THE EFFECT OF ADDING INTRATHECAL MAGNESIUM SULPHATE TO BUPIVACAINE-FENTANYL SPINAL ANAESTHESIA

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ABSTRACT

BACKGROUND

Spinal anaesthesia plays an important role of alleviating pain intraoperatively, extending into post-operative period also. Many drugs have been tried in search for an ideal adjuvant like opioids, soda bicarbonate, ketamine, neostigmine and midazolam. The magnesium sulphate with different mode of action prolong the Bupivacaine-Fentanyl spinal anaesthesia.

MATERIALS AND METHODS

The study was conducted in 70 patients undergoing elective lower extremity surgeries. After routine preoperative assessment as for all elective surgery patients, they were premedicated and patients were randomly allocated into two groups. Group S received Inj. 0.5% Bupivacaine 2 cc+Inj. Fentanyl 0.5 cc + 0.9% NaCl solution 1 cc, Group M received Inj. 0.5% Bupivacaine 2 cc+Inj. Fentanyl 0.5 cc+50 mg of 5% MgSO4 1 cc. On preoperative visit, the patients were explained about the procedure details. Patients were put on sitting position and with strict aseptic precaution lumbar puncture was done. The assigned amount of drug is premixed in a sterile syringe was injected as per the group assigned. After injection patient were put up in supine position. After attaining adequate peak level of sensory block, the surgeon was asked to proceed. If needed oxygen was given through ventimask. The results were observed.

RESULTS

The main finding of this study is that in patients undergoing lower extremity surgery under bupivacaine-fentanyl spinal anaesthesia, the addition of 50 mg IT MgSO4 led to a significant delay in the onset of both sensory and motor blockade and prolonged the duration of spinal anaesthesia without increasing side effects. The mean duration of spinal anaesthesia was significantly prolonged by magnesium to 209 mts. No case had respiratory depression intraoperatively as well as in post-operative period in this study. In this study, the respiratory rate remained unchanged with the baseline and the haemodynamics were stable in the magnesium group.

CONCLUSION

From this study it was concluded that in patients undergoing lower extremity surgery, IT MgSO4 (50 mg), when added to spinal anaesthesia induced by bupivacaine and fentanyl, delayed the onset of both sensory and motor blockade and prolonged the duration of anaesthesia without increasing the incidence of side effects.

KEYWORDS

Spinal Anaesthesia, Intrathecal, Post-Operative.

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BACKGROUND

Spinal anaesthesia plays an important role of alleviating pain intraoperatively, extending into post-operative period also. A pain free post-operative period is necessary for both physical and psychological wellbeing of the patient.

The first neuraxial block performed by J. Leonard Corning by injecting cocaine paved the way for the greatest leap into spinal anaesthesia. He coined the term "Spinal Anaesthesia."

First planned spinal analgesia for surgery in man performed by August Bier on 16th August 1898, in Kiel when he injected 3 mL of 0.5% cocaine solution into a 34-year-old labourer.

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This was followed by successful and enthusiastic practice of spinal anaesthesia by "Rudolph Matas" in New Orleans and "Theodore Tuffier" in France. For lower extremity surgeries, the standard and most frequently employed anaesthetic technique is subarachnoid block. It provides superior analgesia and reduces perioperative complications compared with general anaesthesia.

The first spinal adjuvant adrenaline increase the duration and reduce the toxicity of spinal anaesthesia. From then many drugs have been tried in search for an ideal adjuvant. Like opioids, soda bicarbonate, ketamine, neostigmine and midazolam. The magnesium sulphate with different mode of action prolong the Bupivacaine-Fentanyl spinal anaesthesia.[1,2,3,4]

The demonstration of the opiate receptor in the substantia gelatinosa of the spinal cord (Yaksh and Rudy - 1976) has created interest in the intrathecal administration of opiates.[5]

Opioids are commonly added adjuvant to local anaesthetics in spinal anaesthesia. However, significant adverse effects such as pruritus, urinary retention, respiratory depression, haemodynamic instability and occasionally severe nausea and vomiting may limit their use. Adding magnesium

may also improve the quality and increase the duration of spinal anaesthesia.

