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Comparsion of Three Different Doses of Magnisium Sulphate As Adjuvant To Bupivacaine in Spinal Anaesthesia For Abdominal Hystrectomies

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ABSTRACT

Objectives: To compare three different doses of magnesium sulphate as adjuvant to bupivacaine in spinal anaesthesia for abdominal hystrectomies with respect to the duration of analgesia ,patient comfort and their side effects .

Methods: 120 Patients of age between 35 to 55 years and of ASA I & II physical status who were planned to undergo abdominal hysterectomy in spinal anaesthesia. The study subjects were randomized into four groups consisting 30 patients and they were destined to receive the spinal drug with different concentrations of magnesium sulphate

Results.Onset of motor block for group A was 5.35 ± 0.51min , for group B was 5.28 ± 0.48 min, for group C was 7.31 ± 0.71min and for group D it was 7.8 ± 0.76. Mean difference between groups were significant statistically (P<0.0001) except in group B where it is not significantly different. Mean duration of sensory block for group A was 129.4 ± 7.86 min , for group B was 142.6 ± 5.68 min , for group C it was 164.8 ± 7.12 min and for group D it was 166 ± 6.87 min. Mean difference between four groups were significant statistically (P<0.0001). Mean duration of analgesia for group A was 150.5 ± 5.92 , for group B was 158.8 ± 5.67 for group C was 188.8 ± 8.8 min and in group D it was 190.5 ± 5.14, the mean difference between four groups were significant statistically (P<0.0001).

Conclusions Addition of 50, 75, or 100 mg magnesium sulfate 50% led to a significant delay in the onset of both sensory and motor blockade, and prolonged the duration of sensory and motor blockade without increasing major side effects

KEYWORDS : Magnesium sulphate; bupivacaine; abdominal hystrectomy

INTRODUCTION:-Sub- arachnoid block is administered all around the world for lower limb and lower abdomen surgeries because of its simplicity of technique and the efficient sensory and motor blockade which is achieved with limited complications. Despite its advantages the anaesthesia and analgesia which is achieved by Sub-arachnoid block is often short-lasting limiting its usage in surgeries lasting more than three hours. Recently attempts have been made to prolong the duration of sub-arachnoid blockade by adding various drugs like opioids, ketamine, dexmedetomidine, clonidine, midazolam and magnesium in smaller quantities as adjuvant along with local anaesthetics. Magnesium is the fourth most plentiful cation in the body and the second most plentiful intracellular cation after potassium. Studies have shown that magnesium when added as adjuvant with bupivacaine in spinal anaesthesia it prolonged the duration of the blockade. The purpose of the present study was to compare different doses of magnesium sulphate to find out a dose which is more efficacious in improving the quality of spinal anaesthesia with lesser side effects.

METHODOLOGY: After getting approval from institutional ethics committee the study was conducted in department of anaesthesiology, Netaji Subash Chandra Bose Medical college & Hospital, Jabalpur, Madhya Pradesh, India from a period of October 2012 to October 2013. A total of 120 Patients of age between 35 to 55 years and of ASA I & II physical status who were planned to undergo abdominal hysterectomy in spinal anaesthesia were enrolled in the study. The procedure was properly explained in native language and a written informed consent was obtained from all the study subjects. A detailed history, thorough physical examination, routine investigation like complete blood count, random blood sugar, renal function test, serum electrolytes and any special investigation if required was done for the study. Patients who refused to participate in study, patients with routine contraindication for spinal anaesthesia, patients on long term opioid use or on cancer pain treatment and patients with short stature were excluded from the study.The study subjects were randomized into four groups using Epi info 7™ software each consisting 30 patients. And the patients belonging to the respective groups were destined to receive the spinal drug with different concentrations of magnesium sulphate as described in the Table 1.

Table 1: Different Concentrations Of Magnesium Sulphate

Group	Spinal Drug
Group A	Inj. bupivacaine(0.5%) 3.0ml + Inj. normal saline 0.5ml = Total 3.5ml
Group B	Inj. bupivacaine (0.5%) 3.0ml + inj. magnesium sulphate (50%) 0.1ml (50mg) + Inj. normal saline 0.4ml = Total 3.5ml
Group C	Inj. bupivacaine (0.5%) 3.0ml + Inj. magnesium sulphate (50%) 0.15ml (75mg) + Inj. normal saline 0.35ml = Total 3.5ml
Group D	Inj. bupivacaine (0.5%) 3.0ml + Inj. magnesium sulphate (50%) 0.2ml (100mg) + Inj. normal saline 0.3ml = Total 3.5ml

The following parameters were observed in all the study subjects

Onset of sensory block: Time elapsed from the end of injection to absence of pain sensation to pinprick at the T10 dermatome.

Duration of analgesia: The period from spinal injection to the time of administration of first rescue analgesia for pain postoperatively.

Incidence of side effects.

