Original Article

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Study to Evaluate Usefulness of Magnesium Sulphate and Dexmedetomidine as Adjuvant to Bupivacaine for Lower Limb and Abdominal Surgeries Under Epidural Anaesthesia

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Abstract

Background and Objective: Central neuraxial blockade not only provides good anaesthetic and surgical conditions but it has also advantages over general anaesthesia. To compare time of onset and duration of motor and sensory blockade, duration of analgesia, hemodynamic stability, adverse effects if any and number of rescue analgesia in first 24hours after surgery.

Materials and Methods: After ethical committee permission and patient consent, study was conducted on 90 patients aged 18 to 65 years belonging to ASA- I and II undergoing lower limb and lower abdominal surgeries, were randomly divided into 3 groups. GROUP A received epidural bupivacaine 0.5 % (17 ml) + 1ml 0.9% normal saline. GROUP B received epidural Bupivacaine 0.5 %(17 ml) + 1ml 0.5mcg per kg dexmedetomidine. GROUP C received epidural Bupivacaine 0.5 % (17 ml) + 1ml 50mg magnesium sulphate. Exclusion criteria include patient's with bradyarrythmias, cerebrovascular diseases, neurodegenerative diseases, renal and hepatic diseases, uncontrolled hypertension, bronchial asthma, ischemic heart disease, drug and alcohol abuse and uncontrolled diabetes mellitus.The Statistical software SPSS 22.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc. Test of significance were ANOVA and chi-square test. P value <0.05 statistically significant.

Results: Analgesia in postoperative period and less number of rescue analgesia was better in Group C, Duration of sensory and motor blockade was prolonged and better hemodynamic stability in Group B

Conclusion: Hence addition of magnesium sulphate to epidural bupivacaine provides better post-operative analgesia and dexmedetomidine to epidural bupivacaine increases duration of motor and sensory blockade with better hemodynamic stability.

Keywords: Bupivacaine; Epidural anaesthesia; Dexmedetomidine; Magnesium sulphate.

Key Message: Addition of magnesium sulphate and dexmedetomidine for epidural anesthesia along with bupivacaine has been observed with better hemodynamic stability, increased duration of motor and sensory blockade intraoperatively with good post-operative analgesia.

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Introduction

Many lower limb and lower abdominal surgical procedures are commonly done under neuraxial block, either spinal or epidural anaesthesia. Central neuraxial blockade not only provides us good anaesthetic and surgical conditions but it has also advantages over general anaesthesia. Advantages include less airway related and pulmonary complications that include reduced chances of pulmonary aspiration and decreased stress response.

Epidural anaesthesia is a widely used and a standard technique that is practiced in many surgical procedures. There are various advantages of epidural anaesthesia over spinal anaesthesia that includes slow onset of hypotension, level of blockade and duration of blockade can be extended and the most important is the ability to provide post-operative analgesia through catheter. The most dreaded complication of postdural puncture headache can be avoided in epidural anaesthesia.

Bupivacaine is commonly used drug in epidural anaesthesia. Various drugs have been added as an adjuvant to bupivacaine to prolong duration of anaesthesia and analgesia and also it reduces dose dependent side effects. Dexmedetomidine a well-known alpha 2 agonist, 8 times more potent than clonidine when added as an adjuvant to bupivacaine administered via epidural route produces synergistic anti nociceptive effect and also prolongs the duration of blockade and analgesia.[1]

Magnesium which is a major cation and 4th most abundant mineral in the body produces anti nociceptive effects, due to antagonism of calcium and NMDA receptors. This blocks calcium influx and thus reducing acetylcholine release in neuromuscular junction. NMDA receptors after nociceptive stimuli are involved in pain processing by central sensitization, magnesium prevents this sensitization. Epidural magnesium prolongs duration of analgesia and is a rapid onset of surgical anaesthetic without increasing side effects.[2-4]

Aims and Objectives

To administer epidural bupivacaine with normal saline, epidural bupivacaine with dexmedetomidine, epidural bupivacaine with magnesium sulphate each in 30 patients undergoing lower limb and lower abdominal surgeries and document the time of onset and duration of motor and sensory blockade, duration of analgesia, hemodynamic stability and adverse effects if any.