Magnesium blocks the N-methyl-D-aspartate (NMDA) channels in a voltage dependent way, producing a dramatic reduction in NMDA induced currents. In experimental studies, Intrathecal (IT) administration of magnesium sulphate (MgSO4) significantly potentiated opioids ant nociception in rats during spinal anaesthesia in acute incisional model.[6]

Magnesium has been used safely intrathecally in humans, and its safety profile has been documented by histopathological analysis in experimental studies.[7,8]

Hence, the present study has been undertaken to test the hypothesis that in patients undergoing lower extremity surgeries under Bupivacaine-Fentanyl spinal anaesthesia, the duration of anaesthesia would be prolonged by intrathecal $MgSO_4$ (50 mg).

Regional anaesthesia is the most frequently employed anaesthetic technique for lower extremity surgeries. This study is to assess the effect of intrathecal magnesium sulphate with Bupivacaine-Fentanyl spinal anaesthesia for lower extremity surgeries in prolonging the duration of anaesthesia without increasing the incidence of side effects.

MATERIALS AND METHODS

After getting the approval from the Ethical Committee of the Department of Anaesthesiology, the study was conducted in 70 patients undergoing elective lower extremity surgeries. After getting consent and explaining the procedure details, the anaesthetic technique was performed.

Exclusion Criteria

- Patient refusal.
- ASA III and IV patients.
- Post spinal surgeries.
- Spinal deformity.
- H/o drug allergy.

After routine preoperative assessment as for all elective surgery patients, they were premedicated with injection Midazolam 2 mg IM 30 - 45 minutes before surgery.

Patients were Randomly Allocated into Two Groups

Group S - Received Inj. 0.5% Bupivacaine 2 cc + Inj. Fentanyl 0.5 cc + 0.9% NaCl solution 1 cc

Group M - Received Inj. 0.5% Bupivacaine 2 cc + Inj. Fentanyl 0.5 cc + 50 mg of 5% MgSO4 1 cc

Procedure Details

On preoperative visit, the patients were explained about the procedure details. Then preoperative baseline parameters like pulse rate, blood pressure, respiratory rate were recorded. IV line started with 18 gauge intravenous cannula and infused with crystalloids.

Patients were put on sitting position and with strict aseptic precaution lumbar puncture was done with Quincke standard 23 gauge spinal needle. The assigned amount of drug is premixed in a sterile syringe. After ensuing free flow of CSF, drug was injected as per the group assigned.

After injection patients were put up in supine position. After attaining adequate peak level of sensory block, the surgeon was asked to proceed. If needed oxygen was given through ventimask.

The Following Parameters were recorded

1. Time of highest level of sensory block achieved by pin prick.
2. Degree of motor blockade assessed by using Bromage scale.
3. Pulse rate, Blood pressure, respiratory rate, SpO_2 were monitored every 2 minutes for 10 minutes and every 5 minutes till the end of surgery.
4. Any discomfort like nausea, vomiting, pruritus and shivering.
5. Hypotension is said to have occurred if there was 30% fall from baseline and was treated with 100% O_2, intravenous fluid bolus and Inj. Ephedrine in incremental doses.
6. Bradycardia - if present was treated with Inj. Atropine.
7. Sedation score.
8. Incomplete sensory block.
9. Post-operative observation:
    a. Duration of procedure.
    b. Level at the end of surgery.
    c. Duration of post-operative analgesia.
    d. Two segment regression time (i.e. the time taken to decrease from maximum sensory level by two segments from initial level is noted).

Sedation Score

Brain and Ready Sedation Score was Employed

0 - Fully awake.
1 - Drowsy.
2 - Drowsy but arousable on touch (or) call.
3 - Drowsy but arousable on deep stimuli.
4 - Somnolent.