OBSERVATIONS AND RESULTS All the four groups are comparable in terms of demographic characteristics. The observations and results are summarized as tables and graphs (Table 2 and 3)

TABLE 2: MEAN ONSET OF BLOCK (IN MINUTES)

Groups	Sensory onset in minutes (mean ±SD)	P value
A	2.31±0.49	-
B	3.95±0.47	<0.0001
C	5.36±0.58	<0.0001
D	5.73±0.44	<0.0001

P value is <0.0001

TABLE 3: MEAN DURATION OF ANALGESIA (IN MINUTES)

Groups	Mean	±SD	P Value
A	150.5	5.92	-
B	158.8	5.67	<0.0001
C	188.8	8.8	<0.0001
D	190.5	5.14	<0.0001

P value is <0.0001

The duration of analgesia was recorded as the time from intrathecal injection until the patients request for additional analgesia in postoperative period which was assessed by visual analogue score of ≥4.

STATISTICS Statistical analyses were performed using IBM SPSS 20. All data pertaining to demographic characteristics, sensory block, motor block and adverse effects in the study group were recorded and subjected to statistical analysis. Categorical data were represented as frequency counts (percent) and compared using the chi-square or Fisher's exact statistic as appropriate. Odds Ratio and 95% Confidence Intervals were also presented for 2 x 2 contingency tables. Continuous data are presented as means (± standard deviation) and compared using the t-test or analysis of variance as appropriate.

DISCUSSION Adequate postoperative pain control is essential to prevent adverse consequences of surgical insult. Spinal anaesthesia has the advantage of simplicity of technique, rapid onset of action and reliability in producing uniform sensory and motor blockade. Its main disadvantage relates to its limited duration of action and hence lack of long lasting postoperative analgesia. In recent years, use of intrathecal adjuvants has gained popularity with the aim of prolonging the duration of block, better success rate, patient satisfaction, decreased resource utilization compared with general anaesthesia and faster recovery. Some clinical studies have demonstrated antinociceptive effects for systemically administered magnesium sulphate on the assumption that magnesium acts on NMDA receptors located in the spinal cord[1] whereas, no decrease in postoperative analgesic consumption was observed in a randomized clinical trial using intravenous magnesium (bolus and infusion). Intravenous magnesium for modulation of antinociception via NMDA channel antagonism is insufficient for blood-brain barrier penetration to achieve effective CSF concentration.[2] In addition, the administration of magnesium by systemic route may have unwanted side effects.[3] Considering these factors, recent studies have focused on the antinociceptive effect of intrathecal magnesium.[4,5,6] The intrathecal route is attractive, as it obviates the problems of systemic administration and it solves the problem of transport of the agent across the blood brain barrier. In the dose range necessary for effective enhancement of opiate-based analgesia, there is no evidence that Mg is harmful to neuronal tissue. Indeed, it may offer some degree of protection against hypoxia and ischemia through a combination of spinal cord vasodilatation, calcium antagonism and blockade of the NMDA channel.[7] The efficacy and safety of intrathecal magnesium administration has been evaluated in various animal and human studies.[3] Previous studies have used the dose of (50mg) neuraxial magnesium sulphate either as intrathecal or epidural dose and reported an increase in duration of analgesia and found to be safe and effective.[8,9] The main finding of this study was that in patients undergoing the abdominal hysterectomy under hyperbaric bupivacaine spinal anesthesia, the addition of 50, 75, or 100 mg magnesium sulfate 50% led to a significant delay in the onset of both sensory and motor blockade, and prolonged the duration of sensory and motor blockade without increasing major side effects.Onset of motor block for group A was 5.35 ± 0.51min , for group B was 5.28 ± 0.48 min, for group C was 7.31 ± 0.71min and for group D it was 7.8 ± 0.76. Mean difference between groups were significant statistically (P<0.0001) except in group B where it is not significantly different.Mean time to achieve maximum motor block for group A was 7.18 ± 0.62, for group B was 7.31 ± 0.57 , for group C it was 11 ± 1.23 min. and in group D it was 15.8 ± 0.86 Mean difference between groups were significant statistically (P<0.0001)), except in group B where it is not significantly different.

To conclude adding magnesium sulphate as an adjuvant to intrathecal bupivacaine delayed the onset of both sensory and motor blockade compared to non adjuvant groups. These results are consistent with studies of Ozalevli et al,[9] who too observed a similar delay in onset of spinal anaesthesia when magnesium is added to fentanyl and isobaric bupivacaine, S. Malleeswaran et al [10] also observe similar results in their study when they used mixture of bupivacaine, fentanyl and magnesium intrathecally in patients with mild preeclampsia undergoing caesarean section. Arcioni et al [11]also observed that intrathecal and epidural magnesium sulphate potentiated and prolonged motor block. And our findings are in agreement with the previous report by Unlugence et al,[12] Khalili et al,[13] Mitra Jabalameli et al.[14] The authors suggested that the difference in pH and baricity of the solution by addition of magnesium contributed to the delayed onset, which may also be the case in our study.