To compare the time of onset and duration of motor and sensory blockade, duration of analgesia, hemodynamic stability, adverse effects if any and number of rescue analgesia in the first 24hours after surgery.

Methods

After obtaining institutional ethical committee approval, 90 patients belonging to ASA I and II, aged between 18 to 65 of both genders posted for lower limb and lower abdominal surgeries. Patients were segregated into three groups of 30 patients each group based on computer generated randomisation after informed written consent. Exclusion criteria included patients with bradyarrythmias, cerebrovascular diseases, neurodegenerative diseases, renal and hepatic diseases, uncontrolled hypertension, bronchial asthma, ischemic heart disease, drug and alcohol abuse and uncontrolled diabetes mellitus.

Detailed clinical history of the patient was taken. Proper physical examination was done followed by systemic examination and investigations relevant to epidural anaesthesia were checked. Intravenous line was secured and IV fluid was connected.

GROUP A (control group) received epidural bupivacaine 0.5 % (17 ml) + 1ml 0.9% normal saline.

GROUP B received epidural Bupivacaine 0.5% (17 ml) + 1ml 0.5mcg per kg dexmedetomidine.

GROUP C received epidural Bupivacaine 0.5% (17 ml) + 1ml 50mg magnesium sulphate.

As soon as the patient arrived the OT table, baseline vitals like pulse rate, non-invasive blood pressure, ECG and SPO2 were recorded and continuous monitoring was done. Patient group selection was done with computer generated randomised table. Patient was made to sit and under aseptic precautions parts painted and draped. Skin infiltrated with lignocaine 2% at the level of L3-L4. Then epidural performed with 18G tuhoys needle and space identified by loss of resistance technique and epidural catheter was secured and fixed at appropriate level. Test dose of Lignocaine 2% with adrenaline of 3cc was administered after confirming negative aspiration of blood and CSF. Now the patient was made to lie in supine position and the drug injected according to the group selected by computerised table.

The patients were monitored continuously during surgery and the first 24hours post operatively.

Documentation of onset and duration of sensory and motor blockade, duration of analgesia, hemodynamic stability (by monitoring vital parameters), adverse effects if any and requirement of rescue analgesics (number of doses) was done. Rescue analgesics, anti-emetics was administered whenever required.

Comparison was done between the three groups with the above mentioned variables to evaluate the usefulness of adjuvants (magnesium sulphate or dexmedetomidine) to epidural bupivacaine in order to prolong duration of sensory and motor blockade, duration of analgesia and minimize adverse effects in patients undergoing lower limb and lower abdominal surgeries under epidural anaesthesia.

Sample size of present study was based on time to acquire T10 by Vaibhav Shahi et al in a comparative study of magnesium sulfate vs dexmedetomidine as an adjuvant to epidural bupivacaine observed a variance estimate of four with 95% confidence interval with 80% power with equal allocation to detect a difference of 10% time in achieving T10 blockade, the required sample size per group was 30.

The one-way analysis of variance (ANOVA) was employed to determine whether there were any statistically significant differences between the means of three or more independent (unrelated) groups. Chi-square test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis.

Results

Table 1: Comparison of Various Parameters.

Parameters	Group A	Group B	Group C
Number (n)	30	30	30
Age (years)	33.66.± 9.54	36.66 ± 8.54	35± 8.14
Weight (kgs)	62.8±10.21	69.07±9.19	63.17±9.06
Gender (male/female)	20/10	22/8	21/9
ASA status (I/II)	26/4	20/10	25/5
Surgical time (mins)	85.50±21.24	85.43±21.29	74.33±21.51

ASA: American society of Anaesthesiology.

