To determine the effects of addition of magnesium sulphate to Bupivacaine – fentanyl spinal anaesthesia with respect to sensory and motor blockade

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Abstract:

Background: One of the recent additions to the list of adjuvants that are used intrathecally, is Magnesium. It may improve the quality and duration of spinal anaesthesia. It acts by blocking the N-methyl-D-asparate (NMDA) channels in a voltage dependent way, reducing NMDA – induced currents. While the systemic use of Magnesium sulphate (MgSO4) reduces the postoperative opioid requirements, its intrathecal use is not evaluated extensively.

Objectives: To determine the effect of addition of magnesium sulphate to Bupivacaine – fentanyl spinal anaesthesia with respect to onset of sensory and motor blockade, duration of analgesia and adverse effects if any.

Methods: A prospective non-randomized controlled study was designed to compare the effects of addition of 50 mg of Magnesium sulphate (MgSO4) to Bupivacaine – fentanyl spinal anaesthesia. All adult patients undergoing lower abdominal and lower limb surgeries under Spinal Anaesthesia in the department of anaesthesiology at Vijayanagar Institute of Medical Sciences (VIMS), Bellary were included in the study.

Results: The mean onset of sensory and motor blockade, peak sensory time were comparable between the two groups ($p>0.05$) however there was statistically significant difference between the groups with respect to duration of analgesia (128±8.6 min in fentanyl group and 136±13.1 min in fentanyl magnesium group, $p=0.001$) and the sedation score ($p=0.001$).

Conclusions: Addition of magnesium sulfate (50 mg) to intrathecal fentanyl (25 μg) for elective lower abdominal and limb surgeries has prolonged the duration of fentanyl analgesia without any significant side effects.

Keywords: Bupivacaine, Fentanyl, Spinal anaesthesia, Sensory and motor blockade

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Introduction

Spinal anaesthesia is a very old and well established anaesthetic technique that is simple to perform and has a high success rate and a good safety profile. This technique grew safer over the decades as our understanding of the anatomy and physiology as well as the characteristics of the drugs used for spinal anaesthesia improved. Opioids such as Fentanyl and Sufentanil are commonly added to local anaesthetics to produce spinal anaesthesia. But prominent adverse effects such pruritis, urinary retention, respiratory depression, haemodynamic instability and occasionally severe nausea and vomiting may limit their use.[1-3]

One of the recent additions to the list of adjuvants that are used intrathecally, is Magnesium. It may improve the quality and duration of spinal anaesthesia.[4] It acts by blocking the N-methyl-D-asparate (NMDA) channels in a voltage dependent way, reducing NMDA – induced currents.[5] While the systemic use of Magnesium sulphate (MgSO4) reduces the postoperative opioid requirements, its intrathecal use is not evaluated extensively.[6]

Thus a prospective non-randomized controlled study was designed to compare the effects of addition of 50 mg of Magnesium sulphate (MgSO4) to Bupivacaine – fentanyl spinal anaesthesia.

Methodology

A prospective non-randomized controlled study was designed to compare the effects of addition of 50 mg of Magnesium sulphate (MgSO4) to Bupivacaine – fentanyl spinal anaesthesia. All adult patients undergoing lower abdominal and lower limb surgeries under Spinal Anaesthesia in the department of anaesthesiology at Vijayanagar Institute of Medical Sciences (VIMS), Bellary were included in the study. The study period was from April 2007 to March 2008. After obtaining clearance form VIMS Institutional ethical committee, 100 patients of either sex, prospectively were considered for the study.

Inclusion Criteria

a. Patients belonging to ASA I and II
b. Age between 18 and 45 years of either sex
c. Patients undergoing lower abdominal and lower limb surgeries

Exclusion Criteria

a. Patient refusal
b. Age less than 18 years and more than 45 years

c. ASA grade III and Above
d. Contraindications to Spinal Anaesthesia

All patients in the study or responsible attendant were explained about the study and the procedure and written consent was obtained. All the patients were thoroughly evaluated clinically to rule out any contraindications to the procedure. Routine laboratory investigations were ordered and included

- Blood grouping,
- Rh Typing,
- Haemoglobin percentage,
- Blood sugar levels,
- Blood Urea,
- Serum Creatinine and
- Urine examination.

