 (62.5 %)	15 (37.5%)	40 (100%)	0.053	0.818	NS
Group LD	24 (60%)	16 (40 %)	40 (100%)			

X^2 – Chi-square test, NS – Nothing Significant

Table 3: Time for onset of sensory block (min)

Study group	Onset time	Mean difference	t*Value	P value	Significance
Group LC	8.80 ± 1.18	0.98	3.639	P<0.001	HS
Group LD	7.90 ± 1.21				

*Student's unpaired 't' test, HS – Highly Significant

Table 4: Time for onset of motor block (min)

Study group	Onset time	Mean difference	t*Value	P value	Significance
Group LC	13.48 ± 1.64	3.25	8.32	P<0.001	HS
Group LD	10.23 ± 1.60				

*Students unpaired 't' test, HS – Highly Significant

Table 5: Duration of sensory block (min)

Study group	Duration of block (min)	Mean difference	t*value	P value	Significance
Group LC	305.60 ± 26.61	101.9	18.29	P<0.001	HS
Group LD	407.50 ± 23.07				

*Student's unpaired 't' test, HS – Highly Significant

Table 6: Duration of motor block

Study group	Duration of block (min)	Mean difference	t*value	P value	Significance
Group LC	324.80 ± 24.65	82.3	16.49	P <0.001	HS
Group LD	407.10 ± 19.68				

*Students unpaired 't'test, HS – Highly Significant

In group LC, 62.5 % of the patients and in group LC 60% of the patients were ASA class I, where as 37.5% of patients in group LC and 40% of patients in group LD were ASA class II. Distribution of subjects based on ASA class is comparable, i.e., no significant difference was observed between the groups, as the P value is more than 0.05.

The mean time for onset of sensory block in group

LC was 8.88±1.18 min and in group LD was 7.90 ± 1.21 min. The statistical analysis by student's unpaired 't' test showed that, time for onset of sensory block in group LD was significantly faster when compared to group LC (P < 0.001).

The mean time for onset of motor block in group LC was 13.48 ±1.64 min and in group LD was 10.23 ± 1.60 min. The statistical analysis by student's unpaired 't' test showed that, time for onset of motor block in group LD was significantly faster when compared to group LC (P < 0.001).

Patients of both groups were observed for 12 hours.

The mean duration of sensory block in group LC was 305.60 ± 26.61 min and in group LD was 407.50 ± 23.07 min. The statistical analysis by student's unpaired 't' test showed that, time for duration of sensory block in group LD was significantly longer when compared to group LC (P < 0.001).

The mean duration of motor block in group LC was 324.80 ± 24.65 min and in group LD was 407.10 ± 19.68 min. The statistical analysis by student's unpaired 't' test showed that, duration of motor block in group LD was significantly longer when compared to group LC (P < 0.001).

Table 7: Duration of analgesia (min)

Study group	Duration of analgesia	Mean difference	t*Value	P value	Significance
Group LC	345.92±23.77	111.58	21.16	P<0.001	HS
Group LD	457.50±23.37				

*Students unpaired 't' test, HS – Highly Significant

Table 8: Sedation score

Time of assessment	Scores*	Group LC (%)	Group LD (%)	X^2 Value, Significance
0 min	1	40(100)	40(100)	-
	2	0(0)	0	No Difference
	3	0	0	
5 min	1	40(100)	40(100)	-
	2	0	0	No Difference
	3	0	0	
15 min	1	32(80)	29(72.5)	X^2=0.62 P>0.05(P=0.4)
	2	8(20)	11(27.5)	(Non Significant)
	3	0(0)	0(0)	
30 min	1	25(62.5)	9(22.5)	X^2=16.02
	2	15(37.5)	25(62.5)	P<0.05
	3	0	6(15)	(Significant)
60 min	1	20(50)	9(22.5)	X^2=6.69
	2	17(42.5)	25(62.5)	P<0.05
	3	3(7.5)	6(15)	(Significant)
2 hrs	1	40(100)	40(100)	-
	2	0(0)	0(0)	No Difference
	3	0(0)	0(0)	
6 hrs	1	40(100)	40(100)	-
	2	0(0)	0(0)	No Difference
	3	0(0)	0(0)	
12 hrs	1	40(100)	40(100)	-
	2	0(0)	0(0)	No Difference
	3	0(0)	0(0)	

X^2- Chi-square test

The mean duration of analgesia in group LC was 345.92 ± 23.77 min and in group LD was 457.50 ± 23.37 min. The statistical analysis by student's unpaired 't' test showed that, duration of analgesia in group LD was significantly longer when compared to group LC(P < 0.001).

In both the groups patients are awake and alert and hence had sedation score 1 at 0 min, 5 min, 2hours, 6 hours and 12 hours. Whereas sedation is observed between 15 min and 60 min from the time of drug injection in both the groups.

At 15 min, in group LC, 20% of patients are sedated (with sedation score 2), where as in group LD, 27.5% of patients were sedated (with sedation score 2).

At 30 min, in group LC, 37.5% of patients were sedated (with sedation score 2), where as 85% of patients were sedated (62.5% of patients with sedation score 2 and 15% of patients with sedation score 3) in group LD.

At 60 min, in group LC, 50% of patients were sedated (42.5% of patients with sedation score 2 and 7.5% of patients with sedation score 3), and in group LD, 77.5% of patients were sedated (62.5% of patients with sedation score 2 and 15% of patients with 3).

None of the patients had sedation score 4 and above during the study period.

Statistical analysis of sedation score by Chi-square test showed that the difference in sedation score was significant ($P < 0.05$) at 30 and 60 min. The difference in sedation score at 15 min is not statistically significant though few subjects in both the groups were sedated ($P > 0.05$).

Discussion

The key to successful regional anesthesia is deposition of local anesthetic accurately around the nerve structures. Electrical stimulation or paresthesia, both are relied on surface landmarks identification. However, the limitations of landmark techniques like variations in anatomy and orientation, as well as equipment accuracy, have an effect on success rates and complications. Use of ultrasound for nerve block has overcome these limitations and also shortened the mean time taken for the procedure to administer a block.

An attempt has been made to assess and compare the efficacy of clonidine and dexmedetomidine as an adjuvant to local anaesthetic levobupivacaine in ultrasound guided axillary brachial plexus block in terms of onset time and duration of sensory and motor block, duration of analgesia and sedation. Haemodynamic variables also studied.

A total of 80 patients within the age group of 20-60 years were included in the study. They were randomly divided into two groups, 40 in each group. With levobupivacaine, group LC received clonidine, where as other group, group LD received dexmedetomidine. Both groups were comparable in terms of mean age, sex ratio and ASA class ($P > 0.05$).

Peripheral Action of Clonidine

There have been four proposed mechanisms for the action of clonidine in peripheral nerve blocks. These mechanisms are centrally mediated analgesia, $\alpha_2\beta$ adrenocept or-mediated vasoconstrictive effects, attenuation of inflammatory response and direct action on peripheral nerve. The direct action of clonidine on the nerve can be explained on the basis of a study conducted by Dalle et al. [6], They proposed that clonidine, by enhancing activity-dependent hyperpolarisation generated by the Na/K pump during repetitive stimulation, increases the threshold for initiating the action potential causing slowing or blockage of conduction.

Kosugi et al. [7], examined the effects of various adrenoceptor agonists including dexmedetomidine, tetracaine, oxymetazoline and clonidine, and also an α_2 adrenoceptor antagonist (atipamezole) on compound action potential (CAP) recorded from frog sciatic nerve, and found that CAPs were inhibited by α_2 adrenoceptor agents so that they are able to block nerve conduction.

Popping et al. [8], in their metaanalysis of randomized trials showed the beneficial effect of clonidine on the duration of analgesia with all tested local anaesthetics.

There are still various studies done with clonidine as adjuvant to local anaesthetics.

El Saied et al. [9], conducted a study in which axillary brachial plexus blockade was performed with addition of clonidine to ropivacaine. The study showed that addition resulted in prolongation of sensory and motor block and analgesia without increased incidence of side effects.

In another study Giovanni Cucchiaro et al. [10], evaluated the effects of clonidine on the duration of sensory and motor block and analgesia time in children who underwent a variety of peripheral nerve blocks including brachial plexus block and concluded that the addition of clonidine to bupivacaine and ropivacaine can extend sensory and motor blocks.

Peripheral Action of Dexmedetomidine

Dexmedetomidine and clonidine are both α_2 selective agonists. It is possible that they work in a similar manner and may indicate a class effect.

A study by Brumett *e*tal. [11], showed that dexmedetomidine enhances duration of bupivacaine anaesthesia and analgesia of sciatic nerve block in rats without any damage to the nerve. The analgesic effect of peripheral perineuraldexmedetomidine was caused by enhancement of the hyperpolarisation-activated cation current, which prevents the nerve from returning from a hyperpolarized state to resting membrane potential for subsequent firing.

Kousugi et al. [12], in their study found that high concentrations of dexmedetomidine inhibit CAPs (Compound Action Potentials) in frog sciatic nerves

without α_2 adrenoceptor activation. Their result showed that dexmedetomidine reduced the peak amplitude of CAPs reversibly and in a concentration-dependent manner.

This action was not antagonized by α_2 adrenoceptor antagonists (i.e., yohimbine and atipamezole); rather, α_2 antagonists reduced the CAP peak amplitude. Clonidine and oxymetazoline, two other α_2 agonists, also inhibit CAPs. The maximum effect of clonidine was only 20%. On the other hand, adrenaline, noradrenaline and α_1 agonist phenylephrine and beta agonist isoprenaline had no effect on CAPs.

Conclusion

From our study we conclude that, the addition of dexmedetomidine (1µg/kg) as an adjuvant to levobupivacaine(0.5%) has the following advantages over clonidine (1µg/kg)

1. Faster onset of sensory and motor block
2. Prolonged duration of sensory and motor block
3. Longer duration of post-operative analgesia
4. Comfortable sedation intraoperatively without need for airway assistance

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Original Article

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A Comparative Study of Epidural Fentanyl Citrate Alone and Fentanyl Citrate with Magnesium Sulphate for Post Operative Analgesia

Solanki Rekha N.*, Thakkar Jayshree M., Patel Bipin M.***, Chauhan Arun C.****, Kumar Anupama S.****, Malaviya Gaurav******

Abstract

Background: This study was done to evaluate the efficacy of single bolus administration of Magnesium Sulphate epidurally as an adjuvant to epidural fentanyl citrate for post-operative analgesia with consideration of duration of analgesia and hemodynamic stability after abdominal surgeries and to compare the side effects of both groups. *Method:* One hundred patients received standard general anaesthesia with epidural anesthesia using 10 ml of 0.5% Bupivacaine. After the surgery, patients were randomized into Group-I [Epidural Fentanyl-1µg/ kg in 10 ml saline] and Group- II [Epidural Magnesium-75 mg along with Fentanyl-1 µg/ kg in 10 ml saline]. Supplementary analgesia was provided by Inj. Tramadol- 50 mg when Verbal Rating Score (VRS) was > 4. Patient's first analgesic requirement and duration of analgesia were recorded. *Results:* The duration of analgesia was significantly longer in Group- II (290 ± 50 min) as compared to Group- I (160± 30 min) (*P*- 0.001). The frequency of rescue analgesics required in Group- II (2.1±0.5) was significantly less than that in Group-I (3.3±0.5) (*P*- 0.001). VRS was lower in Group-II up to 4 hours postoperatively (*P*- 0.001). *Conclusion:* The Administration of Magnesium- 75 mg as an adjuvant to Epidural Fentanyl- 1 µg/ kg significantly lowers the Verbal Rating Score (VRS) with prolonged duration of postoperative analgesia as compared with Epidural Fentanyl (1 µg/ kg) alone. Concomitant administration of Magnesium also reduces the requirement of breakthrough analgesics without any significant side effects.