Heart Rate

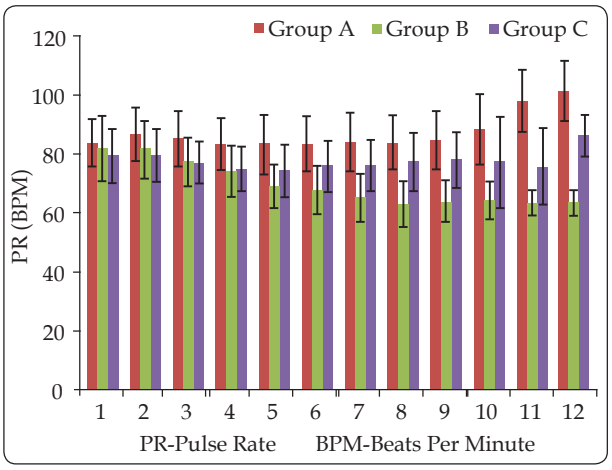

Fig. 1: Showing Comparison of Heart Rate in three Groups.

Baseline HR (bpm) were comparable in three groups, which were 86.43±8.98, 81.57±9.96 and 79.47±8.96 in group A, group B and group C respectively. (fig 1)

In group A there were no significant difference in PR, even after 30 minutes of epidural bupivacaine it remained at 83.97±9.96 and there was increased PR seen after 1hour of epidural bupivacaine with normal saline, it was 101.17±10.3 after 120min of epidural.

In group B after 10minutes of epidural bupivacaine with dexmedetomidine PR dropped to 64.87±8.25 and it remained on the lower side all though the procedure without tremendous increase in PR. It was 63.5±4.32 even after 120minutes of epidural.

In group C, PR remained the same all through the procedure, after 30minutes of epidural bupivacaine with magnesium sulphate it was 75±11.91 and it was 86±7.21 after 120minutes of epidural.

Systolic Blood Pressure

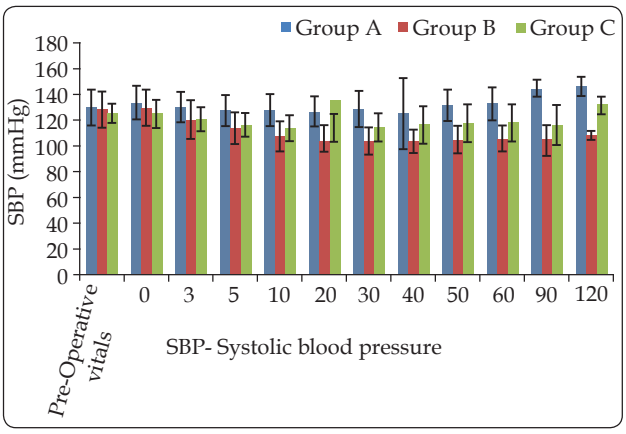

Fig. 2: Showing Comparison of Systolic Blood Pressure in three Groups.

Diastolic Blood Pressure

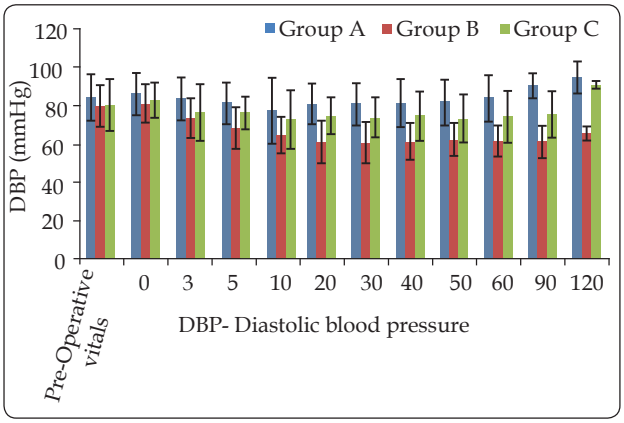

Fig. 3: Showing Comparison of Diastolic Blood Pressure in three Groups.

