



Original Research Article

Effectiveness of low dose epidural magnesium sulphate in labour analgesia

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ARTICLE INFO

Article history:

Received 19-07-2020

Accepted 12-08-2020

Available online 25-11-2020

Keywords:

Break through pain

Combined spinal epidural approach

Epidural adjuvant

Labour analgesia

Magnesium sulphate

ABSTRACT

Background: Magnesium sulphate is common adjuvant in central neuraxial blocks because of its analgesic action due to antagonistic action on N-methyl-D-aspartate receptors. It has been earlier used as epidural adjuvant in labour analgesia in dose of 50 mg. In current study magnesium sulphate was used epidurally in 25 mg dose and its effectiveness was assessed.

Materials and Methods: The current randomized control trial, double blind study was conducted in 100 parturients, divided in group M and C with 50 in each. All the parturient received 15 microgm of fentanyl intrathecally and bolus dose of 8ml 0.1% bupivacaine epidurally followed by epidural infusion of 0.1% bupivacaine at rate of 8ml/hr. In addition to above, group M received 50mg of magnesium sulphate epidurally and group C received volume adjusted sterile saline. The pilot study conducted on 5 parturients, all parturients in group M developed motor block, which was attributed to magnesium sulphate so the dose of it decreased to 25 mg. The synergistic action of magnesium sulphate was evaluated by pain assessment by Visual analogue scale and number of breakthrough pain.

Results: The faster onset of analgesia and better pain relief was found in group M. The breakthrough pain was less in group M in both stage 1 and stage 2 of labour. The duration of labour, incidence of instrumentation, need of caesarean section and neonatal outcome were comparable in both the groups.

Conclusions: Magnesium sulphate is an effective epidural adjuvant in labour analgesia even in 25mg dose without any adverse effect.

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1. Introduction

The labour pain in parturients causes patho-physiological responses leading to hyperventilation, increased work of breathing, increased oxygen consumption, increased plasma levels of cortisol and catecholamine and increased maternal metabolic rate. This leads to decreased uteroplacental blood flow, shift of oxy haemoglobin dissociation curve to left and ultimately maternal as well as foetal metabolic acidosis.¹ Effective pain relief during labour reduces plasma noradrenaline level,² prevents the rise of 11- hydroxyl

corticosteroid during the first and second stage of labour,³ prevents metabolic acidosis by reducing the rate of rise of lactate and pyruvate⁴ and decreases maternal oxygen consumption.⁵

Advances in the field of labour analgesia have treaded a long journey to modern neuraxial labour analgesia, which reflects a shift in the obstetric anaesthesia, where focus is not just on pain relief but on the overall quality of analgesia. Combined spinal epidural approach gives a faster onset of complete analgesia.⁶ This is achieved by using intrathecal lipid soluble opioids, followed by epidural infusion of local anaesthetic agents with or without adjuvants.

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Bupivacaine and ropivacaine are commonly used local anaesthetic agent, which offers the advantage of a longer duration of action and no tachyphylaxis. The continuous infusion of dilute solution of bupivacaine provides stable level of analgesia, a more stable maternal heart rate and blood pressure, with decreased risk of hypotension and less risk of systemic local anaesthetic toxicity.⁷ When used as a sole agent epidurally, bupivacaine is unable to provide adequate analgesia for the total duration of labour, which leads to breakthrough pain and need for frequent boluses. To overcome these difficulties, various adjuvants have been used to improve the quality of analgesia during labour. Fentanyl is the most commonly used adjuvant in labour analgesia, which in higher doses can lead to maternal nausea, vomiting and neonatal respiratory depression.^{8,9}

Magnesium sulphate has antagonistic action on NMDA (N-methyl-D-aspartate subtype of glutamate) receptor¹⁰ in the central nervous system and is widely used as adjuvant in various surgeries through various routes eg, intravenously (IV), intrathecally and epidurally. A study conducted by Hasanein et al.,¹¹ using a single bolus dose of 50mg of magnesium sulphate epidurally for labour analgesia as an adjuvant to bupivacaine and fentanyl reported faster onset, longer duration of action and reduced break through pain. Other studies using intrathecal magnesium sulphate in labour analgesia have also shown longer duration and better quality of analgesia.¹² However, data for the use of epidural magnesium sulphate as an adjuvant to local anaesthetic agents in labour analgesia is limited.

The current study was done to assess the effectiveness of magnesium sulphate as an adjuvant to local anaesthetics administered epidurally in labour analgesia and also to assess whether the same improved quality of analgesia and sparing effect of total consumption of bupivacaine can be obtained even with the low dose of magnesium sulphate (25 mg) given as a single bolus.