In the post-operative period, total duration of analgesia was taken as that period from time of subarachnoid block till patient requirement of analgesic medicine.

Pain was Evaluated using Visual Analog Scale

0 – 1 - Excellent
2 – 4 - Good
5 – 6 - Fair
7 – 8 - Poor
9 – 10 - No relief
Pain score > 6 – supplementary analgesia given.

Motor Block was Assessed by Bromage Scale

0 - Full flexion of knees, feet, able to lift the extended leg.
1 - Unable to lift the extended leg. Just able to flex the knees and full flexion of feet possible.
2 - Unable to flex the knees, but flexion of feet possible.
3 - Unable to move the leg (or) feet.

Also in the post-operative period all patients were followed up for any complications like post-operative nausea, vomiting, pruritus, hypotension and respiratory depression. Statistical significance was brought out by ANOVA table.

RESULTS

In this randomised, single-blinded study conducted in 70 patients, the subjects were allocated into two groups and the following results were observed.

Demographic Data
All 2 groups were comparable in age, sex, duration and nature of surgery as shown in Table 1 and 2 and Fig. 1 and 2.

Highest Dermatomal Level
The onset of sensory level and time to be taken for the maximum level of achieving the sensory level and sedation score were shown as follows and in Table 7, 8 and 9 and Figure 6, 7 and 8.

Maximum Level Achieved
Group S - T6
Group M - T6

Time of Maximum Sensory Level
Group S - 6.51 mts with SD 1.04
Group M - 13.06 mts with SD 2.88

Two Segment Regression Time
Shown in Table 10 as follows:
Group S - 69 mts with SD 6.6
Group M - 75.3 mts with SD 4.9

Onset of Motor Blockade
Onset and duration of motor blockade were shown in Table 11 and 12 and Fig. 9.
Group S - 10.2 mts with SD 1.5.
Group M - 17.3 mts with SD 2.

Duration of Motor Blockade
Group S - 97.8 mts with SD 10.1
Group M - 113.1 mts with SD 9.7

Post-Operative Analgesia
Duration of the procedure and the duration of the post-operative analgesia were shown in Table 13 and 14 and Fig. 10
Group S - 169.4 mts with SD 9.8
Group M - 209 mts with SD 13.4

Haemodynamic Variables
Percentage of fall in the pulse rate and changes in blood pressure in both groups as follows, shown in the Table 3 and 4 and Figure 3 and 4.

Pulse Rate Changes
Fall in Pulse Rate
Group S - 13.7 mts with SD 4.8
Group M - 17.5 mts with SD 6.2

Percentage of Change
Group S - 19.5% with SD 5.9
Group M - 15.4% with SD 5.3

Minimum Pulse Rate
Group S - 71.4/mint with SD 6.3
Group M - 75.4/mint with SD 10.3

Blood Pressure Changes
With regard to blood pressure, more than 30% free from the baseline value was considered hypotension.
Group S - There was no significant fall in BP
Group M - There was no significant fall in BP

Percentage of Fall in Systolic BP
Group S - 14.6% with SD 4.6
Group M - 21.1% with SD 3.8

Respiratory Rate and SPO2
Changes in the respiratory rate and oxygen saturation were shown in Table 5 and 6 and Figure 5 and 6.

Respiratory Rate
Group S - 12.89/min with SD 0.96
Group M - 12.94/min with SD 1.0

SPO2
Group S - 98.94% with SD 0.64
Group M - 99.17% with SD 0.62

Complications
In the post-operative period, all patients were followed up for any complications and are shown in Table 15 and Fig. 11. The complications occurred in both groups were as follows:

Nausea and Vomiting
Group S - 2.9%
Group M - NIL

Pruritus
Group S - 11.4% (4 Cases)
Group M - 8.6% (3 Cases)

Age Group	Group M		Group S	
	No.	%	No.	%
< 3 Years	10	28.6	9	25.7
30 - 39	11	31.4	10	28.6
40 - 49	7	20	6	17.1
50 - 59	6	17.1	7	20
60 and Above	1	2.9	3	8.6
Total	**35**	**100**	**35**	**100**
Range	20 - 65		22 - 65	
Mean	37.5		39.7	
S. D.	11.5		13	
'p'	0.5366 Not Significant			