Mean Arterial Blood Pressure

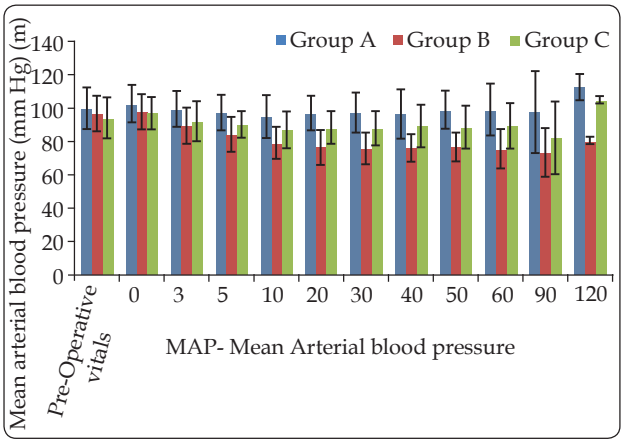

Fig. 4: Showing Comparison of Mean Arterial Blood Pressure in three Groups.

Baseline mean arterial blood pressure in all three groups was 101.90±11.35, 97.17±10.66 and 96.60±9.51 in group A, group B and group C respectively. (fig 4)

In group A MAP remains constant and there is no much fall in MAP, it was 95.70±14.79 after 40minutes of epidural, and it was 111.83±7.65 after 120minutes of epidural.

In group B significant reduction of MAP is seen after 30minutes of epidural and it was 74.93±9.51, it was stable all through the procedure and it was 79.67±2.16 after 120minutes of epidural.

In group C, MAP remains constant without increase or decrease from its basal value, it was 79.67±2.16 after 30minutes of epidural, and it was 104.33±2.08 after 120minutes of epidural.

Time taken for sensory block in group A was 14.12±6.18, in group B it was 4.63±1.22 and in group C it was 5.75±1.71, which signifies that time for onset of sensory block was seen early in group B.

Table 2 shows the time for complete motor blockade in group A was 17.17±2.01, in group B it was 7.02±1.70 and in group C it was 8.10±2.05, which signifies that early onset of motor blockade was seen in group B.

Time taken to achieve T6 level in group A was 13.22±1.43, in group B it was 4.73±1.32 and in group C it was 5.82±1.72, which imparts that time to achieve T6 level was seen early in group B

Time for two segment regression in group A was 86.77±3.60, it was 106.4±8.01 in group B and it was 102.7±8.05 in group C , which signifies that early two segment regression seen in group A, whereas longer time for two segment regression was seen in group B.

Time for recovery from motor blockade in group A was 102.7±8.05, in group B it was 121.6±8.42 and in group C it was 119.87±10.01 which signifies that time for regression of motor blockade in longer in group B when compared to other two groups.

Time taken for first analgesic request in group A was 1.90±0.28 hours, in group B it was 3.18±0.83 hours

Table 2: Comparison of study variables in three groups of patients studied.

Variables	Group A	Group B	Group C	Total	P value
Weight (kg)	62.8±10.21	69.07±9.19	63.17±9.06	65.01±9.83	0.020*
Onset of Sensory Block	14.12±6.18	4.63±1.22	5.75±1.71	8.17±5.65	<0.001**
Onset of Motor Block	17.17±2.01	7.02±1.70	8.10±2.05	10.76±4.96	<0.001**
Time to achieve T6level	13.22±1.43	4.73±1.32	5.82±1.72	7.92±4.07	<0.001**
Duration of Surgery	85.50±21.24	85.43±21.29	74.33±21.51	81.76±21.76	0.071+
Time Two segment regression	86.77±3.60	102.7±8.05	106.4±8.01	98.62±10.94	<0.001**
Recovery from Motor block	97.77±5.03	119.87±10.01	121.6±8.42	113.08±13.53	<0.001**
Time to first Analgesic request	1.90±0.28	3.18±0.83	4.08±0.95	3.06±1.16	<0.001**

+Suggestive significance (P value: 0.05<P<0.10)
*Moderately significant (P value: 0.01<P ≤ 0.05)
**Strongly significant (P value: P≤0.01)

Table 3: Comparative assessment of VAS score in three groups of patients studied.