Keywords: Epidural Adjuvants; Fentanyl; Magnesium; Postoperative Analgesia.

Introduction

Post-operative pain, especially when poorly controlled, results in harmful acute effects (adverse physiological responses) and chronic effects (delayed recovery and chronic pain). The main aim of pain management is to ensure that the patient gets pain relief at appropriate time.

Abdominal analgesia may assist in improving post-operative outcome in cases of abdominal surgeries. The analgesic regimen needs to meet the goal of providing safe, effective analgesia with minimal side effects & allowing the patients to breathe, cough, and move easily with early hospital discharge. These effects reduce pulmonary, cardiovascular, thromboembolism and other complications that may affect the patient.

Providing postoperative pain relief is a challenge task for anesthesiologists. Various adjuvants in addition to opioids have been used epidurally to prolong analgesia and reduced the incidence of adverse events observed when opioids are used alone [1]. NMDA, an excitatory amino acid receptor has been implicated in transmission of noxious stimulus from periphery leading to central sensitization. The duration and intensity of postoperative analgesia is dependent on the degree of inhibition of NMDA receptor signal transmission. Calcium channel blockers and NMDA receptor antagonist have shown to be beneficial in preventing initiation of pain. Magnesium, a divalent cation, through non-competitive mechanism blocks the NMDA receptor in a voltage dependent manner and results in natural calcium antagonism [2,3]. Magnesium has been used as an adjuvant by various routes, including intrathecal, epidural and intravenous in different dosage regimens [4,5,6]. Fentanyl

Author's Affiliation:
*Assistant Professor, **Professor, ***Professor & HOD, ****Resident, Department Anaesthsia, Gujarat Cancer and Research institute, Civil Hospital, Ahmedabad.

Corresponding Author:
Solanki Rekha N., 44, Devshrushti –II Bunglaws, Behind Kena Bunglaws, Motera stadium Road, Sabarmati, Ahmedabad-380005, Gujarat, India.
E-mail: rnsbaps@gmail.com

is a potent opioid agonist and has been widely used in the management of post-operative pain and it is found that epidural route is more effective than Intravenous infusion [7].

We hypothesized that a single bolus dose of Epidural Magnesium will prolong the duration of postoperative analgesia. Thus, we planned a prospective randomized, double-blind study to evaluate the efficacy of single bolus administration of Magnesium-75 mg epidurally as an adjuvant to Epidural Fentanyl- 1 mcg/kg for postoperative analgesia.

Method

After obtaining ethical committee approval and written informed consent, 100 patients of ASA [American Society of Anesthesiologists] physical status I or II patients, 18–65 years of age, undergoing elective abdominal surgery under general anaesthesia were enrolled for the study. Exclusion criteria- History of drug allergy, Cardio-respiratory and liver disease, Regular consumption of analgesics, calcium channel blockers or drug abuse and dependent on narcotic and contraindication to epidural procedure.

A day before surgery, patients were instructed about Verbal Rating Score (VRS) [0: No pain, 10: worst pain). They were advised over night fasting. Tab Lorazepam- 1 mg a night before surgery and Tab Diazepam- 5 mg in the morning on the day of surgery were given orally.

In the operating room monitors were attached for temperature, electrocardiogram, non-invasive blood pressure and pulse oximeter. An intravenous access was established. Inj. Glycopyrrolate- 40 mcg/ kg IV was given before placement of epidural catheter**.** Epidural catheter was placed in L2-L3 or L3-L4 space in lateral position using hanging drop technique and catheter was guided cephalad. Test dose of Inj. Lignocaine hydrochloride (with adrenaline-1:2, 00,000) 3ml 2% with was given. After preoxygenation with 100% oxygen, general anaesthesia was induced with Inj. Fentanyl citrate 2 mcg/ kg, Inj. Thiopentone 5 mg/ kg, Inj. Succinyl choline 2 mg/ kg and Inj. Lignocaine hydrochloride (2%) 2 mg/ kg intravenously.

Patients were intubated with appropriate sized portex tube and cuff was inflated. Anaesthesia was maintained with O_2:N_2O (50%:50%) and Isoflurane. Muscle relaxation was achieved with Vecuronium bromide 0.1 mg/ kg IV initial dose followed by 0.04 mg/ kg/ hr intravenous infusion. Intra-operative epidurally inj. Bupivacaine hydrochloride 0.5% 10 cc was administered. After completion of surgery patients, all patients were reversed with inj. Neostigmine 0.05 mg/ kg with inj. Glycopyrrolate 80 mcg/ kg intravenously, were extubated and transferred to post-operative ward.

Patients were randomized by computer generated random number assignment into 2 groups of 50 each. Group- I (n=50) patients who received Epidural Fentanyl-1 mcg/ kg in 10 mL isotonic normal saline, while patients in Group- II (n=50) who received Epidural Magnesium - 75 mg along with fentanyl- 1 mcg/ kg diluted in isotonic saline to a total volume of 10 mL. The drug was prepared by an independent investigator who was not involved in the perioperative management of the patient. Further observations were noted by an independent investigator who was unaware of the randomization. VRS ≤ 4 was considered adequate pain relief. Whenever patient had VRS > 4, supplementary analgesia was provided by Inj. Tramadol- 50 mg IV. Patient's first analgesic requirement was recorded. The duration of postoperative epidural analgesia was defined as the time from administration of epidural study drug postoperatively to the time to first demand of additional/ rescue analgesia. The frequency of rescue analgesics during 24 hours postoperative period was also noted. Pulse, BP, respiratory rate, verbal rating score, sedation score and SpO_2 were noted initially at 0 and 30 min, then hourly till 6 hours and then at 8 hour, 12 hour and 24 hour duration.

Sedation was evaluated by four point scale:

- 1 = Awake & alert
- 2 = mildly sedated, easy to wake up when spoken
- 3 = moderately sedated, easy to wake up when stimulated
- 4 = deeply sedated, difficult to wake up when stimulated

Patients were monitored continuously for side effects after administration of drug.

Statistical analysis was performed using the statistical software package. Data comparisons were made using unpaired student's t-test and fisher's exact test.

Results

The demographic data were almost comparable in both the groups (P> 0.05). The total numbers and types

Table 1: Demographic data

	Groups	
	Group I	**Group II**
N	50	50
Age (yrs)	54 ±7	56 ± 8
Height (Cm)	159 ± 4	158 ± 8
Weight (Kg)	49 ± 6	50 ± 5
Sex (male/female)	18:32	19:31

Cm-centimeter, Kg-kilogram, Values are mean ± SD

Table 2: Type of surgery

Diagnosis	Surgery	Group I	Group II
Ca. ovary	TAH+BSO	18	20
Ca. cervix	Wertheim's Hysterectomy	8	6
Ca. stomach	Total Gastrectomy	3	5
Ca. colon	Colectomy	9	9
Obstructive jaundice	Whipple's procedure	6	4
Obstructive jaundice	Triple bypass	6	6
Total		50	50

TAH+ BSO-Total abdominal hysterectomy and Bilateral Salpingo-ophorectomy

Table 3: Post-operative VRS Score

Time	Group I	Group II	P value
t = 0	7.1±0.3	7.2±0.4	0.1605
30 min	2.6±0.4	2.5±0.2	0.1171
1 hr	2.4±0.3	1.9±0.6	0.0001
2 hr	3.1±0.6	2.4±0.2	0.0001
3 hr	5.2±0.3	2.8±0.4	0.0001
4 hr	3.8±0.4	3.0±0.2	0.0001
5 hr	3.1±0.2	3.9±0.8	0.0001
6 hr	3.5±0.3	4.8±0.3	0.0001
8 hr	2.8±0.2	1.9±0.3	0.0001
12 hr	3.2±0.4	2.4±0.3	0.0001
24 hr	3.6±0.1	3.7±0.4	0.0895

t-time, Min-minute, hr-hour, mean ± SD

Table 4: Changes in vital parameters

Pulse Rate											
Time	T=0	30 min	1 hr.	2 hrs.	3hrs.	4 hrs.	5 hrs.	6hrs.	8 hrs.	12 hrs.	24 hrs.
Group I	87±9	86±9	83±8	84±10	82±8	80±8	76±7	73±2	78±9	76±10	70±7
Group II	87±12	84±7	83±7	82±6	81±8	78±5	73±6	71±6	74±7	73±7	69±6
P value	1.00	0.24	0.85	0.16		0.17	1.00	0.12	0.04	0.16	0.53
Blood Pressure											
Time	T=0	30 min	1 hr.	2 hrs.	3 hrs.	4 hrs.	5 hrs.	6 hrs.	8 hrs.	12 hrs.	24 hrs.
Group I	90±10	86±9	78±8	77±2	76±5	77±7	71±6	72±5	75±6	72±7	72±5
Group II	92±8	85±7	75±10	75±8	74±8	74±8	69±8	72±9	74±2	77±6	75±6
P value	0.12	0.08	0.10	0.12	0.15	0.33	0.10	0.07	0.08	0.18	0.37
Respiratory Rate											
Time	T=0	30 min	1 hr.	2 hrs.	3 hrs.	4 hrs.	5 hrs.	6 hrs.	8 hrs.	12 hrs.	24 hrs.
Group I	15.4±1.4	15.5±2.2	15.2±2.7	14.7±2.2	14.5±1.2	14.8±1.1	14.6±1.2	14.1±0.9	15.5±0.9	15.0±0.7	15.0±1.8
Group II	15.2±1.3	15.2±1.4	15.0±1.3	14.1±1.3	14.2±1.3	14.4±1.0	14.1±1.4	13.8±1.2	15.0±1.2	14.9±0.6	14.6±2.1
P value	0.46	0.41	0.63	0.10	0.12	0.06	0.05	0.16	0.16	0.44	0.30

t- time, Min-minute, hr-hour, mean ± SD

Table 5: Side effects

	Groups	
Side Effects	**Group I**	**Group II**
Hypotension	2	0
Bradycardia	3	1
Sedation	1	1
Nausea	3	2
Vomiting	1	Nil
Pruritus	Nil	Nil
Urinary retention	Nil	Nil

of surgeries in both groups were comparable. The difference in VRS score was not statistically significant between the two groups at 0 min and 30 min. Both groups had decrease in VRS score. VRS score was significantly lower in Group- II at 1, 2, 3, and 4 hr in the postoperative period (P=0.001). The first breakthrough analgesic requirement of Tramadol- 50 mg in Group- II was between 4 and 6 hrs with average duration of 290 ± 50 min which was significantly longer as compared to Group- I in which first analgesic requirement of Tramadol- 50 mg was between 2 and 3 hrs with average duration of 160 ± 30 min. The frequency of rescue analgesics (Tramadol- 50 mg) required in 24 hrs postoperative period in Group- II was 2.1 ± 0.5 and in Group- I was 3.3 ± 0.5 (P=0.001). Both groups were comparable (P > 0.05) in relation to pulse rate, mean blood pressure and respiratory rate (P > 0.05). Motor blockade was not observed in the study due to the low dose of magnesium. No grave complications were observed in any patient.

Discussion

Post-operative pain is an unpleasant experience for the patient, associated with number of physiological responses and may contribute to post-operative morbidity. Regional anesthesia is a safe, less expensive technique with the advantage of prolonged post-operative pain relief [8]. Epidural analgesia is considered by many as the gold standard analgesic technique for major abdominal surgery [9]. Intra-operatively epidural analgesia reduces stress response, improves quality of muscle relaxation and helps minimize blood loss. Postoperatively epidural analgesia helps in early mobilization of patients and improves gastrointestinal function especially in abdominal surgery.