Any other specific investigations if needed were asked for.

Anaesthetic Procedure

All patients were secured with 20 G Intravenous catheter on the dorsum of the left hand and were preloaded with 10ml/kg of Ringer lactate solution before institution of Spinal Anaesthesia. All patients were administered Inj. Midazolam 0.04mg/kg intravenously as premedication. Basal parameters recorded were Pulse rate, Oxygen saturation (SaO2), Systolic Blood Pressure (SBP), Diastolic Blood pressure (DBP), Mean arterial Pressure (MAP) and Electrocardiogram (ECG). After preloading, patients were placed in the lateral position and the back was painted with betadine and alcohol solutions and draped. Lumbar puncture was done in either L3- L4 or L4 –L5 interspace by midline approach using 23G Quinke needle and intrathecal space was identified by free flow of cerebrospinal fluid from the needle hub. Patients were randomly divided in to two groups Fentanyl (P) and Fentanyl Magnesium (M). "P" group received 2 ml of 0.5% Bupivacaine Hydrochloride, 0.5 ml (25µg of Fentanyl) and 0.5 ml of NS (Normal Saline) [Total volume of 3ml]. 'M' group received 2ml of 0.5% Bupivacaine Hydrochloride, 0.5ml (25µg of Fentanyl) and 0.5ml (50mg) of Magnesium Sulphate [Total volume of 3ml].

Onset and duration of sensory and motor blockade, highest level of sensory blockade attained, time to reach the highest dermatomal level of sensory blockade, time to complete recovery of the motor blockade and the duration of spinal anaesthesia were noted.

The above parameters were described as follows:

1. *Onset of blockade: The time interval from point of intrathecal injection of the study drug to the onset of either sensory or motor blockade.*
2. *Highest level of sensory blockade: The maximum sensory level achieved after the intrathecal injection.*
3. *Time to attain highest level of sensory blockade: the time interval from the onset ofsensory blockade to the time of attainment of maximum level of sensory blockade.*
4. *Duration of analgesia: The time from the onset of the sensory blockade to the first complaint of pain.*

Pulse, oxygen saturation, systolic blood pressure, diastolic blood pressure, mean arterial pressure and Electrocardiogram(ECG) were monitored at various intervals. Any adverse effects were also noted. After 30 minutes of monitoring in PACU patients were transferred to post-operative ward. Patients' first analgesic requirement time were recorded. Adverse events related to drug were observed for 24 hrs.

Statistical Methods: Descriptive statistical analysis was carried out. Results obtained on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. Student t test (two tailed, independent) is used to find the significance of study parameters on continuous scale between two groups Chi-square/ Fisher Exact test are used to find the significance of study parameters on categorical scale between two or more groups.[7-9]

Results

Table 1: Age wise distribution of the study subjects among the two groups

Age group	Group P	Group M	Total
18 – 25 years	16 (32%)	14 (28%)	30 (30%)
26 – 33 years	10 (20%)	16 (32%)	26 (26%)
34 – 41 years	16 (32%)	10 (20%)	26 (26%)
42 – 47 years	08 (16%)	04 (08%)	12 (12%)
48 – 55 years	0 (0%)	06 (12%)	06 (06%)
Total	50 (100%)	50 (100%)	100 (100%)

Chi-square: 5.09, df-4, p value-0.21 (not significant)

Majority (80%) of the patients of either group were in the age range of 18 to 40 years and there was no statistically significant difference in the age distribution of the patients among the two groups.