Variables	Group A	Group B	Group C	Total	P value
VAS First Analgesic	6.47±0.63	4.83±0.75	5.00±0.95	5.43±1.07	<0.001**
VAS 6hrs	6.30±0.65	4.70±1.21	4.47±1.04	5.16±1.28	<0.001**
VAS 12hrs	6.30±0.75	4.77±1.5	4.23±1.19	5.10±1.47	<0.001**
VAS 24hrs	6.13±0.57	4.93±1.31	4.03±1.19	5.03±1.37	<0.001**

+ Suggestive significance (P value: 0.05<P<0.10) * Moderately significant (P value: 0.01<P ≤ 0.05)
** Strongly significant (P value: P≤0.01) VAS: Visual Analogue Scale

and in group C it was 4.08±0.95hours, which signifies that analgesics during post-operative period was better with group C, that is magnesium sulphate.

Average time taken for surgeries in group A was 85.50±21.24, in group B was 85.43±21.29 and in group C it was 74.33±21.51.

Table 3 shows VAS score in all three groups postoperatively in 24hours shown, where it was less in group C after 6hours post operatively, which signifies that post-operative analgesic effect is better with group C.

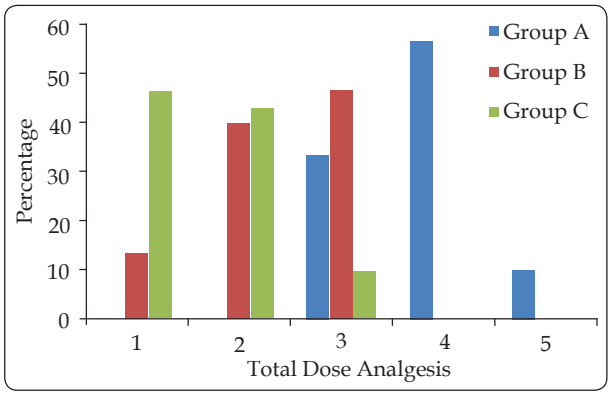

Fig. 5: Showing Total Analgesic Doses Required in 24 Hours in all three Groups.

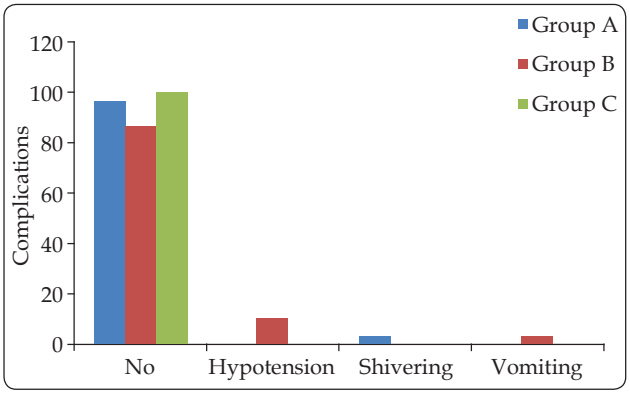

Fig. 6: Complications In Three Groups.

Fig 5 shows the no. of analgesic requests in all three groups which was maximum in group A and minimum in group C, which indicates that group C had better analgesic effect. In group A 10 required 3 doses of top up requirement in 24hours, 17 required 4 doses of top ups. In group C only 3 required 3 doses of top ups, 14 required only one dose and 13 required 2 doses.

Fig 6 shows the complication in three groups intra operatively and post-operative period of first 24hours, where 3 in group B had hypotension and one had vomit. 1 had shivering in group A and no complication was seen in group C.