Epidural fentanyl citrate is selected as 1 mcg/ kg because higher dose of fentanyl citrate may have greater adverse effects than beneficial effect. G. Lyons et al stated that incidence of pruritus was increased significantly with fentanyl citrate 4 mcg/ml [10]. Magnesium, a noncompetitive NMDA receptor antagonist, has a role in prevention of central sensitization from peripheral noxious stimulus. Magnesium has anti-nociceptive effects in animal and human models of pain [11,12].

The results of our study showed that a single bolus of epidural magnesium as an adjuvant to epidural fentanyl results in prolonged duration of analgesia with lower VRS as compared with epidural fentanyl (1 mcg/ kg) alone.

Bilir and colleagues demonstrated that 50 mg epidural bolus magnesium followed by 100 mg/ day epidural infusion resulted in lower VAS score only at first hour postoperatively [16]. This difference of lower VRS score could be due to higher bolus dose of epidural magnesium in our study.

In a study by El-Kerdawy, patients received CSE followed by epidural infusion of magnesium (100 mg/ hr) [13]. They concluded that the time to first analgesic requirement was significantly prolonged in magnesium group when compared with control/ placebo group. The duration of analgesia in their study was much less than in our study (79 vs. 290 min). This may be explained by the fact that we administered epidural magnesium in addition to fentanyl, which could prolong the requirement of rescue analgesia.

Recently this was also confirmed in patients scheduled for cesarean section. Yousef *et al*. administered 10 mL of 5% magnesium epidurally and concluded that the addition of magnesium to epidural bupivacaine and fentanyl in women undergoing elective cesarean section with combined spinal epidural anesthesia improved intra-operative conditions and quality of postoperative analgesia [14].

The frequency of rescue analgesics (intravenous Tramadol 50 mg) required in 24 hrs post-operative period in Group- II and in Group- I were 2.1 ± 0.5 and 3.3 ± 0.5 respectively (P=0.001). Different studies observed that administration of epidural magnesium reduces the rescue analgesic requirement in the postoperative period [5,15,16].

No impact was noted on motor function in our study when magnesium was administered epidurally. There were no increased incidences of side effects in the magnesium group which would be explained by low dose of magnesium sulphate via epidural route. There were no differences in the incidence of side effects between the groups in the studies, nor were any additional adverse events [15,16].

Conclusion

The addition of Epidural Magnesium- 75 mg to Epidural Fentanyl-1 mcg/ kg results in prolonged duration of postoperative analgesia as compared to Epidural Fentanyl-1 mcg/ kg) alone. It also reduces the need for breakthrough analgesics without any side effects.

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7	Indian Journal of Biology	2	5000	3500	400	350
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27	International Journal of Practical Nursing	3	5000	4500	500	450
28	International Physiology	2	7000	6500	700	650
29	Journal of Animal Feed Science and Technology	2	4100	3600	410	360
30	Journal of Cardiovascular Medicine and Surgery	2	10000	8600	910	860
31	Journal of Forensic Chemistry and Toxicology	2	9000	8500	900	850
32	Journal of Microbiology and Related Research	2	8000	7500	800	750
33	Journal of Orthopaedic Education	2	5000	4500	500	450
34	Journal of Pharmaceutical and Medicinal Chemistry	2	16000	15500	1600	1550
36	Journal of Social Welfare and Management	3	7500	7000	750	700
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Oncological Emergencies in Critical Care

Lalit Gupta*, Gaurav Dwivedi*

Abstract

Cancer patients are at risk for several life threatening emergencies, including metabolic, cardiologic, neurologic, and infectious events. These oncologic emergencies can occur at any time during the course of a malignancy, from the presenting symptom to end-stage disease and may require an admission into the intensive care unit (ICU) at any time. Knowledge of such emergencies is critical to the understanding of these emergent syndromes in oncology patients. Each of these disease states requires careful evaluation of the patient's symptoms, monitoring parameters for conditions and supportive care measures and interventions. Many of these high risk situations can be prevented and managed effectively if promptly recognized and timely treated. This review addresses the more commonly encountered emergencies and possible management in cancer patients.

Key words: Hypercalcemia; SIADH; Superior Vena Cava; Leukostasis; Tumor Lysis; Intracranial Pressure.

Cancer is the one of the leading cause of death in the India with over 600 000–700 000 deaths annually. Despite improvements in survival and decreased prevalence of certain malignancies the overall prevalence of cancer is expected to rise. Individuals with malignancy may present with a cancer-related emergency; for many, this will be their initial manifestation of cancer. Efficient diagnosis and proper management of life-threatening complications may facilitate either definitive treatment of the underlying malignancy or palliation.

Cancer and its treatment may lead to a range of potentially life-threatening conditions that require urgent action to correct them. This article includes the following major oncological emergencies:

- Hypercalcaemia.
- Neutropenia.
- Acute tumour lysis syndrome.
- Leukostasis.
- Syndrome of inappropriate antidiuretic hormone
- Raised intracranial pressure.
- Spinal cord compression.
- Superior vena cava obstruction.

Other oncological emergencies include hypoglycemia, pericardial effusion and cardiac tamponade, seizures, hyperviscosity syndrome, leukostasis and airway obstruction [1]. Adverse effects of chemotherapy may also require urgent intervention, like extravasation and anaphylactic reactions [2].

Hypercalcaemia

This is the most common serious metabolic disorder associated with malignancy, affecting up to one third of cancer patients at some point in their disease course [1]. Malignancies most commonly associated include lung cancer, breast cancer, renal cancer, multiple myeloma and adult T-cell lymphoma. Its symptoms may mimic the features of terminal malignancy. Hypercalcaemia is a poor prognostic indicator in malignant disease and may indicate uncontrolled tumour progression and metastasis. The 30-day mortality rate of cancer patients admitted to hospital with hypercalcaemia is almost 50% [2].

The symptoms of hypercalcaemia are nonspecific; delayed recognition can worsen morbidity and mortality [2]. Presenting features include nausea and vomiting, anorexia, thirst and polydipsia, polyuria, lethargy, bone pain, abdominal pain, constipation, confusion and weakness. Renal tract stones may occur. The degree of hypercalcemia can be classified by total serum calcium level as mild (10.5–11.9 mg/dL), moderate (12.0–13.9 mg/dL), or severe (≥14.0 mg/dL).

Author's Affiliation:
*Consultant Anaesthetist & Intensivist HCG- SMH Cancer Curie Centre, New Delhi, India.

Corresponding Author:
Lalit Gupta, Consultant Anaesthetist & Intensivist, HCG- SMH Cancer Curie Centre, 2, Institutional Area, Vikas Marg Extension, Near Metro Pillar No. 116, Karkardooma, New Delhi, Delhi 110092
E-mail: lalit.doc@gmail.com

Clinical effects of hypercalcemia are related more to the rate of rise in serum calcium and the underlying volume depletion resulting from osmotic diuresis than the absolute serum calcium value [2]. Electrocardiographic findings in clinically significant hypercalcemia include prolonged PR interval, widened QRS complex, shortened QT interval, bundle branch block, and brady-dysrhythmias leading to cardiac arrest when serum calcium exceeds 15 mg/dL.

Investigation

Ionised calcium is the most reliable laboratory test. If total calcium is used, it is important to calculate the corrected calcium level to allow for hypoal buminaemia [2]. Other investigations should include alkaline phosphatase, renal function and electrolytes, X-rays (may show lytic or sclerotic lesions of the bone) and a bone scan (to identify any metastases).

Management

There may be a palliative benefit from improving the symptoms of hypercalcaemia, even in patients with advanced malignancies. Urgent intervention is required to treat symptomatic hypercalcaemia. Management includes intensive rehydration and intravenous bisphosphonates. Normal saline infusion is recommended at 200–500 mL/hr and adjusted for a urine output of 100–150 mL/hr, absent any contraindications. However, fluids only modestly decrease serum calcium levels, and ≤ 30% of patients achieve normocalcemia with fluids alone [3]. Loop diuretics to inhibit calcium reabsorption in the ascending loop of Henle [4,5] risk worsening electrolyte abnormalities and volume loss, and should only be used in volume overload. Hemodialysis is generally indicated for congestive heart failure, severe kidney injury (glomerular filtration rate ≤ 10–20 mL/min), clinically significant neurological findings, or calcium concentration ≥18 mg/dL.

Management of calcium metabolism includes eliminating medications (e.g., thiazides) that increase intestinal absorption of calcium and glucocorti-costeroids (Prednisone, 40–100 mg PO; or hydrocortisone, 200–400 mg IV daily for 3–5 days) to decrease extra-renal calcitriol production in lymphoma or myeloma increase renal excretion and inhibit osteoclastic resorption. The bisphosphonates, pamidronate and zoledronate, are first line therapy for MAH. These pyrophosphate analogues bind to hydroxyapatite and inhibit bone crystal dissolution and osteoclastic resorption.

Calcium levels decrease 2–4 days after administration, reach their nadir between 4 and 7 days, and usually normalize for 1–4wks, affording time to treat the underlying malignancy [4].

Neutropenic Fever

Febrile neutropenia contributes to 50% of deaths associated with leukaemia, lymphomas and solid tumours [1]. Neutropenia is most often seen as an effect of cytotoxic therapy. Infection is responsible for at least half of the cases of neutropenic fever. The neutrophil count usually reaches a lowest level 5 to 10 days after the last dose of chemotherapy.

- Gram-positive cocci are now responsible for the majority of culture-positive cases of neutropenic fever, including *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Streptococcus viridans*, *Enterococcus faecalis* and *Enterococcus faecium*. Corynebacterium is the most likely gram-positive bacillus.
- Gram-negative bacilli include *Escherichia coli*, *Klebsiella* spp. and *Pseudomonas aeruginosa*.
- Candida is the most common fungal infection, but aspergillosis and other systemic mycoses can cause more serious infections.
- Often no causative organism is found and the patient improves as the neutrophil count increases.

The vulnerability to infection substantially rises at a neutrophil count less than 1×10^9/L, but the risk continues to increase as the neutrophil count falls.

Management

- The patient should have an infection screen, including blood cultures, urine cultures, swabs of any indwelling catheters, venflons and central lines, CXR, sputum cultures, cultures from any open wounds and stool cultures.
- Empirical antibiotic therapy should be started immediately based on local guidelines, with modification based on the results of microbiological investigations. The addition of antifungal coverage should be considered in high-risk patients who remain febrile after 4 to 7 days of broad-spectrum antibiotics with no identified causative organism.
- Growth colony stimulating factor can be given if the patient is haemodynamically unstable or if the neutropenia is slow to improve. It has been shown to be more effective in refractory gram-

negative and fungal infections than in gram-positive infections.

Acute Tumour Lysis Syndrome

Tumour lysis syndrome is caused by the abrupt release of large quantities of cellular components into the blood following the rapid lysis of malignant cells. It occurs most often in patients with haematologic malignancies, eg acute lymphoblastic leukaemia (ALL) or Burkitt's lymphoma. Treatment-provoked tumour lysis syndrome can occur following chemotherapy, radiotherapy, surgery or ablation procedures [2]. In some cases, tumour lysis syndrome can lead to acute kidney injury and death [6]. Patients particularly at risk have treatment-sensitive tumours, renal impairment or volume depletion. High pre-treatment urate, lactate and lactate dehydrogenase (LDH) are also risk factors. Onset is usually within 1-5 days of starting therapy (but can be delayed by days or weeks in patients with a solid tumour) and symptoms/biochemical features include weakness, paralytic ileus, cardiac arrhythmias, seizures, acute kidney injury, sudden death, hyperuricaemia, hyperkalaemia, hyperphosphatemia and hypocalcaemia.

Investigation

Full metabolic and biochemical profile to detect the above abnormalities. Monitoring of serum lactate, urate and LDH may predict the imminent onset of the syndrome.