Table 2: Comparison of anthropometric measurements among the two groups

Parameters	Group P	Group M	P value*
	Mean ± SD	Mean ± SD	
Height (cms)	168.2 ± 4.5	169.6 ± 5.3	0.57
Weight (Kgs)	59.08 ± 9.5	61.14 ± 7.9	0.08

*Independent t test is applied

The mean height was 168.2±4.5 cms in the fentanyl group (P group) and 169.6±5.3 cms in the fentanyl magnesium group (M group) and not statistically significant (P value = 0.57). The average weight of patients in Group P was 59.08±9.5 kgs and 61.14±7.9 kgs in Group M and was comparable and not statistically significant (P value = 0.08).

Table 3: Comparison of outcome variables among the two groups

Outcome variables	Group P	Group M	P value*
	Mean ± SD	**Mean ± SD**	
Onset of Sensory blockade (min)	7.38 ± 3.6	7.42 ± 3.0	0.81
Onset of Motor blockade (min)	9.92 ± 3.6	10.39 ± 3.2	0.59
Analgesia duration (min)	128.40 ± 8.6	136.80 ± 13.1	0.001
Peak sensory time (min)	8.12 ± 3.1	8.63 ± 2.7	0.67
Sedation Score	2.03 ± 0.2	3.02 ± 0.2	0.001

*Independent t test is applied

The mean duration of onset of sensory blockade from the time of intrathecal injection was 7.38±3.6 minutes in fentanyl group (P group) and 7.42±3.0 minutes in fentanyl magnesium group (M group) and was comparable between the two groups and was not statistically significant (P > 0.05). The mean time of onset of motor blockade was 9.92±3.6 minutes in fentanyl group(Group P) and 10.39±3.2 minutes in the fentanyl magnesium group (Group M) and was not statistically significant (P >0.05).

The mean time to attain peak sensory levels was 8.12±3.1 min in the fentanyl group (P) and was 8.63±2.7 min in the Fentanyl Magnesium group (M) and was not statistically significant.

The mean sedation scores were 2.03±3.1 and 3.02±0.2 in the fentanyl group and fentanyl magnesium group respectively which was statistically significant with a p value of 0.001.

The mean duration of analgesia was 128±8.6 min in the fentanyl group and 136±13.1 min in the fentanyl magnesium group. The mean duration of analgesia was certainly prolonged in the fentanyl magnesium group of patients and was statistically significant when compared to fentanyl alone group.(p value = 0.001).

Table 4: Comparison of adverse effects among the two groups

Adverse effects		Group P	Group M	P value*
Nausea				
	Yes	08 (16%)	08 (16%)	1.00
	No	42 (84%)	42 (84%)	
Vomiting				
	Yes	0 (0%)	0 (0%)	-
	No	50 (100%)	50 (100%)	
Shivering				
	Yes	14 (28%)	06 (12%)	0.15
	No	36 (72%)	44 (88%)	
Pruritis				
	Yes	06 (12%)	14 (28%)	0.15
	No	44 (88%)	36 (72%)	
Urinary retention				
	Yes	0 (0%)	02 (04%)	0.31
	No	50 (100%)	48 (96%)	

Only 8 (16%) patients in both the groups had nausea and were not statistically significant. Likewise adverse effects like vomiting (0% in either groups), shivering (28 % in fentanyl group and 12 % in fentanyl magnesium group), pruritis (12% in fentanyl group and 28 % in fentanyl magnesium group), urinary retention (0% in fentanyl group and 4% in the fentanyl magnesium group) were comparable and not statistically significant with a p value of >0.05.