Table 1. Age Distribution

Sex	Group M		Group S	
	No.	%	No.	%
Male	30	85.7	30	85.7
Female	5	14.3	5	14.3
Total	**35**	**100**	**35**	**100**
'p'	1.0 Not Significant			

Table 2. Sex Distribution

Pulse Rate	Group M		Group S		'P'
	Mean	S.D.	Mean	S.D.	
Baseline	89.2	10.5	88.9	8.3	0.842 Not Significant
Maximum	89.5	10.1	87.5	6.0	0.5464 Not Significant
Change	0.3	3.5	-1.4	4.4	0.1 Not Significant
% of change	0.5	3.9	-1.3	4.7	0.1085 Not Significant
Minimum	75.4	10.3	71.4	6.3	0.1391 Not Significant
Change	-13.7	4.8	-17.5	6.2	0.0068 Not Significant
% of Change	-15.4	5.3	-19.5	5.9	0.0025 Not Significant
Average P.R.	80.6	10.5	77.6	5.8	0.3374 Not Significant

Table 3. Pulse Rate

S. B. P.	Group M		Group S		'P'
	Mean	S.D.	Mean	S.D.	
Baseline	123.3	8.4	124.0	8.8	0.5556 Not Significant
Maximum	121.5	8.2	120.8	6.6	0.6808 Not Significant
Change	-1.8	4.2	-3.3	4.2	0.0144 Significant
% of Change	-1.4	3.4	-2.5	3.4	0.0139 Significant
Maximum	105.4	9.4	97.7	6.5	0.0001 Significant
Change	-17.9	5.8	-26.3	5.8	0.0001 Significant
% of Change	-14.6	4.6	-21.1	3.8	0.0001 Significant
Average SBP	113.6	8.3	107.7	5.9	0.0006 Significant

Table 4. Systolic B. P.

Parameter	Group M		Group S		'P'
	Mean	S.D.	Mean	S.D.	
R. R.	12.94	1.0	12.89	0.96	0.9603 Not Significant
'p'	0.9603 Not Significant				

Table 5. Respiratory Rate/SPO2

SPO2	Group M		Group S	
	Mean	S.D.	Mean	S.D.
SPO2	99.17	0.62	98.94	0.64
'P'	0.1331 Not Significant			

Table 6. SPO2

Onset of Sensorium	Group M		Group S	
	Mean	S.D.	Mean	S.D.
3	-	-	5	14.3
4	-	-	6	17.1
5	18	48.6	19	54.3
6	9	25.7	3	8.6
7	6	17.1	1	2.9
8	2	5.7	1	2.9
Total	**35**	**100**	**35**	**100**
Range	5 - 8		3 - 8	
Mean	5.77		4.77	
S.D.	0.94		1.09	
'P'	0.0001 Not Significant			

Table 7. Onset of Sensory Level (In Minutes)

M.S.L.	Group M		Group S	
	No.	%	No.	%
T6	27	77.1	21	60
T7	4	11.4	12	34.3
T8	4	11.4	2	5.7
Total	**35**	**100**	**35**	**100**

Table 8. Maximum Sensory Level

Time of MSL	Group M	Group S
Mean	13.06	6.51
S.D.	2.88	1.04
'p'	0.0001 Significant	

Table 9. Time of Maximum Sensory Level

2SR Time	Group M	Group S
Mean	75.3	69.0
S.D.	4.9	6.6
'P'	0.0001 Significant	

Table 10. Two Segment Regression Time (Minutes)

Motor Onset	Group M	Group S
Mean	17.3	10.2
S. D.	2.0	1.5
'p'	0.0001 Significant	

Table 11. Motor Onset (Minutes)