2. Materials and Methods

The current study was conducted in a tertiary care centre after approval of Institutional Ethics Committee, in parturients of 18–35yrs age group planned for vaginal delivery, in American society of Anesthesiologists (ASA) class 2, with height in range of 145-175 cm and weight in range of 50-100 kg. Any parturient with allergy to local anaesthetics, coagulation abnormality, infection at site of injection, abnormality of spine, cardiac disease and pre-eclampsia patient who received IV magnesium sulphate for obstetric management were excluded from the study. After taking written and informed consent from the parturients in first stage of labour with cervical dilatation greater than or equal to 3cms were divided randomly by block randomization into two groups, group M and C. All the patients received 15 microgm of fentanyl intrathecally and

bolus dose of 8ml 0.1% bupivacaine epidurally followed by infusion of 0.1% bupivacaine at rate of 8ml/hr through epidural route. In addition to above, group M received 50mg of magnesium sulphate epidurally, after securing the epidural catheter and confirming the position, while group C received volume adjusted sterile saline. All the drugs were prepared by anaesthesiologist not involved in the procedure and assessment of parturients afterwards. The breakthrough pain was managed by bolus dose of 8ml of 0.1% bupivacaine in supine position in first stage of labour and sitting position in second stage of labour, with aim to keep VAS¹¹ (Visual analogue scale) ≤ 3 .

A pilot study was conducted in five parturients, in group M, VAS score was found to be 1 in all the parturients in stage 1, and 2 in stage 2 of labour, with no top up of local anaesthetic requirement. Out of five, three parturients developed motor block of Bromage grade 1 in two parturients and grade 2 in one parturient. Their vitals remained stable and no side effects were noted. Mechanical assistance was needed by 2 (40%) for delivery due to decreased maternal efforts but Apgar scores were 8 and 9 for all neonates at 1 and 5mins respectively. Neonatal resuscitation or neonatal intensive care unit (NICU) admission was not required for any neonate. The higher incidence of motor block and mechanical assistance compared to previous study¹¹ was attributed to lower average height of the parturients in current study and magnesium sulphate. Magnesium sulphate is known to help in faster onset of motor block when used as an epidural adjuvant in 50mg dose for surgical cases,¹⁰ which was an undesirable effect for labour analgesia hence the dose was decreased to 25 mg in current study.

The sample size was calculated based on expected outcome of pilot study. It was decided to have sample size of 100 parturients, with 50 parturients in both the groups, considering risk/prevalence ration of 1.3 and risk/prevalence difference of 20.

On admission, a detailed history, complete general and systemic examination and obstetric evaluation done for all parturients. After securing 18G intravenous cannula and starting crystalloid, spinal anaesthesia (BD Spinal Needle, 26 G) was given by 15microgm fentanyl (1.5ml), followed by securing epidural catheter and confirming the position (Perifix, 18 G B Braun), test drug (25mg magnesium sulphate in group M and equal volume of sterile saline in group C) was given, which was considered as T0. This was followed by bolus(8ml) and then infusion (8ml/hr) of 0.1% bupivacaine, which continued till delivery of the baby. The end point of the study was taken as either normal delivery of the baby or when a decision for operative delivery was taken by the obstetrician.

The parturients were observed for vitals, pain (assessed by VAS), onset of analgesia (VAS ≤ 3), level of sensory block, side effects like hypotension, motor block, pruritus,

nausea, vomiting, progression and duration of labour and mode of delivery were noted. Hypotension more than 10% fall from baseline were treated by 200ml bolus of crystalloid and more than 20% by ephedrine 6-12 mg intravenously. Motor block was assessed by modified Bromage scale.¹¹ The Bromage scale of ≥ 2 was managed by reducing the infusion rate of bupivacaine by 2ml/hr until the Bromage scale was found to be 0. Foetal monitoring was done by recorded on a cardiotocograph and neonatal Apgar score at 1 and 5 minutes noted for all.

Data collected was entered and analysed using Statistical Package for Social Science (SPSS) version 21.0. Results on continuous measurements were expressed in mean \pm standard deviation (SD) and as number (%). Chi-square test was performed to find out the association between various parameters assessed. Significance was assessed at 5% level of significance. Student t test (two tailed, dependent) was used to find the significance of change at different point of time during the study within same group and Student t test (two tailed, independent) was used to find the significance of changes among patients of group M and C.

