ORIGINAL RESEARCH PAPER
VOLUME-6 | ISSUE-5 | MAY - 2017 | ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 78.46
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

# Randomized, double blinded comparison of magnesium sulphate and clonidine as an adjunct to epidural bupivacaine for lower abdominal surgery.

Anaesthesiology

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## ABSTRACT

**OBJECTIVE:** The objective of this study was to compare the effect of magnesium sulphate and clonidine as an adjunct to epidural bupivacaine for lower abdominal surgery in a randomized, double blinded trial.

**MATERIAL AND METHODS:** This is an institution based randomized double blind study. Sixty patients undergoing elective lower abdominal surgery belonging to American society of anesthesiologists (ASA) class I and II were enrolled to receive either magnesium sulphate (group A) or clonidine (group B) along with epidural bupivacaine for surgical anesthesia. All the patients received epidural anesthesia with 19 ml of 0.5% bupivacaine along with either Magnesium sulphate 50 mg (group A) or clonidine 150 mg (group B). The onset of sensory and motor block, duration of block and analgesia; hemodynamic parameters and any adverse events were monitored.

**RESULTS:** Early onset of anesthesia, longer duration of analgesia and sensory, motor blockage were noted in the Clonidine group (Group B). These were stastically significant. There was no significant difference in hemodynamic parameters and side effects among the two groups but incidence of sedation was more in group B.

**CONCLUSION:** Clonidine is a better adjuvant compared to magnesium sulfate in epidural bupivacaine with respect to earlier onset of action and increased duration of sensory motor blockage and arousable sedation.

## KEYWORDS:

Magnesium sulfate, clonidine, epidural bupivacaine.

**Introduction:**

Any unpleasant feeling or experience that originate by intense or damaging stimuli could be termed as pain[1]. Epidural anesthesia is effective in providing surgical anesthesia and prolonged duration of post-operative pain relief with minimum central nervous and cardiovascular toxicities.

In recent years use of adjuvants such as clonidine[2,3], dex medetom i dine[4], ketamine[5], opoid[6], magnesium sulpha te[3,4] gained pop ularity. Neuraxial adjuvants improve and prolong analgesia and also decrease adverse effects associated with high dose of local anesthetic agent. Thus neuraxial adjuvants increase speed of onset, improve the quality and prolong the neural blockage.

Clonidine is centrally acting partial α2adrenergic agonist with selectivity ratio 200:1[7]. Clonidine when used as adjunct, prolongs duration of sensory motor blockage and post-operative analgesia by stimulating the activation of post synaptic α 2 receptor indorsal horn of spinal cord.[8]

Magnesium inhibits calcium influx into cell and non-competively anatagonise NMDA receptors (N methyl – D- asparate), thus preventing development of central sensitization.[9]

This study is designed to evaluate and compare the analgesic efficiency of clonidine and magnesium sulphate as an adjuvant to hyperbaric bupivicane in epidural anesthesia in lower abdomen surgeries.

**Methods:**

After approval from the institutional ethical committee, a hospital based randomized ,double blind , comparative observational study was conducted. Sixty patients undergoing elective lower abdominal surgeries were selected. The age ranged from twenty to sixty years. All were in ASA physical status I and II . The criteria for selection included weight between forty and eighty kilograms and height greater than or equal to 145 centimeters. Patients who had any contraindication for epidural block, those with any adverse reaction to study medication, known hepatic, renal, cardiac, neurological, psychiatric, metabolic or respiratory disease, peripheral neuropathy were excluded from study.

Randomisation was done by using chit in box method,and patients were divided into two groups.

1. Group A(n=30) received epidural bupivacaine0.5%(19ml)+ magnesium sulphate 50 mg (1ml)
2. Group B (n=30) received Epidural bupivacaine0.5%(19 ml)+clonidine 150 mcg(1ml)

Intra-operatively, baseline vitals like heart rate, blood pressure, respiratory rate and oxygen saturation were reorded. Intravenous access was secured and preloading was done with 15ml/kg Lactated Ringer solution.

These patients were given epidural block at L2-L3or L3-4 space with 18 G Touhy neddle and epidural space was identified and confirmed by loss of resistance technique. A test dose of 3 ml of 2% lignocaine and adrenaline (1: 200,000) was given and observed for ten minutes for any adverse events and then followed by total dose of the desired solution slowly (19ml bupivacaineand clonidine or magnesium sulphate).