Management

The key to the management of tumour lysis syndrome includes awareness of its causes, identification of high-risk patients, implementation of appropriate prophylactic measures, vigilant monitoring of electrolyte levels in patients undergoing chemotherapy, and initiation of more active treatment measures when necessary.

- Those at risk should have preventative management by receiving intravenous hydration with normal saline 3-6L/24 hours, with sodium bicarbonate.
- Acetazolamide is used to alkalinise the urine and prophylactic allopurinol/Febuxostat is given.
- Dialysis may be needed in severe cases.

Metabolic Abnormalities in Acute Tumor Lysis Syndrome [7,8,9]

Metabolic Abnormality	Value or change from Baseline	Clinical Implications	Management
Hyper-Kalemia	6.0 mmol/L or 6 mEq/dL Or 25% increase	Muscle cramps Paresthesias Dysrhythmias VF, & Cardiac arrest	• Polystyrene sulfonate 1 gm/kg • Insulin 0.1 unit/kg with dextrose 25% @2 mL/kg • Sodium bicarbonate 1–2 mEq/kg IV push • Calcium gluconate 100–200 mg/kg slow IVinfusion
Hyper-Phospahemia	2.1 mmol/L for Children or 1.45 mmol/L for adults or 25% increase	Nausea Vomiting Diarrhea Lethargy Seizures Acute kidney injury	• Volume loading • Removal of • phosphate from IV fluids • Oral phosphate binders • Hemodialysis
Hypo-Calcemia	1.75 mmol/L or 25% decrease	Muscle cramps Tetany Hypotension Dysrythmia	• Calcium gluconate 50- 100 mg/kg slow I/V • infusion with ECG monitoring. • Give only if symptomatic.
Hyper-Urecemia	476 mmol/L or 8 mg/dL or, 25% increase	Acute Kidney Injury	• Volume loading • Rasburicase (recombinant urate oxidase) • Allopurinol(oral/IV) or Febuxostat

Leukostasis

Leukostasis [1] is associated with a very high white cell count, respiratory failure, intracranial haemorrhage (but it can affect any organ system) and early death. Without prompt treatment the mortality rate can be up to 40%. Leukostasis occurs in 5-13% of patients with acute myeloid leukaemia (AML) and 10-30% in adult patients with acute lymphoblastic leukaemia (ALL). The risk is greater for younger patients, and infants are most often affected. A white cell count greater than 50,000/m^3 indicates a particularly poor prognosis.

There is usually a high fever and examination may show papilloedema, retinal vein bulging, retinal haemorrhage and focal neurological deficits. Myocardial infarction, limb ischaemia, renal vein thrombosis and disseminated intravascular coagulation may occur. Thrombocytopenia is usually present.

Management

- Rapid cytoreduction is the initial treatment, ideally with induction chemotherapy, which can dramatically reduce the white cell count within 24 hours.
- There is a very high risk of tumour lysis syndrome and so close monitoring of electrolytes and prophylaxis with allopurinol or rasburicase are required.
- Leukophoresis is usually started when the blast count is greater than 100,000/m3 or in the presence of symptoms.
- Cytoreduction can also be achieved by hydroxyurea, but is usually reserved for patients with asymptomatic hyperleukocytosis who are unable to receive immediate induction chemotherapy.

Syndrome of Inappropriate Antidiuretic Hormone

When a patient with cancer presents with normovolemic hyponatremia, SIADH should be suspected [1,10]. A bronchogenic carcinoma often is the ectopic source of antidiuretic hormone production, although certain chemotherapy agents can cause SIADH. Patients may present with anorexia nervosa, nausea, myalgia, headaches, and severe neurologic symptoms (e.g., seizures, coma). Laboratory testing may reveal hyponatremia (i.e., serum sodium level less than 135 mEq per L [135 mmol per L]), decreased serum osmolarity (less than 280 mOsm per L [280 mmol per L]), and concentrated urine (100 mOsm per L or more).

It is Often Asymptomatic but may Cause:

- Depression and lethargy.
- Irritability and other behavioural changes.
- Muscle cramps.
- Seizures.
- Depressed consciousness leading to coma.
- Neurological signs (such as impaired deep tendon reflexes and pseudobulbar palsy).

Management

Therapy involves treating the tumor producing the antidiuretic hormone or atrial natriuretic factor along with fluid management, usually fluid restriction or induced diuresis. Appropriate combination chemotherapy should be initiated, and brain metastases, if present, should be treated with radiotherapy.

- Fluid intake should be limited to less than 1,000 mL/d and less than 500 mL/d if the patient responds poorly.
- Refractory cases of hyponatremia or patients who can be treated as outpatients can be managed with 600 to 1,200 mg/d of demeclocycline (Declomycin) in divided doses [18].
- Patients who are symptomatic with coma or seizures can be treated with 3% hypertonic saline by *slow* infusion at a rate sufficient to increase the serum sodium level by 0.5 to 1.0 mEq/L/h.
- Rapid correction (greater than 2 mEq/L/h) may be associated with central pontine myelinolysis.
- Normal saline with IV furosemide may also be effective .

Raised Intracranial Pressure

Cranial metastases affect around a quarter of patients who die from cancer [10]. Lung, breast and melanoma are the tumours that most commonly metastasise to the brain. The clinical picture varies with site of metastases and the rate of rise of intracranial pressure. Small metastases may bleed and cause acute symptoms. Common symptoms and signs include:

- Headache.
- Nausea and vomiting.
- Behavioural changes.
- Seizures.
- Focal neurological deficit.

- Falling level of consciousness.
- Papilloedema.
- Unilateral ptosis or third and sixth cranial nerve palsies.
- Bradycardia (late sign).

Investigation

CT or MRI scanning should be conducted urgently to delineate the lesion, if the result is likely to affect the patient's management.

Management

- If the patient has lost consciousness and requires ventilation, then high respiratory rate should be used to lower pCO_2 which helps reduce intracranial pressure.
- Mannitol may be given as a diuretic along with dexamethasone to reduce symptoms and the likelihood of cerebral herniation.
- Further management may involve cranial irradiation, surgery ± radiation or 'gamma knife' radiosurgery, depending on the site, type and number of metastases.

Malignant Spinal Cord Compression

This condition must be diagnosed and treated quickly to prevent permanent neurological disability. It may occur because of extradural spread from a vertebral body metastasis, direct metastases or from a vertebral crush fracture. Cancers that most often metastasise to bone and cause spinal cord compression are cancers of the breast, kidney, thyroid, prostate and lung). Due to anatomic locations, breast and lung cancer most commonly metastasize to the thoracic spine, whereas abdominal malignanciestypically metastasize to the lumbosacral vertebrae. Spread of pelvic cancers (e.g., prostate) is enabled by valveless venous communication with the lumbar spine.

Back pain, the first symptom in 95% of those with MSCC [11], precedes other symptoms by up to 2 months and offers the opportunity to intervene before incurring long-term morbidity. Approximately half of MSCC patients have bowel or bladder dysfunction [12] and postvoid residual aids diagnosis of cauda equina syndrome. About 75% have focal weakness, which, if untreated, progresses to ataxia and paralysis. Spinal cord imaging (MRI, Gold Standard) is necessary to identify the site of obstruction and plan treatment.

Management

- Treatment goals include maintenance of neurological function, control of local tumor growth, spine stabilization, and pain control.
- Corticosteroids mitigate vasogenic edema resulting from compression-induced ischemia. High-dose dexamethasone (96 mg IV bolus, then 24 mg by mouth every 6 hrs for 33 days, then 10-day taper) had significantly increased preservation of ambulation at 3 months after radiation [13], but it can have serious side effects.
- High-dose steroids are recommended for patients with an abnormal neurological exam and moderate-dose steroids (10 mg IV bolus, then 4 mg qid with 2-wk taper) for all others [14].
- Radiotherapy of radiosensitive tumors is fundamental in MSCC. Nearly half of survivors are ambulatory at 1 yr following radiation.
- The older surgical technique of nonselective posterior laminectomy relieves pressure within the vertebral foramen but does not address the lesion, which is typically in the vertebral body.

Superior Vena Cava Obstruction

This may be due to compression of the superior vena cava, caused by primary or secondary tumours. Lung cancer (~85% of cases), lymphoma and metastatic tumours are the most common causes. Although the signs and symptoms of SVCS vary, the most common finding is facial edema). The frequency of findings differ between malignant and benign etiologies, with dyspnea at rest, cough, chest and shoulder pain, and hoarseness more frequent in the former [15,16].

Management

Therapy is directed at the underlying cause. This is normally chemotherapy for lymphoma/small-cell lung cancer, with early response and resolution of superior vena cava obstruction within weeks being the usual outcome. Radiotherapy is usually used for non-chemosensitive tumours or patients who do not respond to chemotherapy.

Elevation of the head of the bed and supplemental oxygen are standard. Although commonly prescribed, glucocorticosteroids are of unclear benefit except in the cases of lymphoma or thymoma where indicated for the underlying malignancy [17]. Thrombosis-related SVC obstruction is treated with anticoagulation, intravascular device removal, and balloon dilatation or stenting if

significant fibrosis remains.

Median survival of patients with cancer-induced SVCS is roughly 6 months after presentation, but many patients have survived over 2 yrs with appropiate treatment and care [17].

Conclusions

As the number of cancer patients grows, the prevalence of malignancy related life threatening complications will increase. Often the stage of malignancy carries a poor prognosis. Yet diagnosis and management of oncologic emergencies can usually improve the duration or quality of patients' lives.

Further Reading & References

- Palliative and Supportive Care, Bandolier
- Macmillan Cancer Support

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P A Cathetor V/s. A P C O

Manjula Sarkar

Abstract

Cardiac output (CO) monitoring is an integral part of management of patients during cardiac surgery, supramajor surgeries with large fluid shifts and critically ill patients in the ICU. It helps in early identification of insufficient tissue oxygenation and appropriate treatment can be instituted early. Traditionally, CO monitoring is done by thermodilution technique using pulmonary artery catheter. However, it is an invasive modality and several studies criticised and linked it to the increased mortality. This has lead into the development of newer minimally invasive methods most noticeably arterial pressure waveform derived cardiac output (APCO) monitoring system. It is an exciting technology based on normal population arterial waveform algorithm without any need of external calibration and can be attached to the pre-existing arterial line. However, thermodilution is still considered as a gold standard method of cardiac output monitoring.

This article intends to highlight the pro and cons of these two techniques as well as other methods of CO monitoring.

Keywords: Cardiac Output Monitor; Thermodilution; Pulmonary Artery Catheter; Flotrac; LiDCO; Echocardiograhy

P A Cathtor

In medicine *pulmonary artery catheterization* (PAC) is the insertion of a catheter into apulmonary artery. Its purpose is diagnostic; used to detect heart failure or sepsis, monitor therapy, and evaluate the effects of drugs. The pulmonary artery catheter allows direct, simultaneous measurement of pressures in the right atrium, right ventricle, pulmonary artery, and the filling pressure ("wedge" pressure) of the left atriumIn the clinical setting, the perfusion of vital organs usually is assessed by measuring the cardiac output (CO), and usually by thermodilution using a pulmonary artery catheter (PAC).Most clinical assessments have compared less invasive or noninvasive techniques with thermodilutionto achieve clinical relevance and acceptability. Pulmonary artery thermodilution has remained the clinical gold standard for CO. Less Invasive CO monitoring though less precise than PAC but continuous and automatic, improve haemodynamic monitoring in the OR & ICU.

Less invasive cardiac output measurement techniques apart from P A C is arterial wave form analysis require arterial catheter.

Thermodilution most Commonly used Technique

Advantages

- Rapid & easy to use,
- No arterial line required,
- Repeat measurements possible,
- Most Widely Used Measure of Cardiac Output,
- Low Cardiac Output correlated with mortality in multiple studies,
- Readily available in ICU.