Motor Duration	Group M	Group S
Mean	113.1	97.8
S.D.	9.7	10.1
'p'	0.0001 Significant	

Table 12. Duration of Motor Block (Minutes)

Duration of Procedure	Group M	Group S
Mean	107.4	98.8
S.D.	18.1	16.0
'p'	0.0762 Significant	

Table 13. Duration of Procedure (Minutes)

Duration of Post-Op Analgesia	Group M	Group S
Mean	13.06	6.51
S.D.	2.88	1.04
'p'	0.0001 Significant	

Table 14. Duration of Post-Op Analgesia (Minutes)

Complication	Group M		Group S		'p'
	No.	%	No.	%	
N.V.					
Yes	-	-	1	2.9	0.5 Not
No	35	100	34	97.1	Significant
Pruritus					
Yes	3	8.6	4	11.4	0.5 Not
No	32	91.4	31	88.6	Significant
Any Disturbances					
Yes	-	-	-	-	1.0 Not
No	35	100	35	100	Significant

Table 15. Complications

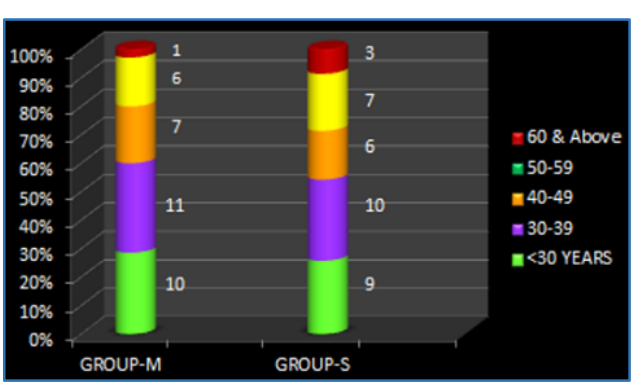

Figure 1. Age Distribution

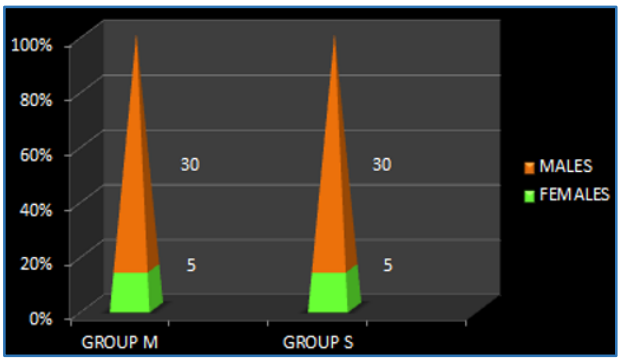

Figure 2. Sex Distribution

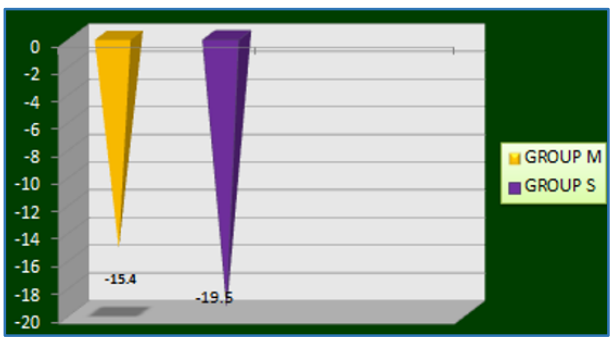

Figure 3. Percentage of Changes in Pulse Rate

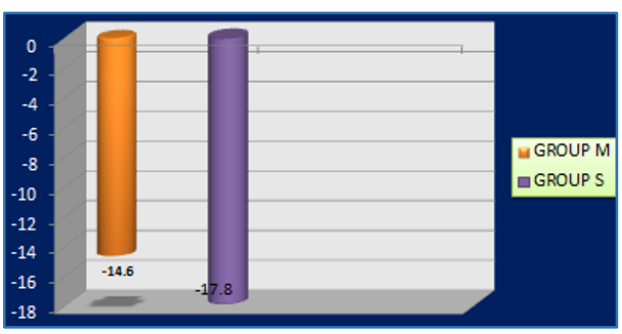

Figure 4: Percentage of Changes in Blood Pressure

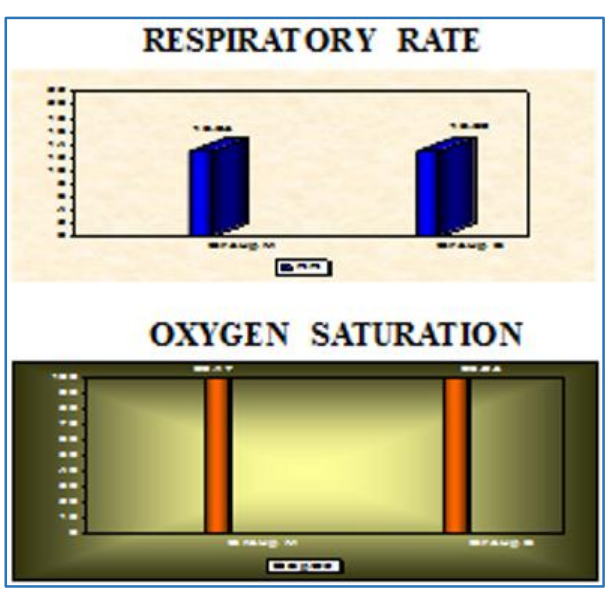

Figure 5. Respiratory Rate and Oxygen Saturation

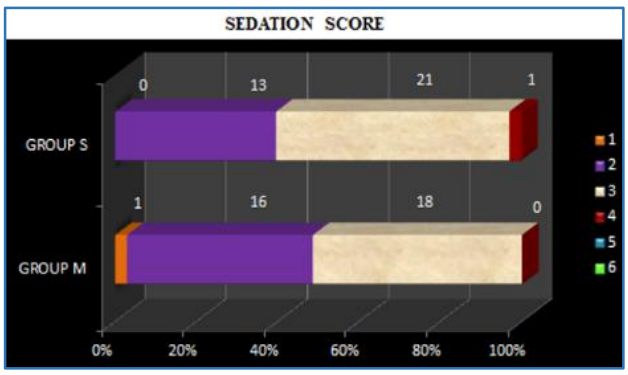

Figure 6. Sedation Score

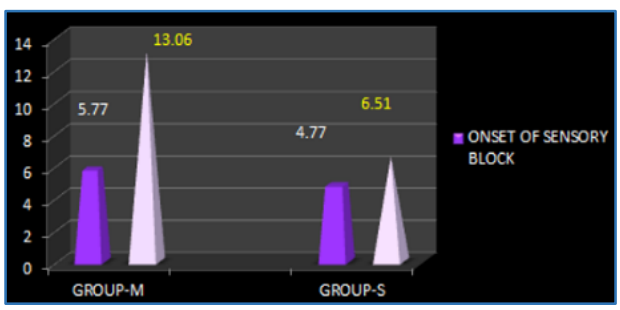

Figure 7. Onset of Sensory Block and Time of Maximum Sensory Level (In Minutes)