Discussion

Central neuraxial blockade is most commonly and widely practised anaesthetic technique in many surgical procedures and bupivacaine is the most commonly used local anaesthetic in this technique. Many adjuvants have been added to bupivacaine to enhance the effect and analgesic quality of bupivacaine in neuraxial blockade. Many such adjuvants like midazolam, opioids and ketamine used in epidural. Opioids been associated with undesirable side effects which includes pruritus, nausea, vomiting, urinary retention, respiratory depression and somnolence.[6,7] there was search for an additive with low incidence of these side effects, where effectively it was replaced with alpha 2 agonists like clonidine and dexmedetomidine.[1]

In the last two decades there has been incredible increase in the use of alpha 2 agonist in epidural anaesthesia. When these drugs are administered in epidural it provides sedation, analgesia, anxiolysis and hypnosis.[10]

In 1999 dexmedetomidine came in clinical practice. Dexmedetomidine in regional anaesthesia was used in animals by many researchers, like Sabbe et al in 1994 and Eisench in 2001. Epidural dexmedetomidine prolongs the duration of analgesia, reduces the number of rescue analgesia. It establishes the faster onset of action of both motor and sensory blockade. Because of stable cardiorespiratory parameters it is even more

preferred adjuvant in regional anaesthesia[11]

The pharmacological properties of alpha 2 agonist have been largely studied and been employed clinically to achieve desired effects in regional anaesthesia. Epidural administration of these drugs is associated with sedation, analgesia, anxiolysis, hypnosis and sympatholysis.[8,9] Introduction of dexmedetomidine, a newer prototype of alpha 2 agonist has widened the scope in regional anaesthesia. It was introduced in clinical practice in 1999. Epidural bupivacaine in a dose of 2mcg/kg given along with intrathecal bupivacaine causes significant prolongation in the duration of analgesia. The number of administered rescue analgesic doses is significantly less in patients receiving epidural dexmedetomidine. The faster onset of action of local anaesthetics, rapid establishment of both sensory and motor blockade, prolonged duration of analgesia in the postoperative period, dose sparing action of local anaesthetics and stable cardiorespiratory parameters make alpha 2 agonist an effective adjuvant in regional anaesthesia.[14]

Parenteral magnesium, used for many years as an antiarrhythmic agent and for prophylaxis in seizures in pre-eclampsia. Noxious stimulation leads to release of neurotransmitters, which bind to various subclasses of excitatory amino acid receptors, including NMDA receptors. NMDA receptor signalling may be important in determining the duration of acute pain. Magnesium blocks calcium influx and non-competitively antagonizes NMDA receptor channels. Magnesium can prevent the induction of central sensitization at the spinal action by blocking NMDA receptors in a voltage dependent manner. With same mechanism of action when small doses of magnesium was added to local anaesthetics for spinal anaesthesia the duration of action of spinal anaesthesia was prolonged and analgesic requirement postoperatively was reduced and side effects of high doses of local anaesthetics and opioids were reduced.[5]

Shahi V, Verma AK, Agarwal A, Singh CS in 2014 conducted a prospective randomized study of comparing dexmedetomidine and magnesium sulphate along with epidural bupivacaine in 120 patients to determine the motor and sensory onset of action and duration of analgesia post operatively, they have concluded that dexmedetomidine group showed rapid onset of action and prolonged duration of action with better post-operative analgesia when compared to magnesium sulphate group.[13]

Sonali Banwait, Sujata Sharma and Rajesh Sood in 2012 evaluated the efficacy of single bolus administration of magnesium epidurally as an adjuvant to epidural fentanyl for postoperative analgesia in 60 patients posted for total hip replacement under combined spinal epidural anaesthesia. The results of the investigations showed that a single bolus of epidural magnesium as an adjuvant to fentanyl for post-operative analgesic requirement results in prolonged duration of analgesia as compared to epidural fentanyl alone. Concomitant administration of magnesium reduces the requirement for breakthrough analgesics with no increased incidence of side effects.[12]

Conclusion:

From our study we conclude that when dexmedetomidine added as an adjuvant to epidural bupivacaine it provides fast onset of motor and sensory blockade with better hemodynamic stability. And magnesium when added as adjuvant to epidural bupivacaine it provides better post-operative analgesics not associated with any complications.

Conflict of Interest: Nil

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