3. Results

Total 100 parturients were recruited in the study (group M=50, group C = 50). Both the groups were age, height, weight and cervical dilatation at which labour analgesia administered were matched. The vitals, including pulse rate, systolic and diastolic pressure were found to be comparable in both the groups M and C till one hour, after that till the end point these were found to be lower in group M, which was found to be statistically significant with $p < 0.05$.

After intrathecal fentanyl administration, the VAS score was 4.92 ± 0.74 in group M and 5.16 ± 0.62 in group C, with p value of 0.084. None of the patient reached VAS ≤ 3 . Time of test drug and bolus dose of local anaesthetic administration was considered as T0, and after that time to achieve VAS ≤ 3 was considered as onset of analgesia. The onset time was 2.39 ± 0.42 minutes in group M and 3.18 ± 0.35 minutes in group C, with p value of < 0.001 . In stage one of labour, throughout the VAS score was lower in group M, and this trend was statistically significant with p value of < 0.001 . To maintain VAS ≤ 3 , none of the parturient needed any bolus dose in group M, while in group C, 17(34%) parturients needed single bolus dose and 7(14%) needed two bolus dose of 0.1% bupivacaine. In second stage of labour in group M, 45(90%) parturients did not need any bolus dose and 5(10%) needed one bolus dose. Whereas in group C, 44(88%) parturients needed two bolus dose and 6(12%) needed one bolus dose.

All the parturients achieved sensory block of T6-T8, and none developed any hypotension, motor block, postdural puncture headache, nausea and vomiting. Pruritus of grade 2 and 3 were found in 3(6%) parturients in group M and 2(4%) in group C. The duration of labour was comparable

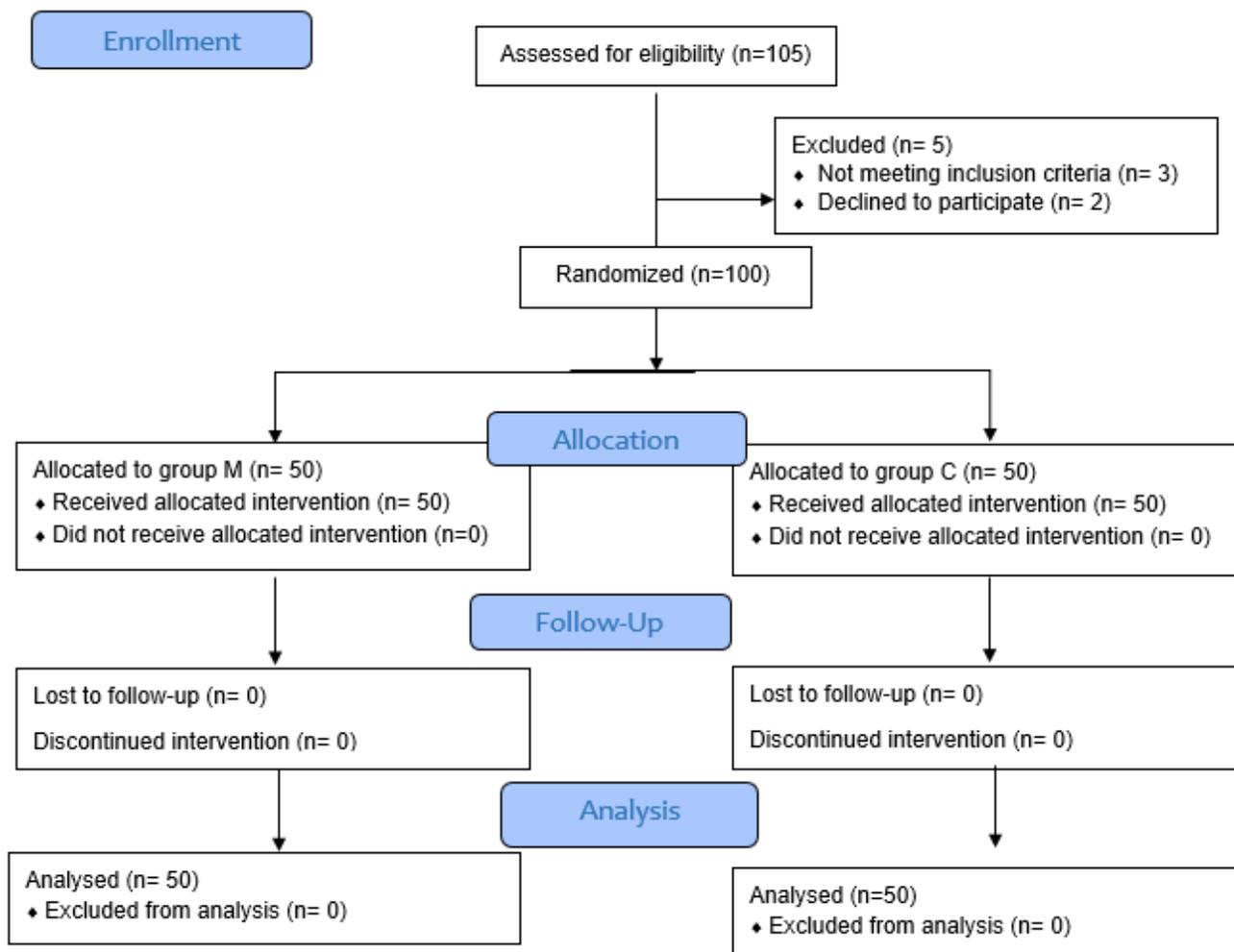
in both the groups, it was 3.08 ± 1.28 hours in group M and 3.18 ± 1.12 hours in group C, with p value of 0.678. 62% parturients in group M and 56% in group C had normal vaginal delivery, without any mechanical assistance. Distribution of mode of delivery was statistically similar in two groups with p value of 0.924. Incidence of instrumentation by forceps and ventouse application were similar in both the groups. The caesarean section was needed in 18% parturients in group M while 24% in group C, which was comparable in both groups with p value of 0.773. Furthermore, for foetal distress caesarean section was done in 1(2%) parturient in group M and 3(6%) parturients in group C. Other indications of caesarean section were cephalopelvic disproportion and failure to progress. Neonatal outcomes were comparable in both the groups with p value of 1. One neonate in group M needed neonatal resuscitation with ambu bag and mask and was shifted to NICU for further monitoring. The baby was discharged after 24 hrs of NICU care. Intubation was not needed in any neonate in both the groups.