The time of injection, onset of sensory block and intensity of sensory block, motor block and total duration of analgesia was noted.

Sensory block was assessed by using pin prick method while motor blockade was assessed by modified Bromage score. Grading of motor block was done by modified bromage score (0=no motor block; 1=inability to raise extended leg; 2=inability to flex knee; 3=inability to flex ankle and foot).

Standard monitorning consisted of pulse oximetery, ECG and noninvasive blood pressure in the two groups. Time for two segment regression was also noted between the two groups.

Sedation was graded by five point scale (1-alert and wide awake; 2-arousable to verbal command; 3-arousable with gentle tactile stimulation; 4-arousable with vigorous shaking; 5-unarousable)

Duration of motor block was assessed by recording the time elapsed from the maximum to the lowest modified Bromage score.

Pain was assessed by visual analogue scale(VAS).The patients were asked to evaluate their pain on standard 100 point visual analogue pain scale(VAS 0 = no pain,VAS 100 = worst possible pain). In event of pain, (VAS≥40) rescue analgesia was given.Duration of analgesia was defined as time from epidural injection to the first dose of rescue analgesia which was given when VAS was 40.

Statistical analysis was performed with the SPSS, version 21 for Windows statistical software package (SPSS inc., Chicago, IL, USA). The Categorical data was presented as numbers (percent) and were compared among groups using Chi square test. The quantitative data was presented as mean and standard deviation and were compared by students t-test. Probability was considered to be significant if less than 0.05.

**Results:**

**Table1:** The demographic profile of patients in 2 groups.

| Parameters | Group A | Group B | P- value |
|---|---|---|---|
| Number of patients | 30 | 30 | |
| Age(in years) | 42.9 ± 8.6 | 39.9 ± 8.8 | 0.1922 |
| Weight(in kg) | 58.5 ± 12.4 | 59.3 ± 10.9 | 0.7994 |
| Height(in cm) | 165.2 ± 8.7 | 164.3 ± 8.4 | 0.6959 |
| BMI(kg/sqmtr) | 21.6 ± 5.3 | 22.1 ± 4.4 | 0.7265 |
| ASA | 1.3 ± 0.4 | 1.1 ± 0.3 | 0.2031 |

The two groups were comparable with regard to demographic data as shown between the groups.

**Table 2: Comparison of block characteristics.**

| Variables | Group A | Group B | P- Value |
|---|---|---|---|
| Onset of sensory block (in minutes) | 16 ± 1.66 | 14.33± 1.58 | <0.01 |
| Onsetof motor block (in minutes) | 19.67 ± 2.92 | 17.13 ± 2.05 | <0.01 |

The time taken to achieve sensory block in Group B was14.33±1.58 and in Group A was 16±1.66,the time taken to achieve motor block in Group B was 17.13± 2.05 and in Group A was 19.67±2.92.The difference between the groups was statistically significant.(p<0.01)

**Table 3: Comparison of study variables of two groups**

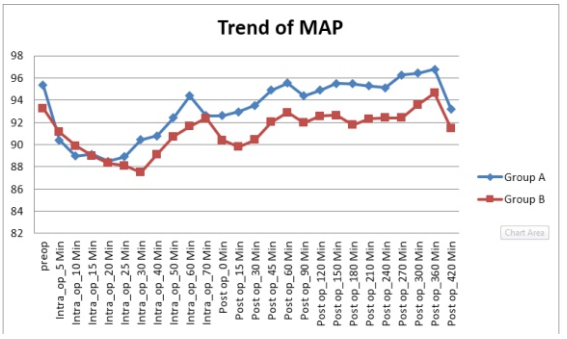
| Variables | Group –A | Group - B | P value |
|---|---|---|---|
| Time taken for 2 segment regression (in min) | 144.5 ± 9.8 | 167.8 ± 10.5 | <0.01 |
| Duration of Motor Block (in min) | 278.8 ± 24.0 | 325.6 ± 34.5 | <0.01 |
| Duration of Analgesia (in min) | 336.87 ± 16.96 | 408.4 ± 17.34 | <0.01 |

The time for two segment regression in GroupB (167.8 ± 10.5) is more than Group A (144.5 ± 9.8). The duration for motor block in GroupB (325.6 ± 34.5) is again more than Group A (278.8 ± 24.0).The duration for analgesia in GroupB (408.4 ± 17.34) is also more than Group A (336.87 ± 16.96).All these values are significant with p value less than 0.01.

