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Original Research

Evaluation of intrathecal clonidine and magnesium sulphate used as an adjuvant with bupivacaine in lower abdominal surgery

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***ABSTRACT*:**

Background: Various drugs used as adjuvants to spinal anaesthesia are known to provide intra- and post-operative analgesia. The present study was designed to evaluate and compare the analgesic efficancy of clonidine and magnesium sulphate when used as an adjuvant to intrathecal bupivacaine. **Material and methods:** The present prospective, placebo-controlled study was done in 40 patients of age 20-50 years with the American Society of Anesthesiologists' (ASA) physical status grade I or II, height between 140 to185cm, weight between 40 to 80 kg, posted for elective lower abdominal surgery under spinal anaesthesia over the period of 6 months was done. Patients in Group A received 3 mL of 0.5% hyperbaric bupivacaine with 1 mL of normal saline, those in Group B received 3 mL of 0.5% hyperbaric bupivacaine with 1 mL (30µg) of clonidine (1:5 dilution) and patients in Group C received 3 mL of 0.5% hyperbaric bupivacaine with 1 mL (50mg) magnesium sulphate (1:10 dilution).Statistical analysis was done with Statistical Package for the Social Science version 21.0.0 (SPSS Inc., Chicago, Illinois, USA) and p value <0.05 was taken to be statistically significant. **Results:** Results of the study shows that mean age of Group C was more than Group A and Group B. Duration of surgery for Group C was more than group A and Group B. Onset of motor block for Group C (8.14±4.6) was more than Group A and Group B. Duration of motor block for Group C (136.88±39.5) was more than Group A and Group B. **Conclusion:** Intrathecal clonidine long-lasting post-operative analgesia along with earlier onset and prolonged duration of sensory and motor blockade compared to both magnesium and control. Intrathecal magnesium also increased the analgesic duration compared to control but it was associated with delayed onset of both sensory and motor blockade compared to both clonidine and control.

Key words: Bupivacaine, magnesium sulphate, clonidine.

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INTRODUCTION:

Intrathecal adjuvants are increasingly used for better post-operative pain management. Intrathecal opioids are used to potentiate post-operative analgesia but they have adverse effects which raises the necessity to look for better alternatives.[1] Intrathecal clonidine potentiates post-operative analgesia by hyperpolarising Aδ and C fibre in the substantia gelatinosa of the spinal cord.[2] The combination of epidural clonidine with bupivacaine for analgesia has been extensively studied and it has been shown to improve analgesia. 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.[3,4] Magnesium prevents the development of central sensitisation of pain by antagonistic action on N-methyl-D-aspartate receptors in the spinal cord. The calcium channel blocking property of magnesium also contributes to its antinociceptive effect.[5]Antinociceptive of Mg effects appear to be relevant not only to chronic pain[6] but it also determines, in part, the duration and intensity of postoperative pain.[7] These effects are primarily based on the regulation of calcium influx into the cell, i.e. natural physiological calcium antagonism. Mg is a noncompetitive antagonist to NMDA receptors and has the potential to prevent central sensitization from peripheral nociceptive stimulation. Intravenous (i.v.) administration of Mg, even at high doses, is associated with limited passage across the blood-brain barrier.[8] The present study was designed to evaluate and compare the analgesic efficacy of clonidine and magnesium sulphate when used as an adjuvant to intrathecal bupivacaine.

MATERIAL AND METHODS:

The present prospective, placebo-controlled study was done in 40 patients of age 20-50 years with the American Society of Anesthesiologists' (ASA) physical status grade I or II, height between 140 to185cm, weight between 40 to 80 kg, posted for elective lower abdominal surgery under spinal anaesthesia over the period of 6 months was done. Before the commencement of study approval of the Institutional Ethical Committee and written informed consent from all patients was obtained. All the patients underwent a thorough pre-operative examination, including history, general physical examination and necessary blood investigations.

EXCLUSION CRITERIA

Patients with any contraindication to spinal anaesthesia or major neurological, cardiovascular, metabolic, respiratory, renal disease or coagulation abnormalities were excluded from this study.

METHOD

After taking written informed consent, on the day of surgery, 30 patients were randomised into three groups of 10 patients using computerised randomisation method. All the patients were fasted for at least 6 h before the procedure. After arrival of patients in the operation theater a base line pulse rate, blood pressure, ECG, respiratory rate, SpO_2 were noted. The drugs were prepared by an anaesthesiologist who was not involved in the study. Intravenous (IV) line was secured with 18-gauge cannula and ranitidine 50 mg IV and metoclopramide10 mg IV were administered. All the patients were pre-loaded with Ringer's lactate 15 mL/kg over 10 min. Under all aseptic precautions, spinal anaesthesia was performed at the L_3–L_4 interspace, with the patient in sitting position. A total of 4 ml study drug was injected over 30 seconds through a 25-gauge spinal needle. The intrathecal drug compositions depended on the group to which patients were randomised. Patients in Group A received 3 mL of 0.5% hyperbaric bupivacaine with 1 mL of normal saline, those in Group B received 3 mL of 0.5% hyperbaric bupivacaine with 1 mL (30µg) of clonidine (1:5 dilution) and patients in Group C received 3 mL of 0.5% hyperbaric bupivacaine with 1 mL (50mg) magnesium sulphate (1:10 dilution). All the study drugs were prepared in identical volume (4 mL) and in an identical syringe by an anaesthesiologist who was not involved in the anaesthetic management of the patients. The patients were placed in supine position with head down tilt immediately after spinal injection to achieve the satisfactory level of the block (up to T_6 spinal level). Then, the patients were kept in horizontal position.Sensory block was assessed by the pinprick method bilaterally along the mid-clavicular line with a 25-gauge hypodermic needle at 2 min interval till the highest level of block was achieved and the required time was noted. Motor block was assessed according to the modified Bromage scale.[9] Duration of motor block was the time elapsed from the maximum to the lowest Bromage score I–IVas follows: 0-no paralysis, 1-inability to raise extended leg. 2- inability to flex knee, 3-Inability to flex ankle joint.Intraoperatively, monitoring of blood pressure, pulse rate, saturation and respiratory rate were done at 5 min interval. The time from intrathecal injection to first rescue analgesia (total duration of analgesia) was recorded and this was the end point of our study.