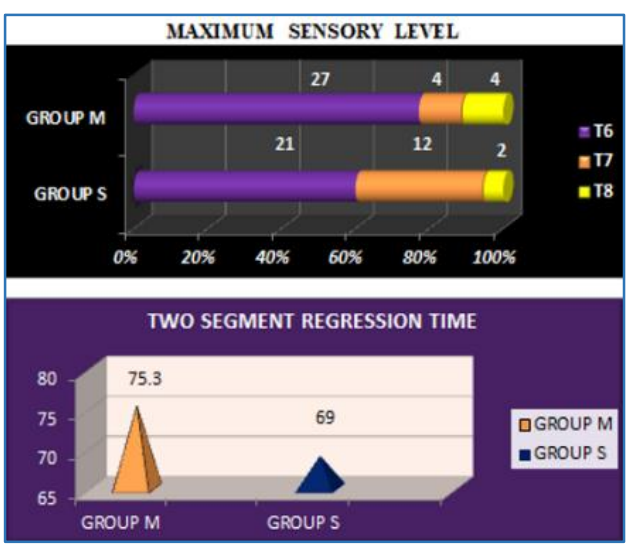

Figure 8. Maximum Sensory Level

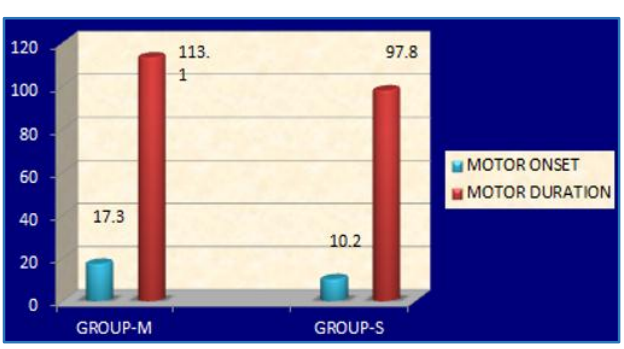

Figure 9. Onset and Duration of Motor Blockade

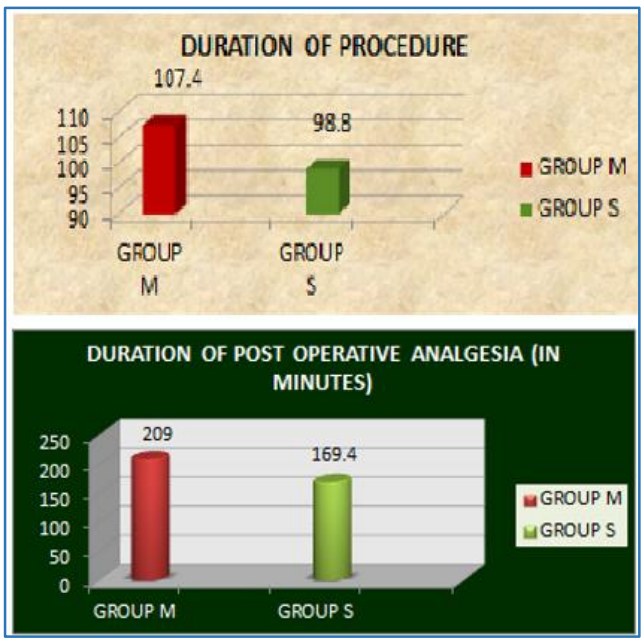

Figure 10. Duration of Procedure and Duration of Post-Operative Analgesia (In Minutes)

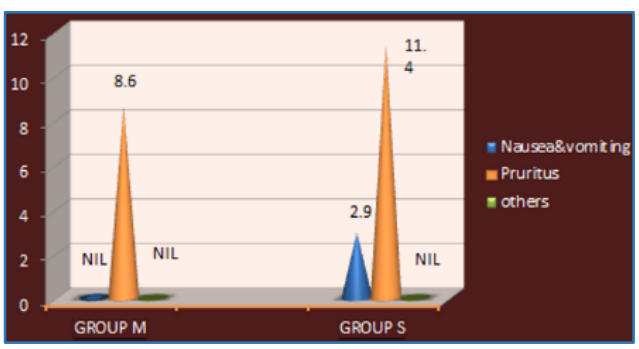

Figure 11. Complications

DISCUSSION

The pain we perceive after a burn, bite (or) pinch is readily identifiable but difficult to define, because it is differently perceived at different threshold.

Pain is defined as psychical adjunct of protective reflex by Sherington in 1906.

The International Association of Society for Pain (IASP) defined it as "An unpleasant sensory and emotional experience associated with actual (or) potential tissue damage (or) described in terms of such damage."

The use of opioids to control pain exists even in ancient history and opioids are still the primary analgesic chosen for severe pain. But adding magnesium sulphate to Bupivacaine-Fentanyl spinal anaesthesia prolong the post-operative analgesia in a different mechanism, mainly by NMDA blockade.