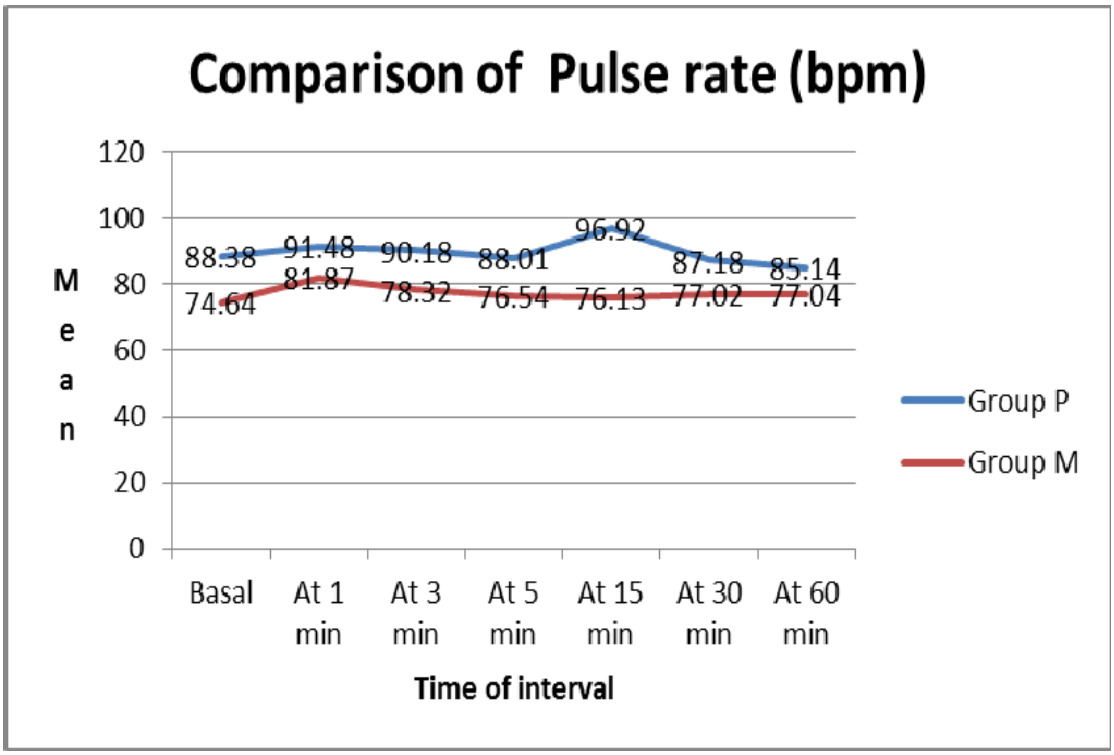
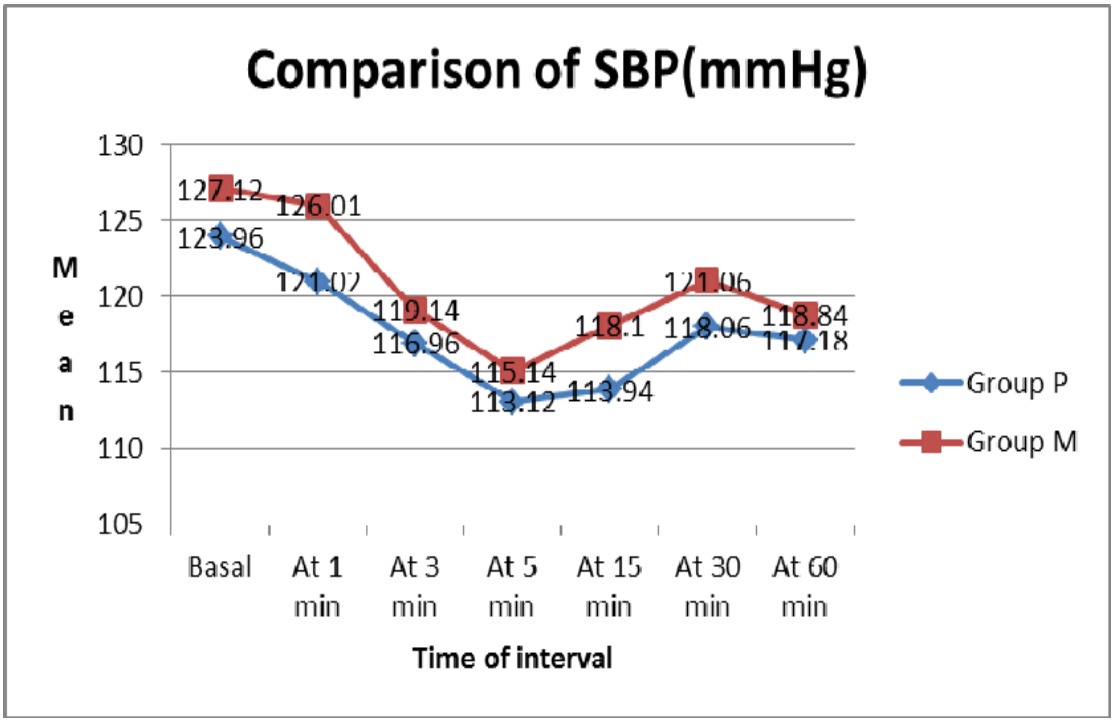