STATISTICAL ANALYSIS

Statistical analysis was done with Statistical Package for the Social Science version 21.0.0 (SPSS Inc., Chicago, Illinois, USA) and p value <0.05 was taken to be statistically significant.

RESULTS:

In our study total participants were 30 and the study groups were divided into 3 groups each group contain 10 participants each. Mean age of Group C was more than Group A and Group B. Duration of surgery for Group C was more than group A and Group B. Onset of motor block for Group C (8.14±4.6) was more than Group A and Group B. Duration of motor block for Group C (136.88±39.5) was more than Group A and Group B.

Table 1: Demographic detail

Parameters	Group A	Group B	Group C	P-value
Mean age	40.90±6.44	39.45±7.87	41.54±8.58	0.188
Sex(m/f)	3/7	4/6	4/6	0.798
Weight(kg)	57.88±8.13	58.45±9.34	58.14±7.67	0.896
Height (cm)	156.23±8.00	157.46±11.76	156.88±9.57	0.504
Duration of surgery(min)	70.86±4.78	69.78±7.89	72.54±8.78	0.894

Table 2: Spinal block characteristics

Parameters	Group A	Group B	Group C	P-value
Onset of sensory block (mins)	**5±1.4**	**3±1.8**	**8±1.5**	**<0.01**
Duration of sensory block(mins)	**96±23.5**	**169±24.8**	**132±18.9**	**<0.01**
Onset of motor block(mins)	**6±1.1**	**5.±1.8**	**8.14±4.6**	**<0.01**
Duration of motor block(mins)	**115.23±8.60**	**217.46±45.76**	**136.88±39.5**	**<0.01**

Onset of sensory block for Group C (8±1.5) was more than Group A and Group B. Duration of sensory block for Group B (169±24.8) was more than Group A and Group C.

DISCUSSION:

Previously many drugs have been used as an adjuvant with local anesthetics. The reasonably extensive clinical experience with clonidine reflects the broader experience with alpha2 -adrenergic agonists in regional anaesthesia. Epidural clonidine appears to offer unique advantages over existing adjuvants. Clonidine also produces side effects like hypotension, bradycardia, and sedation.[10]

In our study total participants were 30 and the study groups were divided into 3 groups each group contain 10 participants each. Mean age of Group C was more than Group A and Group B. Duration of surgery for Group C was more than group A and Group B. Onset of motor block for Group C (8.14±4.6) was more than Group A and Group B. Duration of motor block for Group C (136.88±39.5) was more than Group A and Group B.

Ko et al concluded that MgSO4 50mg/kg IV failed to demonstrate an increase in the CSF MgSO4 level. Also they did not found any significant increase in the post-operative analgesia.[11]

Intrathecal clonidine in diferrent doses such as 50 mcg and 75 mcg showed enhanced post-operative analgesia with clonidine compared to intrathecal bupivacaine in lower abdominal surgery.[12,13]

Intrathecal Mg was used in order to increase the analgesic duration of opioids in humans, and they demonstrated that addition of 50 mg intrathecal Mg to intrathecal fentanyl led to better analgesia during painless delivery. These results were comparable with those of animal studies, where intrathecal Mg increased the analgesic time of opioids.[14]

Mg blocks N-Methyl-D-aspartate (NMDA) channels in a voltage-dependent way and produces a dramatic reduction of NMDA-induced currents.[15] Noxious stimulation leads to the release of glutamate and aspartate neurotransmitters, which bind to the NMDA receptor. Activation of these receptors leads to calcium entry into the cell and initiates a series of central sensitization such as wind-up and long-term potentiation in the spinal cord in the response of cells to prolonged stimuli.[16]NMDA receptor signalling may be important in determining the duration of acute pain. [17] Mg blocks calcium influx and noncompetitively antagonizes NMDA receptor channels. [18]

Eisenach et al showed in their study that Clonidine prolongs and intensifies epidural anaesthetics without increasing hypotension during epidural anaesthesia. In his study clonidine has produced hemodynamic stability which was similar to our study.[19]

CONCLUSION:

Intrathecal clonidine long-lasting post-operative analgesia along with earlier onset and prolonged duration of sensory and motor blockade compared to both magnesium and control. Intrathecal magnesium also increased the analgesic duration compared to control but it was associated with delayed onset of both sensory and motor blockade compared to both clonidine and control.

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