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Comparative Study Of Clonidine And Magnesium Sulfate Used As Adjuvant To Epidural Bupivacaine In Lower Abdominal Surgery.

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ABSTRACT

Background: A lot of researches have been going on to find out ideal adjuvant to bupivacaine in epidural anaesthesia for post-operative pain management without any side effects. Antinociceptive effect of magnesium in epidural route has been recently studied. **Aim:** This study was conducted to evaluate the onset, duration of sensory and motor block and side effects of clonidine and magnesium sulfate when used as an adjuvant to bupivacaine in epidural anaesthesia in lower abdominal surgery. **Methods:** A prospective randomized double blind study was conducted on 60 patients of ASA status I and II, posted for lower abdominal surgery. All patients were randomly allocated into two groups of 30 each; group BC was bupivacaine - clonidine group and group BM was bupivacaine – magnesium sulfate group. Group BC patients received epidural 18 ml of 0.5% bupivacaine and clonidine 2mcg/kg. Group BM patients received epidural 18 ml of 0.5% bupivacaine and magnesium sulfate (50 mg). The onset, extent, duration of sensory and motor block, and side effects were observed. **Results:** Magnesium sulfate with bupivacaine had an earlier onset of sensory and motor block but duration of postoperative analgesia was more in clonidine group which was statistically significant. Sedation scores were statistically significant with BC group in comparison to BM group. Both groups were haemodynamically stable in perioperative period. **Conclusion:** Magnesium sulfate is a better alternative to clonidine as an adjuvant to bupivacaine in epidural anaesthesia in lower abdominal surgeries for rapid onset of action but clonidine provides prolonged duration of action and delays requirement of rescue analgesia.

Keywords: Clonidine, magnesium sulfate, bupivacaine.

INTRODUCTION

Pain is defined by the International Association for Study of Pain (IASP) as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.[1] Epidural anaesthesia is a safe and popular technique not only for surgical anaesthesia but also for post-operative analgesia. It has been shown to blunt the stress response to surgery, decrease intraoperative blood loss, reduce the incidence of postoperative thromboembolic events and decrease morbidity and mortality in high risk surgical patients. It can be used to provide prolonged analgesia in postoperative period which can be achieved with various adjuvants like opioids and other drugs. Clonidine has been used as an adjuvant to local anaesthetics in regional anaesthesia. It is an alpha-2 adrenergic agonist that produces analgesia via a non-opioid mechanism. It is also helpful in sparing local anaesthetic doses, which consequently reduces the incidence of side effects associated with larger doses of local anaesthetics. The combination of epidural clonidine with bupivacaine for analgesia has been extensively studied and it has been shown to improve analgesia.[2] After sodium, potassium and calcium, magnesium is the most abundant cation in our body. It has antinociceptive effects in animal and human models of pain.[3] Noxious stimulus produces an influx of calcium ion through both voltage sensitive calcium channels that facilitates presynaptic release of neurotransmitters and post synaptic N-methyl D-aspartate calcium channels which triggers the sequence of events leading to cellular hyper excitability.[4] Studies in animal models of persistent pain in which central sensitization is present support this theory. Magnesium is a relatively harmless molecule, non-expensive and may provide postoperative analgesia for its antinociceptive effect.[5] These effects are primarily based on physiological calcium antagonism, that is voltage-dependent regulation of calcium influx into the cell, and noncompetitive antagonism of N-methylD-

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aspartate(NMDA)receptors.[6] As, there is no ideal adjuvant drug available for postoperative epidural analgesia, the present study was conducted to compare epidural plain bupivacaine with clonidine and bupivacaine with magnesium sulphate in patients undergoing lower abdominal surgery in respect of onset and duration of sensory block ,onset and duration of motor block, hemodynamic parameters and incidence of side effects.

MATERIALS AND METHODS

After the approval of the Institutional Ethical Committee randomized double blind prospective study was done in 60 patients posted for elective lower abdominal surgery. Patients included in the study were of ASA grade I and II,of age from 20 to 60 years, of either sex and of weight 40-70kg. Patients having local infection in the lumbar region, known hypersensitivity to amide local anaesthetic,bleeding diathesis,spinal deformity and chronic pain syndromes, known neurological, cardiac, renal, metabolic and psychological disorder were excluded from this study.