Fig. 1



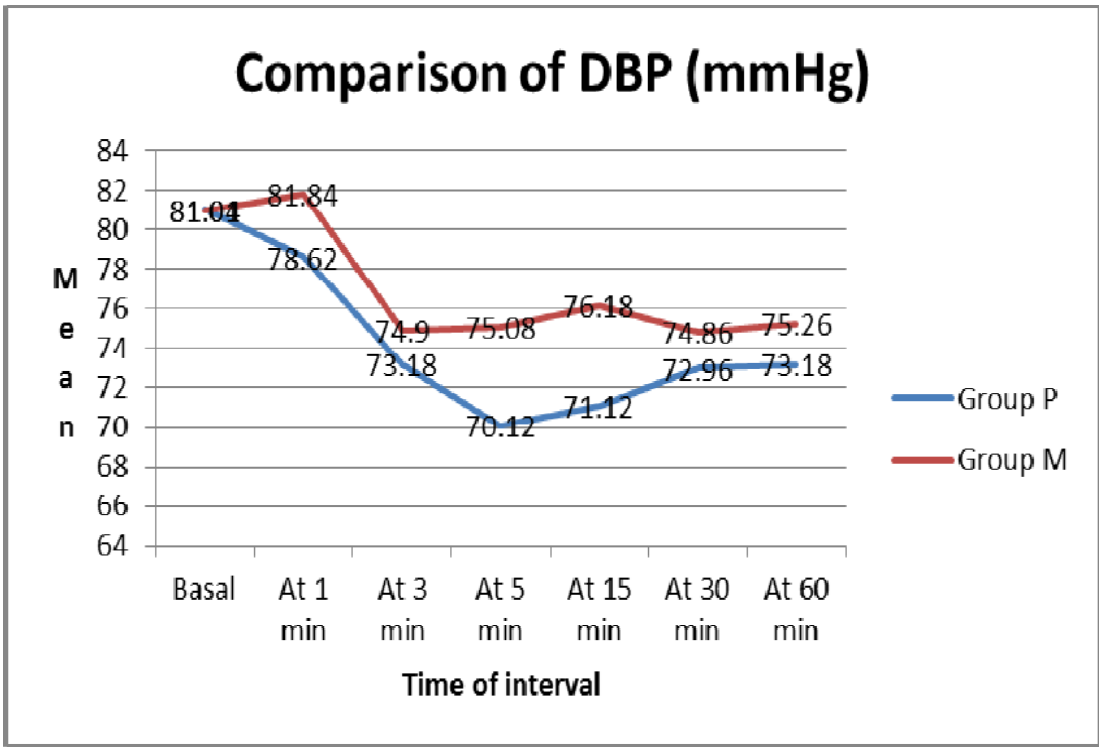


Fig. 2: Comparison of systolic and diastolic BP among the two gorups

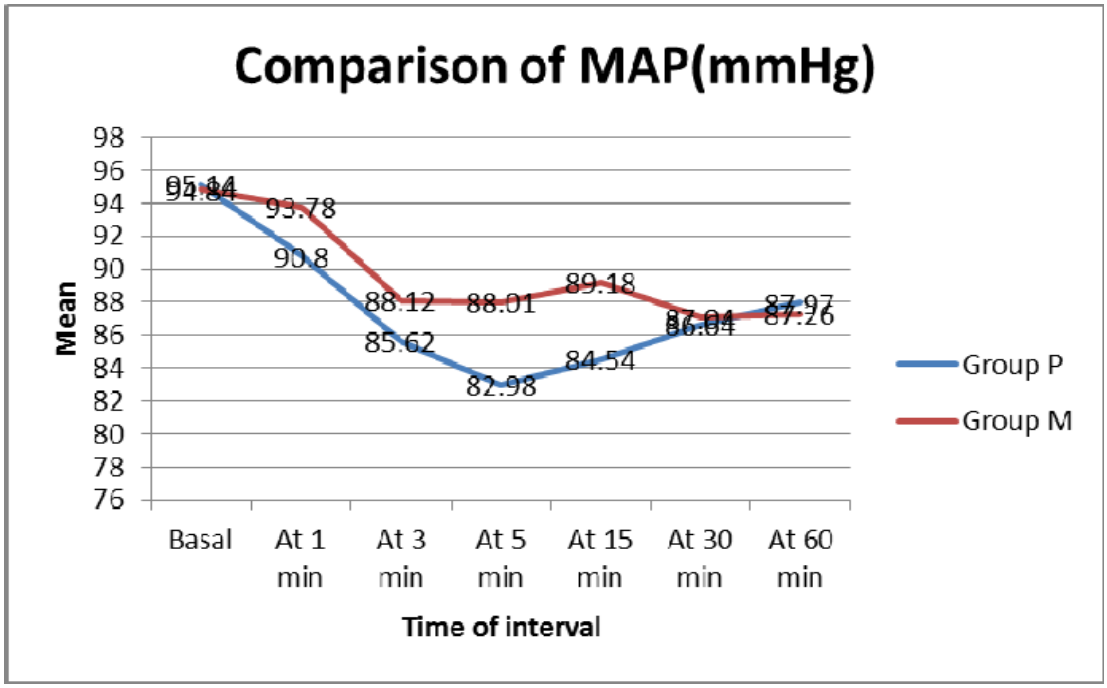


Fig. 3

The mean basal pulse rate was 88.38±12.4 per minute in the Fentanyl group and 74.64±13.8 per minute in the Fentanyl Magnesium group and was statistically significant (p value of 0.001). Similarly the mean pulse rate at all-time intervals i.e, at 1 min, 3 min, 5 min, 15 min, 30 min and 60min between the two groups were statistically significant (p value < 0.05).

The average basal systolic blood pressure (SBP) was 123±11.9 mmHg in the Fentanyl group and 127±15.1 mmHg in the Fentanyl Magnesium group and was not statistically significant. Similarly the SBP at all other time intervals i.e 1 min ,3 min , 5 min, 15 min, 30 min and 60 min in both the groups were comparable and not statistically significant (p value > 0.05).

The average basal diastolic blood pressure (DBP) in the fentanyl group was 81.04±9.3 mmHg and 81.01±9.0 mmHg in the Fentanyl Magnesium group and was comparable and was not statistically significant. While the DBP was comparable at all other time intervals (1min, 15min, 30min, 60 min) and was not statistically significant ,but was statistically significant at 3 min and 5 min time interval.

The average basal mean arterial pressure was 95.14±8.6 mmHg in the fentanyl group and 94.84±11.8 mmHg in the Fentanyl Magnesium group and was comparable and not statistically significant (p value of 0.91). The mean arterial pressure was comparable at all other time intervals i.e, 1min, 3 min, 5min, 15 min, 30 min and 60 min and were not statistically significant (p value > 0.07).

Discussion

Spinal anaesthesia is the one of the simplest and most reliable regional anaesthetic techniques and provides a useful technique of choice for surgeries involving lower abdomen and lower limbs. There has been a significant transformation in the choice of local anaesthetics for use during spinal anaesthesia and the adjuvant that are used along with local anaesthetics for intrathecal use.