Disadvantages

- Intracardiac shunts,
- Tricuspid or pulmonic valve regurgitation,
- Inadequate delivery of thermal indicator,
- Warming of iced injectate,
- Thermistor malfunction from fibrin or a clot Pulmonary artery blood temperature fluctuations,
- Post–cardiopulmonary bypass status,
- Rapid intravenous fluid administration,
- Respiratory cycle influences,
- Indicator is time consuming,

Author's Affiliation:
Professor, Anaesthesia, Seth G. S. Medical College & KEM Hospital, Parel, Mumbai – 400 012.

Corresponding Author:
Manjula Sarkar, Professor, Dept. of Anaesthesia, Seth G. S. Medical College & KEM Hospital, Parel, Mumbai – 400 012.

E-mail: drmanjusarkar@gmail.com

- expensive& cumbersome to prepare.

Why Monitor Cardiac Out Put ?

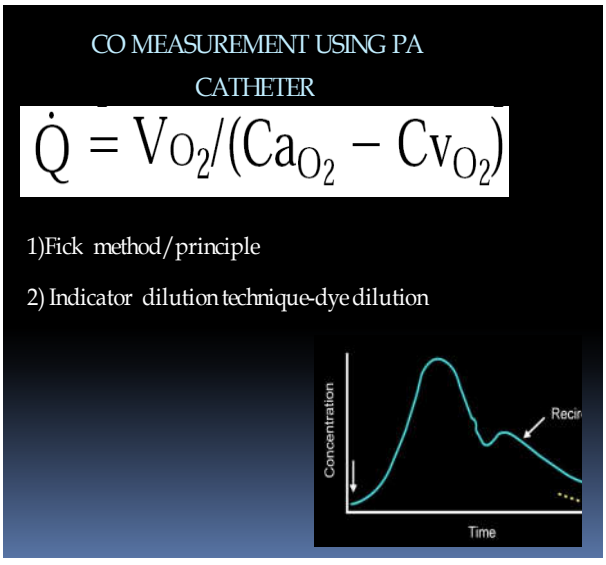
Global assessment of circulation,Critically ill low cardiac output- increase mortality & morbidity-inadequate blood flow to the organs, Clinical assessment of cardiac output-inaccurate "It is well known that the blood volume and cardiac output are usually diminished in traumatic shock before the arterial blood pressure declines significantly" Blalock A, (1943) Surgery 14: 487-508 BP does not change until late due to these compensatory response, CVP & PAOP represent the end diastolic pressures of RV & LV respectively, Do not translate in to systolic function or cardiac output,Cardiac output and other haemodynamic parameters DD of shock,establishing the right treatment plan and monitoring and refining it in real time.

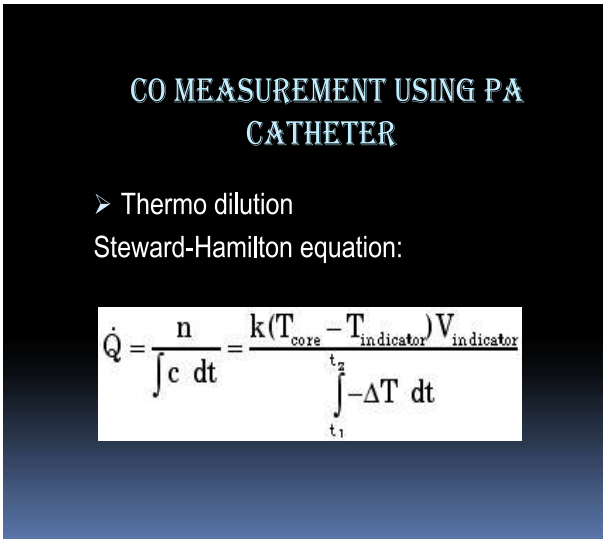
Determinants of Cardiac Out Put

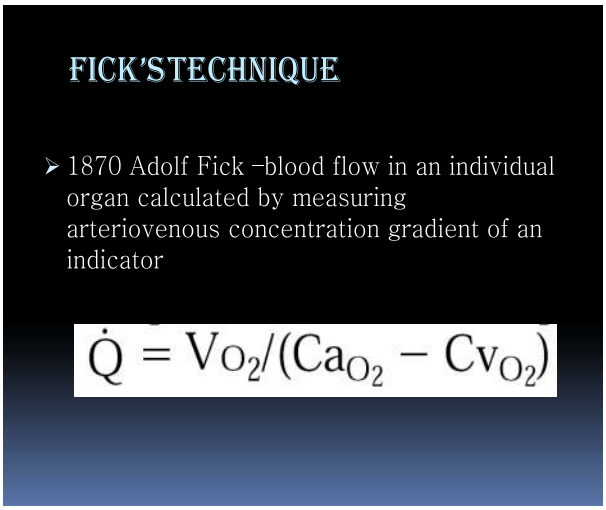
- *Intrinsic Factors:* Heart Rate,Myocardial contractility.
- *Extrinsic Factors :* Preload, Afterload.

Characterstics of Ideal Cardiac out put Monitor

- Precise,
- No bias,
- Non-invasive,
- Readily available in the ICU,
- Leads to treatment changes/improvement in outcome.







Advantages

- Accurate & precise compared to electromagnetic flow probe

Disadvantages

- Not easy to perform in OR.
- Cumbersome.
- Time consuming.
- Repeat measurements not practical.

Dye dilution 1890 George Stewart - Concept of Indicator Dilution

- William Hamilton-measurement of cardiac output using indicator dilution technique
- Ideal indicatorStable.
- Nontoxic.

- Easily measured.
- Uniformly distributed within fluid compartment.
- Not lost from circulation during the first trasit.
- Rapidly dissipated to avoid recirculation.

Dye Dilution

The cardiac output (blood flow) is amount of indicator injected, divided by average concentration in arterial blood.

- Cardiac Output(ml/min)= mg of dye injected x 6 {Avgconc of dye Duration of in each ml of blood for [X] curve induration of curve } second.

Pulse Contour Analysis Technique

The pulse contour technique of measuring cardiac output relies on the principle that the arterial pressure waveform is related to the stroke volume.This was described by Frank and colleagues in 1930and has been studied with varied success ever since. A recent publication describing a novel time-averaged approach to this technique reviews the traditional Windkessel model of the circulation, which is the underlying principle of arterial waveform analysis (Figure 1). Although it is possible to obtain an arterial waveform with noninvasive monitors, pulse contour cardiac output devices currently available require an invasive arterial waveform.There are three techniques. In addition, two of the three require an external calibration with a known cardiac output. One relies on lithium indicator dilution (PulseCO, LiDCO Limited, Cambridge, United Kingdom), where the radial artery lithium concentration is measured after a venous injection of lithium. The other is calibrated with a transpulmonarythermodilution technique (PiCCO, Pulsion Medical Systems, Munich, Germany), applies to the circulation (left), ABP should decay like a pure exponential during each diastolic interval with a time constant (T) equal to the product of the TPR and the nearly constantAC. Thus, an exponential is fitted to the diastolic interval of each ABP pulse to determine T(right) and the time-averaged ABP (MAP) is divided by T to estimate proportional CO. Newerarterial waveform analysis techniques may use significant modifications of this equation or differentequations altogether. Abbreviations: ABP, arterial blood pressure; AC, arterial systemcompliance; MAP, mean arterial pressure; TPR, total peripheral resistance. (Reproduced andtext modified from Mukkamala R, Reisner H, Hojman M, et al. Continuous cardiac outputmonitoring by peripheral blood pressure waveform analysis. IEEE Trans Biomed Eng 2006:53:459–67; with permission.Copyright 2006 IEEE.)

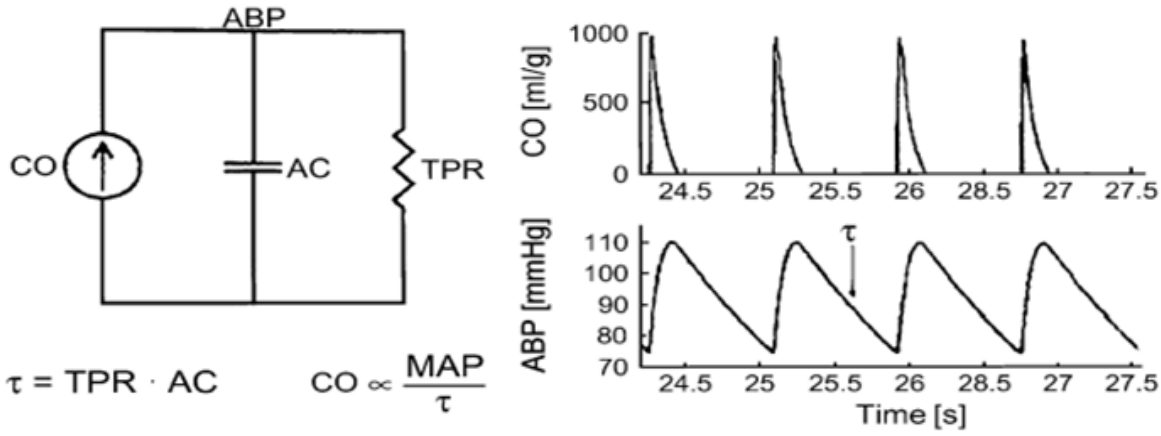


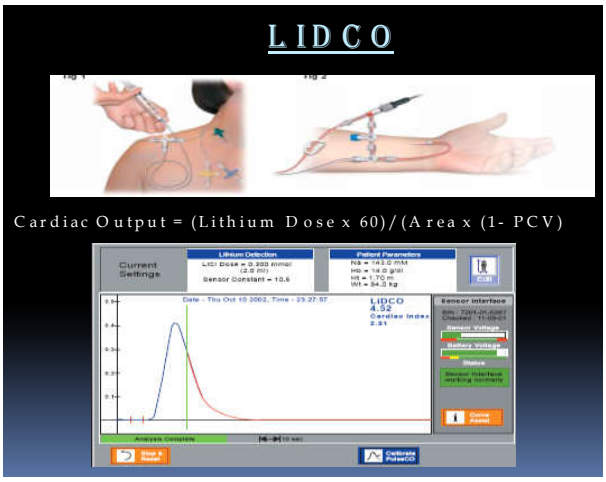
Fig. 1A: Mathematical model for deriving cardiac output from an arterial pressure waveform.According to the ''Windkessel'' model, which assumes Ohm's law (described for electrical circuits)