Table 1: Comparison of parturient characteristics

	Group M	Group C	Total
Age			
<30 years	35(70.0%)	40(80%)	75(75%)
>30 years	15(30.0%)	10(20%)	25(25%)
Height (cm)			
144-154	24(48%)	32(64%)	
155-164	25(50%)	18(36%)	
165-174	1(2%)	0(0%)	
Weight (kg)			
50-69	25(50%)	25(50%)	
70-89	25(50%)	25(50%)	
ASA			
Grade 1	39(78%)	41(82%)	
Grade 2	11(22%)	9(18%)	

Table 2: Comparison of the number of bolus doses of local anaesthetic required by the parturient during stage one and two of labour to maintain VAS ≤ 3

Number of bolus in stage one	Group M (n = 50)	Group C (n = 50)
0	50(100%)	26(52%)
1	0(0%)	17(34%)
2	0(0%)	7(14%)
Number of bolus in second stage		
0	45(90%)	6(12%)
1	5(10%)	44(88%)



Graph 1: CONSORT flow diagram

Table 3: Comparison of mode of delivery

Mode of delivery	Group M	Group C	Total
Normal vaginal delivery	31(62%)	28(56%)	59(59%)
Cesarean section	9(18%)	12(24%)	21(21%)
Forceps delivery	7(14%)	7(14%)	14(14%)
Ventouse extraction	3(6%)	3(6%)	6(6%)
Total	50(100%)	50(100%)	100(100%)

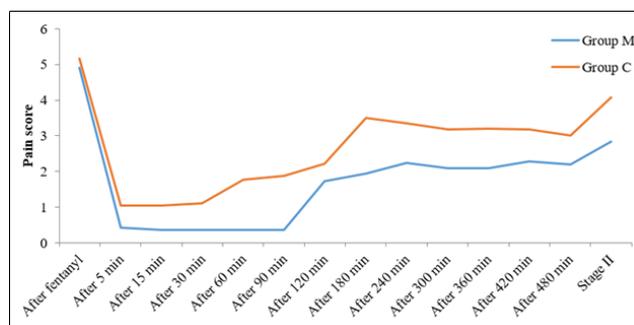


Fig. 1: Pain score during study period

4. Discussion

4.1. Quality of analgesia

The current study demonstrates that magnesium sulphate is an effective epidural adjuvant in labour analgesia even in lower dose of 25mg. Few previous studies had shown

the prolonged analgesic effect, better motor block, muscle relaxation and decreased requirement of other analgesic in postoperative period, when 50 mg magnesium sulphate was used as intrathecal and epidural adjuvant for caesarean section patients.^{10,13,14} Buvanendran et al¹² study on labour

analgesia, using 50mg of magnesium sulphate intrathecally with bupivacaine, fentanyl and adrenaline epidurally, found no difference in the VAS scores between the groups, but the duration of analgesia was significantly longer in magnesium group. Hasanein et al¹¹ used 50mg magnesium sulphate epidurally for labour analgesia concluded that the duration of analgesia was prolonged in magnesium group with greater satisfaction scores and decreased breakthrough pain.