Opioids such as Fentanyl and Sufentanil are commonly added to local anaesthetics to produce spinal anaesthesia. But prominent adverse effects such pruritis, urinary retention, respiratory depression, haemodynamic instability and occasionally severe nausea and vomiting may limit their use.[1-3]

Fewer studies[10,11] have compared the addition of magnesium sulphate as an adjuvant to local anaesthetic especially hyperbaric bupivacaine and we undertook this prospective randomized controlled study to evaluate any advantages with the addition of magnesium to bupivacaine fentanyl spinal anaesthesia.

M.Ozalevli et al[11] in their study had used 50 mg of intrathecal magnesium added to hyperbaric bupivacaine - fentanyl combination in patients undergoing lower extremity surgery. **A Buvanendran** et al[4] studied the effect of adding magnesium (50mg) to fentanyl intrathecal analgesia in labouring patients as part of combined spinal – epidural technique. **S.Malleeswaran** et al[12] in their study of sixty women of mild preeclampsia undergoing caesarean section have used 0.1ml of 50% magnesium sulphate (50 mg) along with bupivacaine – Fentanyl combination.

Based on the above studies, we fixed the intrathecal dose of fentanyl at 25 µg. Though higher doses did not cause any major side effects, we preferred to use a smaller dose of spinal magnesium doses of 50 mg, that would not cause any side effects36. And we undertook a study in 100 ASA I/ II patients posted for elective lower abdominal and lower limb surgeries with 50 patients in each group, Group P (fentanyl) and Group M (fentanyl+ magnesium).

The demographic criteria were noted and various study parameters such as onset of sensory and motor blockade, peak sensory level attained, duration of analgesia, hemodynamics and side effects were noted and compared among the two groups.

Age and gender distribution: In the present study both groups were comparable with respect to age (Group P 40.92 yr, Group M 39.6 year, p=0.583) and sex (both groups having 36 males and 14 females, p=1).

Study parameters: The mean duration of onset of sensory blockade from the time of intrathecal injection was 7.38±3.6 minutes in fentanyl group (P group) and 7.42±3.0 minutes in fentanyl magnesium group (M group) and was comparable between the two groups and was not statistically significant (P > 0.05). The mean time of onset of motor blockade was 9.92±3.6 minutes in fentanyl group(Group P) and 10.39±3.2 minutes in the fentanyl magnesium group (Group M) and was not statistically significant (P >0.05). Highest level of sensory blockade achieved in both the groups was T6 and statistically similar between the groups (p=0.324). Time taken for highest sensory level was comparable in both the groups.

Duration of Analgesia*:* In the present study, there was significant prolongation of duration of analgesia in Group M (137 min) compared to Group P (128 min) with p < 0.001. Out of 50 patients in Group P maximum duration of analgesia was 150 min and minimum was 115 min with a Mean of 128.0 and SD of 8.6. In Group M maximum duration of analgesia was 180 min and minimum was 112 min with a Mean of 137 min and SD of 13.3. Noxious stimulation leads to the release of neurotransmitters, which bind to various subclasses of excitatory amino acid receptors, including NMDA receptors. NMDA receptor signalling may be important in determining the duration of acute pain.[13] Therefore, NMDA receptor antagonists may play a role in the prevention and treatment of post-injury pain. Magnesium blocks calcium influx and non-competitively antagonizes NMDA receptor channels.[14] Mg can have an effect on pain when used alone, but it has also been shown that it can reveal the analgesic properties of opioids.[15] In this way the co-administration of magnesium and an opioid is expected to prolong fentanyl analgesia. Our results were comparable with that of M Ozalevli et al[11] who had a similar duration of analgesia of 155 (130 – 220) min in Group S and 173 (130 – 240) min in the Group M who also showed statistically significant increase in the duration of analgesia with the addition of magnesium to Bupivacaine fentanyl intrathecal use. A Buvanendran et al,[4] in their study fifty patients found that addition of Magnesium sulphate to intrathecal fentanyl has significantly prolonged the duration of analgesia in labouring parturients (Group FM 75min with a range of

30 – 140 min Vs Group F 60 min with a range of 25 – 133 min) . This study is also in concurrence with findings of our study.