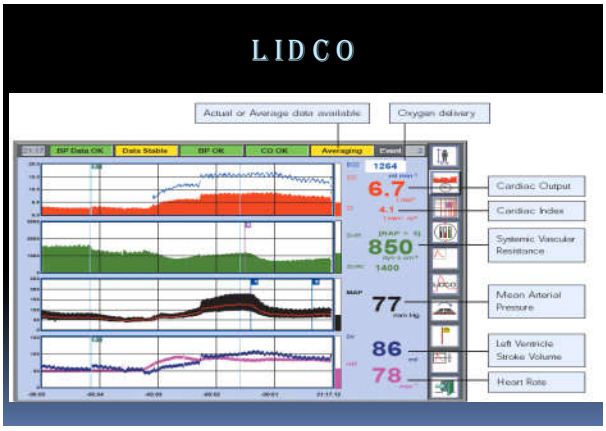
where a central venous injection of cold or room temperature injectate is sensed by a thermistor-tipped catheter placed in the radial artery. Both the lithium indicator dilution and transpulmonary thermodilution techniques (ie, the calibration techniques for the noninvasive pulse contour) have been shown to correlate well with standard thermodilution. Neither of these pulse contour techniques is truly noninvasive; however, they do not require a pulmonary artery catheter. The third and most recently introduced technique (Flotrac,) does not require external calibration, but it has not been compared adequately with other techniques to warrant conclusions regarding reliability or clinical utility. Although all techniques of pulse contour analysis use the arterial waveform, just how the

waveform is analyzed differs significantly. In the case of PulseCO, a proprietary algorithm uses beat duration, ejection duration, mean arterial pressure, and themodulus and phase of the first waveform harmonic in order compute beat-to-beat stroke volume. Both this latter publication and a more recent independent evaluation of this system in 22 postoperative patients showed the pulse contour analysis to compare well with lithium indicator dilution.Certain patient populations cannot be analyzed adequately with this technique, including those on lithium therapy and patients with significant cardiac dysrhythmias, severe aortic incompetence, or a poor arterial waveform. Calibrations with lithium indicator dilution are recommended every 8 hours; if done more frequently, serum lithium levels may interfere with the calibration. A major advantage of the PulseCO system is that the calibration with lithium can be done with a peripheral venous catheter; it therefore only requires the peripheral venous catheter and radial arterial catheter. The PiCCO system uses a more traditional Windkessel model for waveform analysis The proprietary algorithm was revised recently to take into account the shape of the systolic portion of the arterial waveform. Earlier studies with this system showed a fair correlation with thermodilution[in patients after cardiac surgery, the new algorithm correlated well with thermodilution during changes in preload]. Both long radial artery catheters and brachial artery catheters appear to be acceptable alternatives to femoral artery catheters for the transpulmonarythermodilution calibrations. In addition to providing stroke volume and CO, this system can be used to calculate extravascular lung volume. The most recent entry into the field of pulse contour cardiac output analysis is the Flotrac sensor. The product information available from the manufacturer states the proprietary algorithm takes into account the pulse pressure, known determinants of arterial system compliance (such as age, sex, and body surface area), and other undefined aspects of the arterial waveform to calculate stroke volume without the need for external calibration.

Transpulmonary Lithium Indicator Dilution &Arterial Waveform Analysis LiDCO

Central/peripheral venous acess is required. Absence of renal dysfunction or dialysis is ensured. An isotonic (150 mM) solution of lithium chloride - 0.15 -0.30 mmol for an average adult -patient weight (> 40kg) is injected. Ion selective electrode is attached to peripheral arterial catheter which measures Lithium Dilution Curve to derive CO. Thistechnique calibrates software which performs continuous arterial wave analysis by a pulse power method.





Advantages of LIDCO

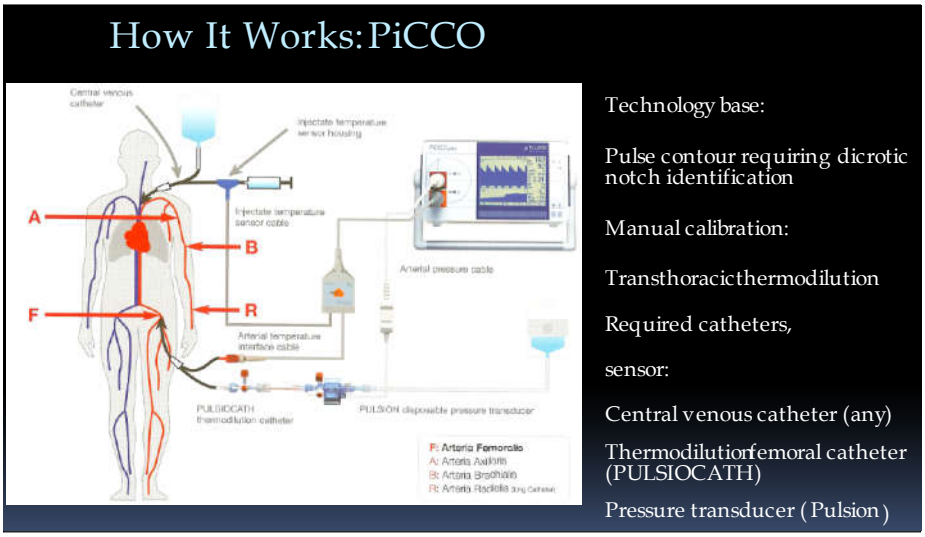
- Compared well with electromagnetic flow probes &thermodilution technique.
- Continuous real-time cardiovascular monitoring.
- Minimally invasive.
- Safe,Simple to use in conscious as well as unconscious patients.
- Newer complete noninvasive LIDCO monitor which derives CO from finger probe (similar to pulse oxymeter) has recently been launched but the accuracy and validation is still not conclusive.

Disadvantages

- NDMR interferes with the lithium sensitive electrode.
- Dysrhythmias result in irregular data output.
- Damping of waveform results in eror.

Transpulmonary Thermo Dilution &Arterial Waveform Analyses (PiCCO)

Cold saline is injected via central venous catheter and temperature of arterial blood in femoral or brachial artery is measured. CO calculated using modified Stewart Hamilton equation.



Advantages

- Compared well with electromagnetic flow probes &thermodilution technique.
- Enables continuous hemodynamic monitoring.
- Measures Transpulmonary cardiac output (C.O.), Intrathoracic blood volume (ITBV), Extravascular lung water (EVLW), Stroke volume variation (SVV) in conscious as well as unconscious patients.

Disadvantages

- More invasive than LiDCO.
- Specific thermistor tipped catheter.
- Damping of waveform or change in aortic compliance results in error.
- Needs Recalibration.
- Dependent on Compliance of Arterial Tree.
- Little Validation in Patients with Shock.

Flotra or Vigilio

It is the technique of arterial pressure waveform analysis without external calibration. Patient demographic data is used to calculate CO. The device connects to any existing peripheral arterial line using the FloTrac pressure transducer and CO is displayed on a continuous basis after entering patient height, weight, and age. The FloTrac sensor measures variation in arterial pulse pressure.The Vigileo monitor uses the FloTrac measurements to continuously compute stroke volume. Age, gender, height, and weight determine patient-specific vascular compliance. The vigileo monitor supports both the flotrac sensor for continuous cardiac output and the presep central venous catheter for continuous central venous oximetry (scvo2).The vigileo monitor continuously displays and updates continuous cardiac output, cardiac index, stroke volume, stroke volume index, systemic vascular resistance, systemic vascular resistance index, and stroke volume variation every 20 seconds when used with the flotracsensor.These parameters help guide the clinician in optimizing stroke volume through precision guided management of preload, afterload, and contractility. The vigileo monitor uses the patient's arterial pressure waveform to continuously measure cardiac output with inputs of height, weight, age and gender, patient-specific vascular compliance is determined. The flotrac sensor measures the variations of the arterial pressure which is proportional to stroke volume. Vascular compliance and changes in vascular resistance are internally compensated for. Cardiac output is displayed on a continuous basis by multiplying the pulse rate and calculated stroke volume as determined from the pressure waveform. The flotrac sensor is easily setup and calibrated at the bedside using the familiar skills used in pressure monitoring."Validation of a continuous cardiac output measurement using arterial pressure waveform", critical care, mar 05 supplement (abstract) Dr Mcgee's study is the largest validation study of its kind. The study was conducted in 4 centers, 2 american and 2 european, in both ORs and ICUs, over a wide range of ages. This study presents a "real life" validation as patient sample bias often caused by homogeneous demographics and the effect of a limited number of participatingclinical sites has been minimized. APCO responds quickly to changes in cardiac output. One of the most significant factors affecting differences in the magnitude and timing of changes in trends between the two

continuous technologies, APCO and CCO, is the averaging time. The APCO algorithm detects changes in vascular tone via analysis of waveform characteristics. CO systems based upon an indicator dilution method of calculating CO require regular calibration because they do not compensate continuously for changes in vascular tone. APCO does not require a manual method of recalibration.

Advantages

- Continuous monitoring.
- No Calibration.
- Less invasive.

Source of Error

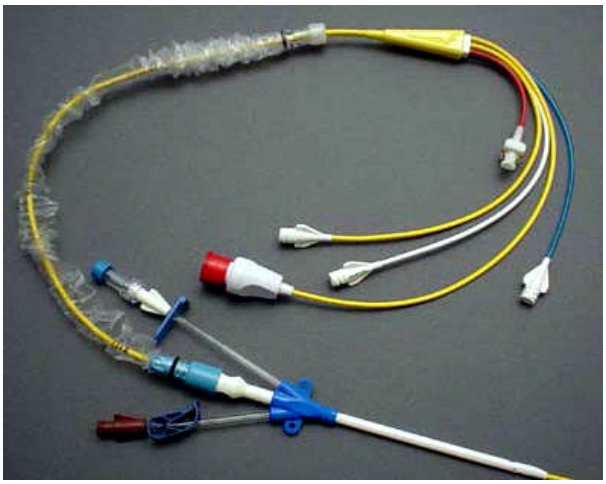
- Dysrhythmia.
- Sensor heightAortic balloon pump.
- Patient arm movement.
- Line bubbles.
- Pressure dampening.

PA Catheter

❖ *General Indications are*

- Management of complicated myocardial infarction.
- Assessment of respiratory distress.
- Assessment of type of shock.
- Assessment of therapy
  - o Afterload reduction
  - o Vasopressors
  - o Beta blockers
  - o Intra-aortic balloon counter-pulsation
- Assessment of fluid requirement in critically ill patients
  - o Hemorrhage
  - o Sepsis
  - o Acute renal failure aka Acute Kidney Injury
  - o Burns
- Management of postoperative open heart surgical patients.
- Assessment of valvular heart disease.
- Assessment of cardiac tamponade/constriction.

Note: No study has definitively demonstrated improved outcome in critically ill patients managed with PA catheters. Therefore, the primary justification has been on the basis of clinic experience.



Procedure

The catheter is introduced through a large vein—often the internal jugular, subclavian, or femoral veins. From this entry site, it is threaded, often with the aid of fluoroscopy, through the right atrium of the heart, the right ventricle, and subsequently into the pulmonary artery.The standard pulmonary artery catheter has two lumens (Swan-Ganz) and is equipped with an inflatable balloon at the tip, which facilitates its placement into the pulmonary artery through the flow of blood. The balloon, when inflated, causes the catheter to "wedge" in a small pulmonary blood vessel. So wedged, the catheter can provide an indirect measurement of the pressure in the left atrium of the heart, showing a mean pressure, in addition to a, x, v, and y waves which have implications for status of the left atria and the mitral valve. Left ventricular end diastolic pressure (LVEDP) is measured using a different procedure, with a catheter that has directly crossed the aortic valve and is well positioned in the left ventricle. LVEDP reflects fluid status of the individual in addition to heart health.

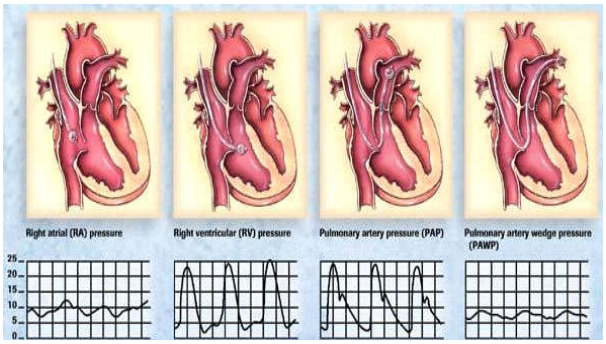


Fig. 2: This is a typical waveform progression as the pulmonary artery catheter floats throigh Cardiac chambers. Monitoring these waveform tells clinicians where in the heart the catheter is as it advances.