During pre-anaesthetic checkup detailed history of present illness, and any relevant past history of disease was recorded. Laboratory investigations were noted. The patients were explained in detail about the procedure of lumbar epidural block. All their queries and doubts were answered to get their confidence. Patients were kept fasting overnight.All patients received Tab Alprazolam 0.25 mg orally night before surgery. All patients had an intravenous line with 18G cannula after arriving in the operation theater. Base line pulse rate, blood pressure, ECG, respiratory rate, SpO2 were noted. All patients were preloaded with 15ml-20ml/kg of Ringer's Lactate solution over 15-20 minutes before administering epidural block. The drugs were prepared by an anaesthesiologist who was not involved in the study. Epidural anaesthesia was administered with 18G Tuohy needle in sitting position. Epidural space(L2-3) was identified by loss of resistance to air technique. After negative aspiration test for blood and CSF, a test dose was administered with 3 ml of inj. Lignocaine hydrochloride 2% with adrenaline (1:200000). After ensuring proper epidural placement of the needle tip, the study drug was slowly injected with repeated aspiration test. After placement of study drug, epidural catheter was introduced. Monitoring of vital signs was continued throughout the procedure. The patients were made supine. No other analgesic was given to the patients intraoperatively. Group BC (n=30) patients received total volume of 18ml of study drug (17ml of plain 0.5% bupivacaine + clonidine 2mcg/kg made up to 1ml by adding normal saline. Group BM (n=30) received a total volume of 18 ml of study drug (17 ml of 0.5% bupivacaine + 50 mg magnesium sulphate, 1ml). The patients were administered O2, 3 L/min through face mask. Onset of sensory block was assessed by pin prick method at every minute interval. Time duration was assessed from local anaesthetic solution injection to epidural space to start of loss of pain sensation to pin prick. Duration of sensory block was assessed every 15 minutes postoperatively by pin prick method. Duration was assessed from onset of sensory block to regression of dermatome of two segments. Motor block was assessed by modified Bromage scale as follows:[7] 0 - no paralysis,1-inability to raise extended leg.2-inability to flex knee,3-Inability to flex ankle joint. Analgesia was assessed every 15 minutes postoperatively by 10 cm Visual Analogue Scale (VAS) 0 - no pain,10 - worst possible pain. Time to rescue analgesia was assessed from onset of sensory block to first request for rescue analgesic or VAS score 5 or more.[8]

Inj Tramadol 2mg/kg was given intravenously as rescue analgesic. Haemodynamic parameters like heart rate, systolic BP, diastolic BP, respiratory rate were noted at 0, 15, 30, 60, 75, 90, 120, and at 240 mins from administration of epidural anaesthesia. Side effects like nausea, vomiting, hypotension,sedation, shivering, headache, etc were noted.Sedation was assessed on 4 point sedation scale.0-awake and alert,1-mildly sedated,2-moderately sedated,3-deeply sedated.[9]

Statistical evaluation

Sample size calculation was done by taking duration of analgesia as primary outcome. It was estimated that minimum 26 patients will be required per group to detect 60 minutes difference in this parameter with 80% power and 5% probability of type I error. This calculation assumed a standard deviation of 75 minutes in duration of analgesia. For statistical analysis, raw data entered into a MS Excel spread sheet and analyzed by SPSS 21 (statistical software version 21). Unpaired student's t– test was used to compare normally distributed numerical variables. All analysis were two-tailed and p value <0.05 was taken to be statistically significant.

RESULTS

There was no statistical difference regarding age, sex, weight, height and duration of surgery. [Table 1].

Table 1: Demographic characteristics.

Parameters	GROUP BC (mean±SD)	GROUP BM (mean±SD)	P value
Mean Age (years)	37.70±9.87	38.33±9.88	0.69
Sex distribution (m/f)	16/14	15/15	0.96
Weight (kg)	58.66±6.91	57.33±7.93	0.55
Height (cm)	165.33±8.25	163.4±9.44	0.91
Duration of surgery (min)	120.66±35.52	125.90±33.15	0.94

Time to achieve both sensory and motor block was less in BM group than BC group which was statistically significant.[Table-2]

Table 2: Epidural block characteristics

Block characteristics	GROUP BC (mean± SD)	GROUP BM (mean± SD)	P Value
Onset time of sensory block at T 10 (mins)	8.75±4.84	6.14±2.51	0.013
Time to max sensory block (mins)	14.54±3.36	11.94±3.25	0.001
Time for complete motor block (onset in mins)	17.4±4.24	14.86±6.45	0.04
Total ephedrine requirement (mg)	8.35±3.8	7.95±6.5	0.21

Mean time to two segment regression, mean time to sensory regression at S 1, mean time to regression to bromage 1 and time to first rescue top up was delayed in BC group compared to BM group which was statistically significant. [Table 3].

Table 3: Epidural block characteristics

Parameters	GROUP BC (mean±SD)	GROUP BM (mean±SD)	P Value
Mean time to two segment regression (mins)	155.6±10.45	138.95±10.26	0.0004
Mean time to sensory regression at S 1(mins)	345.84±35.24	298.5±35.60	0.0001
Mean time to regression to bromage 1(mins)	285.92±28.64	245.12±31.26	0.0001
Time to first rescue top up (mins)	350.95±25.5	300.10±24.85	0.0001

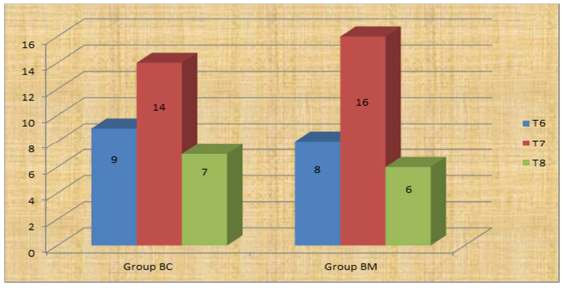

Figure 1: Distribution of block height between study groups

The bar diagram [Figure 1] showing distribution of block height between the groups and it showed no significant differences between the groups.