Onset and level of sensory and motor blockade: In study conducted by M Ozalveli et al,[11] where they used intrathecal Bupivacaine- fentanyl in Group S and Bupivacaine-fentanyl with 50 mg Magnesium in Group M , they found that the median time to reach the highest dermatomal level of sensory block was 17 min in Group M and 13 min in Group S and found to be statistically significant.($p < 0.05$) . The mean degree of motor blockade was also lower in Group M at 5,10 and 15 min ($P < 0.001$) and was statistically significant when compared to Group S. Also they found that the median duration of spinal anaesthesia was longer in the group M ($P < 0.001$).

The onset of sensory blockade in our study was 7.38±3.6 minutes in fentanyl group (P group) and 7.42±3.0 minutes in fentanyl magnesium group (M group) and was not statistically significant which correlates well with the study by M.Ozalevli et al[11] (12.5± 3.8 in Group S vs 16.5±2.4 in Group M). Slight prolongation in the onset of the sensory blockade in the above study could be because of use of median instead of mean time of onset.

Our study has shown that there was prolongation in the time to attain peak sensory levels in the Magnesium group, Group M (8.63± 2.7 vs 8.12 ±3.1in group P) though it was not statistically significant which correlates well with the above study although the duration to attain peak sensory level was prolonged slightly .

Haemodynamic changes: Right from the start of the study the pulse rate was significantly higher in the fentanyl group of patients (Fig no. 1-3) when compared to the patients in the Fentanyl Magnesium group. Significant difference in the pulse rate either group of patients could be because of significant effects of magnesium on the Heart. This observation was not statistically significant in the studies by M. M Ozalevli et al,[11] A Buvanendran et al,[4] and S. Malleeswaran et al.[12]

The other parameters like Systolic blood pressure (SBP), Diastolic Blood Pressure (DBP) and Mean arterial pressure (MAP) were comparable in the two groups in our study and not statistically significant which correlates well with the studies mentioned above. Thus addition of 50 mg of magnesium sulphate to intrathecal bupivacaine fentanyl is not associated with significant variations in the cardiorespiratory variables like HR, SBP, DBP, MAP SpO2 and RR.

Adverse effects: Only 8 (16%) patients in both the groups had nausea and were not statistically significant. Similarly 14 patients in fentanyl group and 6 patients in fentanyl magnesium group had shivering, pruritis (12% in fentanyl group and 28 % in fentanyl magnesium group), urinary retention (0% in fentanyl group and 4% in the fentanyl magnesium group) were observed. These adverse effects were not statistically significant and comparable. Neither there were differences in the incidence of these side effects between the groups in the above mentioned studies, nor were any additional adverse events.

Many authors have studied the role of Mg for intrathecal and postoperative analgesia. Buvanendran et al,[4] demonstrated in pregnant women that, if Mg 50 mg and fentanyl 25 µg were given intrathecally, the median duration of analgesia was significantly prolonged compared with plain intrathecal fentanyl. Similarly, in another study by Ozalevli et al,[11] it is reported that the addition of intrathecal magnesium 50 mg to spinal anaesthesia prolongs the period of anesthesia without additional side-effects. Bilir et al,[16] showed that epidural administration of magnesium reduced postoperative epidural fentanyl consumption in comparison with the saline group. Arcioni et al,[17] also showed that epidural magnesium supplementation of spinal anaesthesia has reduced postoperative morphine requirements.

Conclusion

Addition of magnesium sulfate (50 mg) to intrathecal fentanyl (25 µg) for elective lower abdominal and limb surgeries has prolonged the duration of fentanyl analgesia without any significant side effects.

Limitation

The present study has certain limitation. The dose of magnesium used was decided on the dose used in the previous studies and not on the patient's factors. Preoperative magnesium levels were not recorded as it can affect the pharmacodynamics of the intrathecal magnesium.

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