Mean duration of sensory block for group A was 129.4 ± 7.86 min , for group B was 142.6 ± 5.68 min , for group C it was 164.8 ± 7.12 min and for group D it was 166 ± 6.87 min. Mean difference between four groups were significant statistically (P<0.0001). Mean duration of 2 segment regression of sensory block for group A was 80.16 ± 5.11 min , for group B was 89 ± 5.93 min , for group C it was 95.5 ± 6.34 min and for group D it was 97 ± 5.66 min. Mean difference between four groups were significant statistically (P<0.0001). Mean duration of motor block for group A was 106.5 ± 6.84 min , for group B was 119.5 ± 4.61min , for group C it was 134.1 ± 5.98 min , and for group D it was 138.4 ± 4.61 min, and the mean difference between four groups were significant statistically (P<0.0001). These results are in corroboration with H. Unlugenc et al [12]and S. Malleeswaran et al [10]who showed prolongation of duration of sensory and motor block in magnesium group.Mitra Jabalameli et al [14]used different doses of magnesium i.e. 50, 75 and 100 mg with 0.5% bupivacaine in caesarean section and observed maximum duration of sensory and motor block with 100 mg group, Khalili G et al [13]observed prolongation of the duration of the sensory block with 100 mg intrathecal magnesium. Jehan Ahmed Sayed et al [15]showed the prolongation of onset as well as time to regression of sensory block was more with 100 mg of magnesium as compared to 50 mg.

Our study is also in agreement with the previous experience of Ozalevli et al,[9] Malleeswaran et al [10]who postulated that fentanyl plus magnesium sulphate is hyperbaric as compared with CSF and would limit cephaled spread. They explained this delay by the difference in pH and baricity of the solution containing magnesium.Mean duration of analgesia for group A was 150.5 ± 5.92 , for group B was 158.8 ± 5.67 for group C was 188.8 ± 8.8 min and in group D it was 190.5 ± 5.14, the mean difference between four groups were significant statistically (P<0.0001). In our study duration of analgesia was taken as the period from spinal injection to the time of administration of first rescue analgesia for pain postoperatively when requested by the patien. Magnesium prolongs the duration of spinal anaesthesia, given during abdominal hysterectomy. This drug is the analgesic and antinociceptive additive drug. When it is used with local anaesthetic, it resulted in prolongation of analgesia without significant complication [16].This prolongation of anaesthesia is consistent with the experimental synergistic interaction between spinal local anaesthetics and NMDA antagonists, like magnesium, which use antinociceptive effects via different mechanisms, hence, the rationale for combining the two.

The dose of magnesium used in the present study was based on data from Buvanendran *et al* [6]where 50 mg of spinal magnesium sulfate potentiated fentanyl antinociception. Larger doses have also been used. In 1985, Lejuste [16]described the inadvertent intrathecal injection of 1000 mg of magnesium sulfate, producing a dense motor block followed by complete resolution within 90 min, with no neurological deficit at long-term follow up. Further examination is required to determine whether larger doses of magnesium produce greater potentiation of spinal analgesia without causing any neurological deficit when injected intrathecally. Malleeswaran et al *[10]*found that the addition of intrathecal magnesium increased the duration of spinal anaesthesia by 42 min. Huban Dayioglu et al [17]also conclude that addition of magnesium sulphate to spinal anaesthesia prolonged the time to first analgesic requirement. These results are consistent with various previous studies conducted by Ozalevli M et al [9],Jehan Ahmed Sayed et al,[15] Mitra Jabalameli et al,[14] Buvanendran A et al,[6] Arcioni R et al.[11] Though intravenous magnesium is known to cause hypotension when used to treat eclampsia, we found no significant hemodynamic effect following the addition of magnesium to our spinal solution. This may be attributed to the absence of systemic vasodilator effects of spinal magnesium. This finding also corroborate with study of Malleeswaran et al [10]and H. Dayioglu et al [17] as they too doesn't find any difference regarding hypotension and bradycardia after addition of intrathecal magnesium (50 mg). Mitra Jabalameli et al [14]concluded that higher dose of magnesium (100mg) might result in increasing some of side effects (hypotension, nausea and vomiting)..

In our study, higher dose (100 mg) of magnesium sulfate resulted in increasing some of side effects (hypotention, respiratory depression, nausea, and vomiting).These patients needed to use supplemental drug such as ephedrine or metoclopramide. An increased risk of respiratory depression has been reported with magnesium sulfate therapy[18], and an increased incidence of respiratory depression may be expected when other drugs are combined. Total analgesic requirements for 24 h following surgery were lower in patients who received higher dose of intrathecal magnesium sulfate ($P < 0.001$). It is likely that magnesium sulfate can potentiate opioid analgesic effect by both central and peripheral mechanism[19] **.** Compared to published data and from the clinical point, the 100 mg magnesium sulfate 50% used in our study does not seem to have more desirable effect than 75 and 50 mg. Although 75 mg magnesium sulphate decrease the postoperative analgesic requirement.

CONCLUSION

To conclude,75mg of magnesium sulphate given intrathecally with hyperbaric bupivacainein abdominal hysterectomy provides safe and effective anaesthesia.This dose is enough to cause a significant delay in the onset of block and also increase the duration of post operative analgesia without causing significant increase in side effects.

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