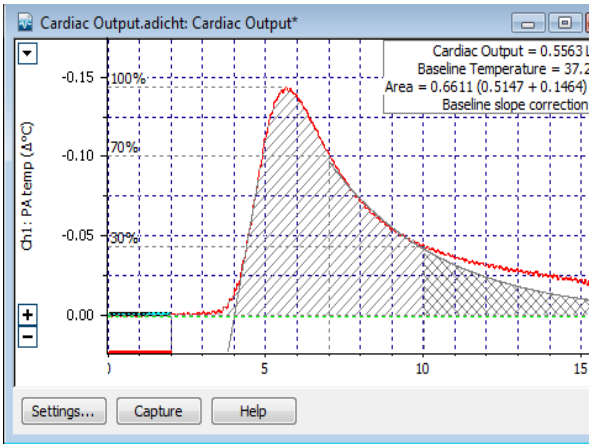
Technical Developments

Thermal Dilution

After Swan developed the initial balloon tip, Ganz used Fronek's idea and added a small thermistor (temperature probe) about 3 cm behind the tip. Either cold 10 ml of saline (0.9% NaCl) under 10° Celsius or room temperature (not as accurate) is injected into an opening in the right atrium. As this cooler fluid passes the tip thermistor, a very brief drop in the blood temperature is recorded. A recent variation in design is the incorporation of a heating coil on the catheter (30 cm from the tip, residing in the atrium area) which eliminates the cold fluid bolus, a major factor in human technique variation.

By attaching both the injector site and the ventricular thermistor to a small computer, the thermodilution curve can be plotted. If details about the patient's body mass index (size); core temp, Systolic, diastolic, central venous pressure CVP (measured from the atrium by the third lumen simultaneously) and pulmonary artery pressure are input, a comprehensive flow v/s. pressure map can be calculated. this measurement compares left and right cardiac activity and calculates preload and afterload flow and pressures which theoretically if stabilized or adjusted with drugs to either constrict or dilate the vessels to raise or lower the pressure of blood flow to the lungs, respectively, in order to maximize oxygen for delivery to the body tissues. The true art remains with the consultant in balancing fluid load.

Temperature-versus-time curve



Pharmacotherapy Lumens

Modern catheters have multiple lumens — five or six are common — and have openings along the length to allow administration of inotropes and other drugs directly into the atrium. Drugs to achieve these changes can be delivered into the atrium via the fourth lumen, usually dedicated to medication. Common drugs used are various inotropes, norepinephrine or even atropine. A further set of calculations can be made by measuring the arterial blood and central venous (from the third lumen) and inputting these figures into a spreadsheet or the cardiac output computer, if so equipped, and plotting an oxygen delivery profile.

SvO_2 Measurement

One further development in recent years has been the invention of a catheter with a fiber-optic based probe which is extended and lodged into the ventricle wall providing instant readings of SvO2 or oxygen saturation of the ventricle tissues. This technique has a finite life as the sensor becomes coated with protein and it can irritate the ventricle via the contact area.

Complications

(a) Complications of Central Venous Puncture

Arterial puncture, arterial or venous hematoma, arteriovenous fistula (AVF), pseudoaneurysm formation, thoracic duct injury, pneumothorax/ hemothorax, thrombosis and air embolization.

(b) Complications related to PAC Insertion and Manipulation: Cardiac Arrhythmias

The incidence ofarrhythmia has been reported to range from 12.5% to over 70% during PAC insertion (16–18). The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Pulmonaryartery versus central venous catheter to guide treatment of acute lung injury. N Engl J Med 2006 ;354: 2213–2224. Iberti TJ, Benjamin E, Gruppi L, et al: Ventricular arrhythmias during pulmonary artery catheterization in the intensive careunit. Prospective study. Am J Med 1985;78:451–454 18. Groeneveld ABJ, Thijs LG: Hemodynamic monitoring in septicshock. Springer, Berlin 1991;179–196.

(c) Mechanical Complications

Mechanical damage to cardiac structures (i.e., valves, chordae) can occurduring PAC placement/ manipulation but is uncommon (~0.9%) (25–29). Arnaout S, Diab K, Al-Kutoubi A, et al: Rupture of the chordate of the tricuspid valve after knotting of the pulmonary artery catheter. Chest 2001; 120: 1742–

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Thrombosis and Venous Embolism Infections

Complications associated with short- or long-term presence of the PAC inthe cardiovascular system Pulmonary Artery Rupturep Fortunately this complication is rare (incidence of 0.03%–0.20%) [7–8].

PAC Knotting: The incidence of PAC knotting is estimated to be 0.03% of all PAC placements.

Balloon Failure and breaking of the *PAC* with repeated inflation, cracks within the PAC balloon can occur resulting in up to 17% balloon rupture rate in early PAC series.

(d) Incorrect Interpretation/use of PAC-Derived data

Evidence of Benefit

Several studies in the 1980s seemed to show a benefit of the increase in physiological information. Many reports showing benefit of the PA catheter are from anaesthetic, and Intensive Care settings. In these settings cardiovascular performance was optimized thinking patients would have supra-normal metabolic requirements.

Evidence of Harm or Lack of Benefit

Contrary to earlier studies there is growing evidence the use of a PA catheter (PAC) does not necessarily lead to improved outcome [2].The following explanations have been advanced. One explanation could be that nurses and physicians were insufficiently knowledgeable to adequately interpret the PA catheter measurements. Also, the benefits might be reduced by the complications from the use of the PAC. Furthermore, using information from the PAC might result in a more aggressive therapy causing the detrimental effect. Or, it could give rise to more harmful therapies (i.e. achieving supra-normal values could be associated with increased mortality).

Utility of Pulmonary Artery Catheterization

This interpretation of Adolph Ficks' formulation for Cardiac Output by time/temperature curves is an expedient but limited and invasive model of right heart performance. It remains an exceptional method of monitoring volume overload leading to pulmonary edema in an ICU setting.

A feature of the pulmonary artery catheter that has been largely ignored in the clinical setting is its ability to monitor total body oxygen extraction by measuring the mixed venous oxygen saturation. Regardless of the value obtained by measurements of the cardiac output, the mixed venous oxygen saturation is an accurate parameter of total body blood flow and therefore cardiac output. The assumption that a low mixed venous oxygen saturation (normal = 60% except for the coronary sinus where it approximates 40% reflecting the high metabolic rate of the myocardium) represents less than adequate oxygen delivery is consistent with physiological and metabolic observations. High oxygen extraction is associated with low cardiac output and decreased mixed venous oxygen saturation. Except during hypothermia and in severe sepsis, low mixed venous oxygen saturations are indication of inadequate hemodynamics. The ability of the pulmonary artery catheter to sample mixed venous blood is of great utility to manage low cardiac output states.

Non-invasive Echocardiography and pulse-wave cardiac output monitoring are concordant with (and much safer) if not better than invasive methods defining right and left heart performance. The advent of MRSA and similar hospital based catheter infections now clearly limits the utility of this type of invasive cardiac ICU intervention.

Conclusions

APCO, a less invasive technique requiring simply an arterial catheter, does not require calibration.

APCO correlated well with ICO and CCO showing comparable bias and precision.

APCO performed well in the real world setting of both medical and surgical critically ill patients.

The development of an accurate less invasive simple method of measuring cardiac output may contribute to the expansion of hemodynamic monitoring to patients currently not monitored.

P A Cathetor is more invasive but gives accurate parameters for diagnosing the problem and perfact treatment.

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Journal of Animal Feed Science and Technology	2	4100	410
Journal of Cardiovascular Medicine and Surgery	2	9100	910
Journal of Forensic Chemistry and Toxicology	2	9000	900
Journal of Microbiology and Related Research	2	8000	800
Journal of Orthopaedic Education	2	5000	500
Journal of Pharmaceutical and Medicinal Chemistry	2	16000	1600
Journal of Practical Biochemistry and Biophysics	2	5500	550
Journal of Social Welfare and Management	3	7500	750
New Indian Journal of Surgery	3	7100	710
Ophthalmology and Allied Sciences	2	5500	550
Otolaryngology International	2	5000	500
Pediatric Education and Research	3	7000	700
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Urology, Nephrology and Andrology International	2	7000	700
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Indian Journal of Emergency Medicine	2	12000	1200
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Case Report

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Stress Induced Postoperative Takotsubo Cardiomyopathy

Taaeba I. Syed*, Vrishali Ankalwar, Deepak Ruparel***, Naresh G. Tirpude******

Abstract

The Takotsubo cardiomyopathy is a rare hemodynamic dysfunction, only recently reported . While the diagnostic criteria have been established and the outcome is known as favourable, the pathophysiological mechanisms are not entirely understood. Here we present the case of a patient scheduled for laparoscopic hysterectomy, who postoperatively developed a Takotsubo cardiomyopathy, supposedly triggered by an acute hypertensive crisis and emotional stress.

Keywords: Takotsubo Cardiomyopathy; Transient Left-Ventricular Apical Ballooning Syndrome; Stress-Induced Cardiomyopathy And Broken Heart Syndrome.

Introduction

Takotsubo or "stress induced cardiomyopathy" is a rare disorder which usually manifests as myocardial infarction. It is characterized by reversible left ventricular dysfunction with apical akinesia.

A Case Report

A peri-menopausal woman (45 year old), ASA I, a diagnosed case of dysfunctional uterine bleeding (DUB) was posted for laparoscopic hysterectomy under general anaesthesia. During her preanesthetic check up, patient had no history of any medical illness or surgical procedure in the past. Her all laboratory investigations were within normal limits.

Preoperatively patient was anxious and was much worried about the surgery. The counselling of patient was done to relieve her anxiety. Tab. Alprazolam 0.5 mg was given orally a night prior the surgery. At operation theatre, after the checking of consent & case paper, Multipara monitor cables were connected to the patient. IV access was achieved. General anaesthesia was administered with IV Midazolam 1.5 mg, IV Fentanyl 80 mcg, IV Propofol 2 mg/ kg and IV Vecuronium 6 mg. The endotracheal intubation was done without any difficulty. General anaesthesia was maintained with N2O: Oxygen in 60: 40% & Sevoflurane 1.5-2% and intermittent doses of Inj. Vecuronium and Fentanyl. The positive pressure ventilation was done via anaesthesia ventilator and $etCO_2$ was maintained between 32-36 mm/ Hg. The pneumo-peritoneum insufflation pressure was constantly maintained at 12-14 mm/ Hg. Intra-operatively patient's vitals were stable except that there was a transient increase of Blood pressure i.e. 170/100 mm/ Hg (Highest reading during intraoperative monitoring). It was managed with Inj. Nitro-glycerine (NTG) drip for a period of 20 minutes.

On completion of surgery, the reversal of anaesthesia was done with Inj. Neostigmine & Inj. Glycopyrrolate. After reversal of anaesthesia, the skeletal motor power was not adequate. Hence patient was shifted with endotracheal tube in situ to post anaesthesia care unit (PACU) and respiration was supported with CPAP. After two hours of reversal of anaesthesia, patient regained adequate skeletal motor tone and she was extubated.

After one hour of tracheal extubation, patient suddenly complained of chest pain and pink frothy secretions were coming out of mouth. Patient became suddenly dyspnoeic. Within few minutes, the patient developed pulse less ventricular tachycardia. Cardio-version was done with 200 J, she was reintubated and mechanical ventilation was initiated. Inotropic support was started with Inj. Dobutamine and

Author's Affiliation:
*Junior Resident, **Associate Professor,***Assistant Professor, ****Professor & Head, Dept. of Anaesthesiology, Govt. Medical College, Nagpur.

Corresponding Author:
Taaeba I. Syed, Plot No.- 1004, Last bus stop, Hasan bagh ,Kharbi road, Nagpur- P.C. 440 009, Maharashtra.

E-mail: taaebaiffat@gmail.com

Inj. Noradrenaline in titrated doses. ECG showed ST elevation. CPK-MB and Troponin-T levels were found to be minimally raised. X ray chest showed bilateral pulmonary oedema.