Advantages of Intrathecal Magnesium in this Study

The main finding of this study is that in patients undergoing lower extremity surgery under bupivacaine-fentanyl spinal anaesthesia, the addition of 50 mg IT MgSO4 led to a significant delay in the onset of both sensory and motor blockade and prolonged the duration of spinal anaesthesia without increasing side effects.[9,10,11,12]

The delay in onset observed in this study with IT magnesium during IT bupivacaine and fentanyl has not been reported previously except Ozalevli et al. It is possible that the solution to which MgSO4 was added had a different pH, which might explain our findings. However, we cannot offer a satisfactory explanation for this delay and further studies are needed.

Duration of Post-Op Analgesia

The mean duration of spinal anaesthesia was significantly prolonged by magnesium[13,14,15,16,17] to 209 mins., compared with 169.4 mins. in Group S, which is consistent with the findings of Buvanendran et al[(4)] and Ozalevli et al.

Two-Segment Regression Time

Two-segment regression time was significantly prolonged in Group M "P" 0.0001.

Haemodynamics

The haemodynamics were stable in Magnesium group than Group S (P - 0.0001). This observation is similar to et al.

Sedation

There is no significant difference between two groups.

Pruritus

The incidence of pruritus in Group M is 8.6% and in Group S is 11.4%. Nausea and vomiting was found in one case in Group S.

Respiratory Depression

The use of IT opioids is associated with the risk of respiratory depression.[18,19,20] However, fentanyl, a lipid-soluble opioid binds fairly rapidly with the opioid receptors in the dorsal horn of the spinal cord leaving only small amounts of substance for cephalad migration to the fourth ventricle in contrast with the less lipid-soluble morphine. Varassi et al[(19)] reported that the subarachnoid administration of 25 mg of fentanyl during spinal anaesthesia in non-premedicated men did not cause early respiratory depression in elderly patients. An increased risk of respiratory depression in labouring. No case had respiratory depression intraoperatively as well as in post-operative period in this study. In this study, the respiratory rate remained unchanged with the baseline.

The safety of IT magnesium administration has been evaluated in animal and human studies. In rats, boluses of magnesium produced transient motor and sensory block with no adverse clinical or histological consequences. In a randomised, controlled canine study, no neurological deficit or change in cord histopathology was reported following IT magnesium administration (45 - 60 mg). A recent human study found no deleterious effects of IT magnesium on spinal opioid analgesia in labouring parturients. Thus, IT MgSO4 seems to have a good safety profile.[21,22,23,24,25]

The dose of magnesium used in this study was based on data from Buvanendran et al and Ozalevli et al, where 50 mg of IT MgSO4 potentiated fentanyl antinociception. Larger doses have also been used. In 1985, Lejuste[(17)] described the inadvertent IT injection of 1000 mg of MgSO4 producing a dense motor block followed by complete resolution within 90 mins. with no neurological deficit at long-term followup. Further investigation is required to determine whether larger doses of magnesium produce greater potentiation of spinal analgesia without causing any neurological deficit when administered intrathecally.

CONCLUSION

This study is conducted in patients aged 20 - 65 years. Magnesium sulphate is added intrathecally in the dose of 50 mg to Bupivacaine Fentanyl spinal anaesthesia for lower extremity surgeries.

Magnesium sulphate delayed the onset of both sensory and motor blockade and prolonged the duration of anaesthesia; in Group M the haemodynamics were stable with significant prolongation of post-operative analgesia than other group.

In Group F 11.8% of the patients had intraoperative discomfort who needed supplemental intravenous analgesia.

From this study, it was concluded that in patients undergoing lower extremity surgery, IT MgSO4 (50 mg), when added to spinal anaesthesia induced by bupivacaine and fentanyl, delayed the onset of both sensory and motor blockade and prolonged the duration of anaesthesia without increasing the incidence of side effects.

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