**Table 4: Side Effects**

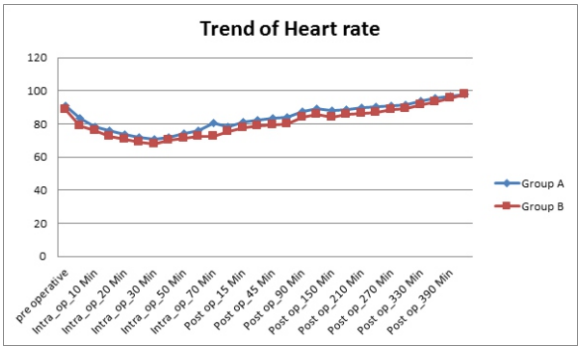
| Characteristics | Group A | | Group B | |
|---|---|---|---|---|
| | No. | % | No. | % |
| Hypotension | 3 | 10 | 1 | 3.3 |
| Bradycardia | 2 | 6.7 | 1 | 3.3 |
| Nausea and vomiting | 3 | 10 | 4 | 13.3 |
| Sedation scores 1 | 30 | 100 | 10 | 33.3 |
| Sedation scores 2 | 0 | 0 | 8 | 26.7 |
| Sedation scores 3 | 0 | 0 | 12 | 40 |
| Sedation scores 4 | 0 | 0 | 0 | 0 |
| Sedation scores 5 | 0 | 0 | 0 | 0 |
| Shivering | 3 | 10 | 1 | 3.3 |

**Graph 1:**




There was no significant difference in mean arterial blood pressure perioperatively between both groups.

**Graph 2:**




There was no significant difference in heart rate perioperatively between both groups

**Discussion:**

Neuraxial adjuvants are used to improve and prolong duration of block and analgesia and decrease the dose of local anaesthetic to which it is added.They also hasten the onset of anesthesia and improve quality of block.

Noxious stimulation leads to the release of neurotransmitters,which causes activation of NMDA receptors which further cause central sensitization and pain[12].Magnesium blocks calcium influx and non-competitively antagonizes MMDA receptors.[9]

In our study onset of sensory and motor block was statistically earlier in clonidine group as compared to magnesium. Clonidine is known to fasten the onset and prolong the duration of motor and sensory block due to presynaptic inhibition of transmitter release and post synaptic hyperpolarization of dorsal horn neurons[8]. Similar results were found by Pramila Soni et al[2]in their study where onset of anesthesia was earlier in clonidine group than control group. Vaibhav Shahiet.al[4] also found earlier onset of anesthesia with alpha-2 agonist as compared to magnesium. In contrast to our study Ghatak et al[3] found earlier onset with magnesium than clonidine group.

Time for two segment dermatomal regression was prolonged in clonidine group when compared to magnesium group which was similar to studies of Ghatak et al[3]and Thimmppa[10].

Duration of analgesia was also significantly more in clonidine group than magnesium.The similar results were also found by Ghatak et al[3],Wasim Mohammad et al[11],and Pramila Soni et al[2]. Clonidine causes spinal cord antinoception,by stimulation of α2 receptors in dorsal horn,mimicking the activation of descending inhibitory pathways.[13]

Duration of motor block was also significantly prolonged in clonidine group than magnesium.In concordance to our study,Thimmpaet al[10] and Vaibhav Shahi et al[4] also proved prolongation of block on addition of clonidine as adjuvant to epidural anesthesia.

In our study,we have observed heart rate and blood pressure remained stable and there was no significant difference between the two groups.This was similar to study of Ghataket al[3] and Wasim Mohammad[11]were also haemodynamic stability was maintained after addition of clonidine.However,Guptaet al[14]found significant fall in blood pressure at 30 min post epidural block in the clonidine group.The α2 adrenergic agonist reduce sympathetic drive and may affect blood pressure and heart rate as seen in some studies.

In our study sedation was found in patients in clonidine group but the sedation was mild i.e. patient was sleeping comfortably,but responding to verbal commands,similar to the results of Ghatak[3] and Thimmappa[10].There was no other significant side effects in terms of nausea,vomiting,hypotension,bradycardia or shivering.

**CONCLUSION:**

Clonidine when used as an adjuvant to 0.5% hyperbaric bupivacaine in epidural anesthesia resulted in prolonged post-operative analgesia along with duration of both sensory and motor blockade with faster onset as compared to magnesium sulphate without significant adverse effects and hemodynamic alterations.

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