In current study, VAS score remained ≤ 3 up to 120 minutes in both the groups, after which in group C, pain score was > 3 in stage 1 and > 4 in stage 2, for which top up dose of local anaesthetic were required. In group M, lower VAS score was noted and need of top up doses were less. As bupivacaine and fentanyl were common in both the groups, so decreased VAS scores achieved in group M was probably effect of magnesium sulphate.

4.2. Onset of analgesia

The onset of sensory analgesia gets accelerated by epidural administration of magnesium sulphate, this conclusion was made based on meta analysis which included eighteen published trial of magnesium sulphate, as an adjuvant, in central neuraxial blocks.¹⁰ Similar findings were noted by Hassanein et al.,¹¹ with 50mg magnesium sulphate as adjuvant in labour analgesia. In current study, after epidural administration of magnesium sulphate, the time to achieve VAS ≤ 3 was 2.39 minutes in magnesium group and without magnesium, it was found to be 3.18 minutes. The time taken for the onset of analgesia was faster and statistically significant with a p value of < 0.001 .

4.3. Maternal hemodynamic and side effects

The maternal hemodynamic parameters remained stable after magnesium sulphate administration in epidural and intrathecal route in dose of 50mg.^{11–14} In current study hemodynamic parameters including mean blood pressure and heart rate were comparable in both the groups for one hour, after which it was found to be lower in group M, which could be the result of better analgesia. The incidences of hypotension were found to be similar in both the groups.

Stocks et al.,¹⁵ documented the incidence of pruritus with different doses of intrathecal fentanyl. The incidence of pruritus with 15 mcg of intrathecal fentanyl was found to be 60%. They concluded that the addition of bupivacaine to fentanyl could have led to an alteration of the fentanyl dose–response in relation to pruritus. In current study, with 15 mcg of fentanyl intrathecally, the incidence of pruritus was found to be 15%, with grade 2 and 3. There are few studies with 15 mcg of intrathecal fentanyl, so incidence of pruritus needs further evaluation with larger sample size.

4.4. Outcome of pregnancy

In the study conducted by Buvanendran et al,¹² the distribution of spontaneous vaginal delivery, assisted vaginal delivery, mean duration of labour for vaginal delivery, caesarean section was comparable in groups with and without magnesium sulphate. For caesarean section, the mean duration of labour was 502 min in magnesium group while in the control group it was 577 min, which seems to be longer. Hasanein et al,¹¹ found no significant difference in the duration of first and second stage of labour. The comparison of outcome of pregnancy was not done in the study.

In current study, the longer duration of labour in group M was probably due to more number of parturients in group M with first pregnancy. Duration of labour based on first pregnancy, second pregnancy and more than two pregnancies were comparable in group M and C. The incidence of mechanical assistance for vaginal delivery and caesarean section were comparable in group M and C. With respect to indications for cesarean delivery, the incidence of failure to progress was same in both the groups while foetal distress and cephalopelvic disproportion were more in the group C. The distribution of indications for caesarean section were statistically similar in the two groups with a p value of 0.773. So, magnesium as an epidural adjuvant did not lead to any prolongation of labour or altered outcome of pregnancy.

4.5. Neonatal outcome

Hasanein et al¹¹ found that the partial pressure of oxygen and carbon dioxide in umbilical artery, base deficit, lactate concentrations, and Apgar scores at 1, 5 and 10 min were comparable between the two groups.

In current study, Apgar scores at 1min and 5mins was statistically similar with p value of 1. One neonate in the study group needed neonatal resuscitation with ambu bag and mask and was shifted to NICU for further monitoring. The baby was discharged after 24 hrs of NICU care. Intubation was not needed in any neonate in both the groups.

5. Conclusion

Low dose of magnesium sulphate reduced the breakthrough pain, thereby decreased the number of bolus doses of local anaesthetic agents, accelerated onset of analgesia and also prevented its side effects, maintained stable maternal hemodynamic without affecting outcome of pregnancy.

6. Limitations

The total duration of analgesia was not assessed as the end point of study was till delivery of baby or decision of caesarean section by the obstetrician.

7. Source of Funding

Not applicable.

8. Conflict of Interest

None.

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Cite this article: Sinha S, Zachariah VK, Priya P, Kakkar R, Kumar A. Effectiveness of low dose epidural magnesium sulphate in labour analgesia. *Indian J Clin Anaesth* 2020;7(4):613-618.