After 24 hours, 2D-Echo was done which showed left ventricular ejection fraction of 20 % with left ventricular apical hypokinesia. Repeat 2D echo on 3rd day showed mild improvement in ejection fraction of up to 30 %. Coronary angiography was done on 3rd day which did not reveal any coronary blockage (Proximal/ distal). Mechanical ventilation and Inotropic support was continued for the next 2 days.

Patient was extubated on 5th post-operative day as her vital parameters and laboratory parameters were satisfactory. Unfortunately after 6 hours of extubation, patient developed hypotension and cardiac arrest.

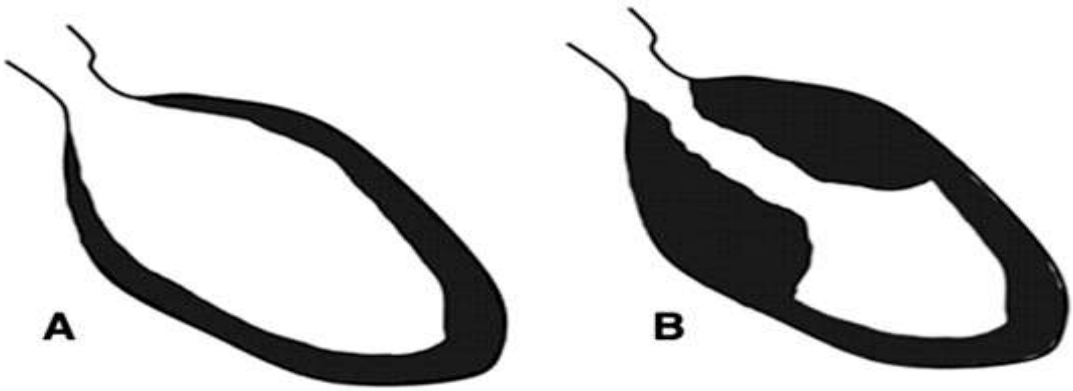

Fig. 1: Normal heart (A) and Tako-Tsubo sign (B) with apical ballooning (end-systolic view).

Inspite of all efforts of resuscitation, patient could not be revived and succumbed to death.

Discussion

Takotsubo cardiomyopathy (TCM) or "broken heart syndrome" is a clinical entity characterised by transient left ventricular dysfunction and apical dyskinesia with minimal increases in cardiac enzymes in the absence of coronary blockage/ occlusion.

Dote et al, first described this syndrome in Japanese patients; the name relates to the peculiar shape of left ventricle, which resembles an octopus-fishing pot called Takotsubo and can be visualised by end-systolic ventriculography [1].

Although the world wide incidence is unknown, TCM accounts for approximately 1% of admission for suspected for acute myocardial infarction in Japan; most cases are reported in post menopausal woman aged 60 -75 years [2-7]. Psychological, emotional (fear, grief, anger) & physical stresses (surgery, asthma, chemotherapy, stroke) are known triggers for onset of TCM. Initial signs and symptoms are similar as that of with acute coronary syndrome i.e. chest pain, dyspnoea and ST segment changes on ECG. The most common ECG finding in Takotsubo cardiomyopathy is ST segment elevation (as seen in our patient), but ECG may be normal or may show T or Q wave abnormalities, diffuse often deep T wave inversion in the right pre-cordial leads mimicking STEMI can occur. In classic MI, size of infarct corresponds to the amount of myocardium supplied by obstructed artery. In Takotsubo, area of affected myocardium is much larger than normal distribution of a single coronary artery [8].

Pathogenesis

Although the exact aetiology of Takotsubo cardiomyopathy is remain unclear. Various mechanisms proposed is: 1) Multi vessel coronary artery spasm 2) Impaired cardiac micro vascular function and 3) Endogenous catecholamine induced myocardial stunning and micro-infarction. In TCM, catecholamine level reaching 7-34 times as high as published normal values and 2-3 times as high as level in patient with MI have been reported. Possibility of genetic predisposition may also exist [9].

Clinical Features of Takotsubo Cardiomyopathy:

1) Presentation of acute chest pain, or dyspnoea after emotional and physiological stress, 2) ECG abnormalities that mimic an acute MI, 3) Transient akinesia or hypokinesia of left ventricular apex and mid ventricle with basal hyperkinesias, 3) Absence of obstructive coronary lesion on coronary angiography, 4) Absence of other catecholamine-surge state, including Pheochromocytoma, recent head trauma and intra cranial bleeding. Recovery of

left ventricular function may occur within 2 - 4 wks of presentation.

Treatment

It is mainly supportive with diuretics, beta blockers, ACE inhibitors and if necessary, mechanical ventilation and intra-aortic balloon pump. Prophylactically warfarin may be used to prevent LV apical thrombus, which may be formed due to stasis of blood in akinetic segment. Although most patient of TC recover without any complication, 15-45% may develop life threatening complications like Cardiogenic shock, ventricular fibrillation, cardiac arrest and even death (RARE) .

In the present case anxiety and acute hypertensive crisis might have triggered TCM. We could not rule-out the possibility that CO_2 insufflation (Carbo-peritoneum) might have been the trigger factor of TC. Anderson et al. [10] found that increased catecholamine blood levels five minutes after peritoneal insufflations with CO2 may trigger Takotsubo Cardiomyopathy. This is less likely, considering that our patient's et CO_2 was low (30-31 mmHg) throughout the whole procedure [10]. Although this patient showed mild improvement in ejection fraction within 72 hours but she could not recover completely and succumbed to death due to cardiac arrest, which is a rare complication of reversible TCM.

Conclusion

Takotsubo syndrome (Stress induced Cardiomyopathy) is an adverse event whose relationship with anaesthesia and surgical stress should be studied because of its specific course, which is different from typical myocardial ischemia [11].

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Vigilance and Checking of Anaesthesia Machine is a Must for Patient Safety in Anaesthesia

Sandeep Sahu*, Ganpat Prasad**

Anaesthesia machine or modern anaesthesia workstation is required to deliver O_2, anaesthetic gases and volatile anaesthetic in desired concentrations to patients.The older anaesthesia machines were completely mechanical systems that have a number of limitations and drawbacks.There are multiple exposed connections which are subject to disconnection or misconnection, kinking, or obstruction. So that even a small leaks and its flow meters makes them unfit for low flow anaesthesia. Most old anaesthesia ventilators are 'bag in bottle' double circuit machines that consume oxygen for powering the ventilator with lack of internal positive end-expiratory pressure valve. And also there were no performance feedback mechanisms in old machines [1].

Anaesthesia machines had evolved from simple mechanical pneumatic devices to sophisticated, computer-based, fully integrated anaesthesia systems. Modern anaesthesia workstation had replaced the older anaesthesia machines even in developing countries also. The need of greater patient safety and the technological innovations made the development of these newer advanced anaesthesia gas delivery systems cum patient information systems.It had physiological and other optional monitoring of the patients which provides detailed information on not only the cardiorespiratory status of the patient but also have in built high end ventilators to meet the requirement in operation theatres.

The limitations and hazards of modern workstation are continued movement of a descending bellows despite a leak or disconnection in the machine. In the ascending bellows system a small amount of PEEP transmitted to the patient during ventilation .Augmentation of tidal volume when the oxygen flush is activated in the inspiratory phase of ventilator delivered breath in machines without fresh gas delivery. Although workstation had battery backup butfunctioning depends on the electricity. Inability to detect the carbon monoxideproduction. Besidesall this, human error due to ignorance or lack of understanding or training of newer modern anaesthesia workstation and systems are always challenging [2].

For the patient safety maintenance and checking each component of anaesthesia machine and workstation daily prior to use is a must. A detailedanaesthesia machine/workstation checking involves the proper functioning of the pneumatic, electrical, electronic and other components of the machine in a systematic manner. An approach may involve checking the integrity of the high pressure, intermediate pressure and low pressure system with checking of electrical/electronic components of anaesthesia machine and its breathing circuits system. There are several international guidelines are available for anaesthesia machine check [3-5].

Manual inspection and checking the machine for leaks/malfunction is not done frequently or incompletely done. Leak test was carried out almost perfectly but other tests were not performed routinely by anaesthesiologists. Therefore an idea to putanesthesiologists under an obligation to use the check sheet before anaesthesia and file the sheet in the medical may be useful [5]. Most modern anaesthesia delivery systems perform the self-test or automatic machine check and have ability to detect and report the faults.The modern machines being more sophisticated and increasingly complex, many conventional tests of machine check cannot be applied and it is difficult for anaesthetist to determine a problem.

With the development of new workstation most of the hazards and drawbacks of older anaesthesia machines had been improved but still some are

Author's Affiliation:
*Additional Professor, **Student, Department of Anaesthesiology & Emergency Medicine, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, UP-22604, India.

Corresponding Author:
Sandeep Sahu, Additional Professor, Department of Anaesthesiology & Emergency Medicine, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, UP-22604, India.

remaining as water vapour condensation inside the machine components, bobbins of the flow meters may get stuck to the inner wall of the flow meter (due to dirt and static electricity), possibility of leak from the selectatec system of vaporisers in the event of accidental removal of O-ring during the process of mounting or dismounting of the vaporisers [1,2].

Also new problems are also coming day to day practise such as leak or obstruction attributable to newer mechanical, electronic and electric components and gadgets. Besides human error and other factors a lot of incidents had been reported in literature regarding malfunctioning of workstations in last decades.Leakage from the vaporizer of the anesthetic machine despite the normalities on performing the initial leak test. The vaporizer of the anesthetic machine was found compressed by computer keyboard of Electronic Medical Records which caused a leak from vaporizer [6]. Complete internal fresh gas flow disconnect within a DrägerFabius GS anesthesia machine without any alarms being triggered. Despite the advent of highly automated machines, manual checkout procedures remain crucial to minimizing undiagnosed failures [7]. Broken transverse pin on the back of a Drager D-Vapordesflurane vaporiser caused significant anaesthetic machine (Datex-OhmedaAestiva 15) leak during a routine anaesthetic machine check in the morning before commencement of the day list [8]. Interruptions in the supply of breathing gas during general anesthesia caused by malposition of the DragerVapor 2000® vaporizer, which was accidentally tilted and lifted off the Selectatec manifold of the anesthesia machine. The gas-sampling tubing had become lodged in the gap between the adjustable pressure-limiting valve dial and its housing causing leak into the high end Dragger Primus anaesthetic machine, which took place despite a full machine check as per guidelines. but the leak in the catheter mount was not detected by any of these tests [9]. Adverse events are known to have occurred due to problems with tracheal tube connectors so routine testing for both integrity and leakage of catheter mounts be carried out along.During an anaesthetic machine check, yellow discolouration of liquid desflurane was seen in the D-Vapor (Draeger Medical UK Ltd.) vaporiser window due to contamination [10].

Sophisticated and advance technology demands up gradation not only of anaesthesia machines but also of doctors using it and of those who are caring them. There should be proper training before using new workstation whichstarts from self-routine test before first use. Also emphasis should be onthe manual inspection to rule out any possible malfunction before using on the patients. There should be strict institute protocols for machine check as per any of the existing guidelines and label this in medical records to see proper functioning because safety is always first.

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28	International Physiology	2	7000	6500	700	650
29	Journal of Animal Feed Science and Technology	2	4100	3600	410	360
30	Journal of Cardiovascular Medicine and Surgery	2	10000	8600	910	860
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42	Physiotherapy and Occupational Therapy Journal	4	8500	8000	850	800
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44	Indian Journal of Emergency Medicine	2	12000	11500	1200	1150
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46	Indian Journal of Trauma & Emergency Pediatrics	3	9000	8500	900	850
47	International Journal of Pediatric Nursing	3	5000	4500	500	450
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