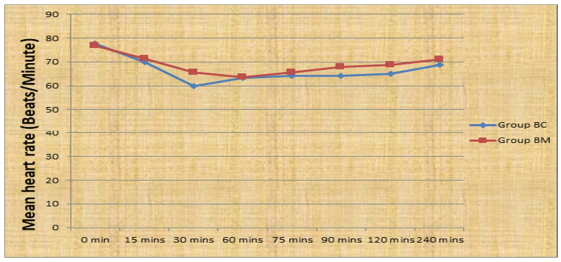

Figure 2: Comparison of mean heart rate variability between study groups

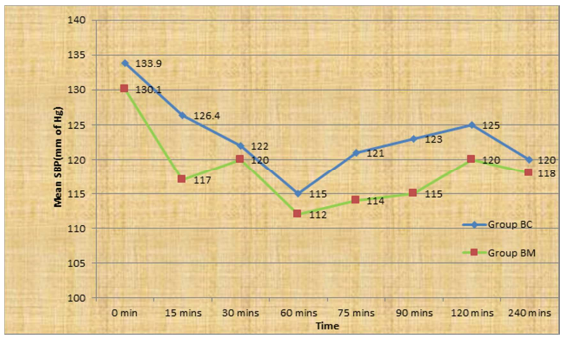

Figure 3: Comparison of mean systolic blood pressure (SBP) variability between study groups.

There was no significant deference in hemodynamic parameters between the two groups [Figure 2 & 3]

Table 4: Incidence of side effect between two groups

Side Effects	Group Bc	Group Bm	Significance (P Value)
Nausea and vomiting	4 (13.33%)	7(23.33%)	0.317
Shivering	2(6.67%)	4(13.33%)	0.389
Sedation	8(26.66%)	1(3.33%)	0.03
Headache	3(9.99%)	1(3.33%)	0.605

Sedation was significantly high in BC group compared to BM group. There was no significant difference in incidence of other side effects between study groups [Table 4].

DISCUSSION

Many drugs has been used as an adjuvant with local anaesthetics in regional anaesthesia. Epidural clonidine appears to offer unique advantage over other agents. Clonidine can produce side effects like hypotension, bradycardia, and sedation.[10] Till now very few studied magnesium as an adjuvant in epidural anesthesia. Mechanism of intrathecal MgSO4 is postulated to be supraspinal. However Ko et al, with 50mg/kg IV failed to demonstrate an increase in the CSF MgSO4 level. Also they did notfound any significant increase in the post-operative analgesia.[11] Bilir A et al showed that epidural magnesium reduces postoperative analgesic requirement. The primary mechanism of action of MgSO4 is antagonism of NMDA receptors. Quicker onset and relatively prolonged analgesia of MgSO4 with bupivacaine may be due to their direct effects on the nerve roots in the epidural space.[12] Ghatak et al showed that addition of magnesium sulphate, as adjuvant to epidural bupivacaine reduces the time of onset of anaesthesia in comparison to clonidine. Both clonidine and magnesium groups were similar in respect to haemodynamic parameters.[13] Their findings were similar to ours. Eisenach et al showed in their study that clonidine prolongs aepidural anesthesia without increasing hypotension. In his study clonidine has produced haemodynamic stability which was similar to ours.[14] Riham et al

showed that epidural single dose magnesium sulphate when added to bupivacaine and fentanyl in labor analgesia resulted in significantly faster onset and longer duration of action of epidural analgesia compared to bupivacaine and fentanyl only.[15] It was observed in the present study that addition of 50mg of MgSO4 to 0.5% bupivacaine administered epidurally reduces the onset of sensory and motor block compared to epidural 0.5% bupivacaine with clonidine which was statistically significant. There were no significant change in blood pressure, pulse rate and respiratory rate in both groups. There was no significant increase in side effects except sedation. Duration of analgesia is significantly high in BC group compared to BM group. Vital parameters were well maintained during intraoperative and postoperative period. Sedation was found more in BC group in comparison to BM group which was statistically significant. Few other side effects like nausea, vomiting, and shivering were found in both study groups but they were statistically not significant.

CONCLUSION

Epidural magnesium sulfate with bupivacaine produces rapid onset of sensory and motor block without any side-effects but addition of clonidine to epidural bupivacaine produces prolonged duration of analgesia.The results of the present study conclude that magnesium may be a useful alternative to clonidine as an adjuvant to epidural bupivacaine.

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