Original Article

A comparative study of intrathecal magnesium sulphate with Bupivacaine and Fentanyl versus intrathecal Bupivacaine and Fentanyl for spinal anaesthesia in patients undergoing lower abdominal oncosurgeries

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Abstract

Background: Spinal anaesthesia is used widely and safely over 100 years especially for operations involving the lower abdomen and perineum. Although hyperbaric Bupivacaine 0.5% is extensively used intrathecally, it does not produce prolonged postoperative analgesia. Hence, opioids like morphine and fentanyl which have synergistic effects are used for prolonged postoperative analgesia. Non-opioid adjuvant drugs like Magnesium sulphate are becoming increasingly popular approaches for perioperative pain management. **Aims and Objectives:** The present study was carried out to know the effects of adding intrathecal magnesium sulphate to Bupivacaine and Fentanyl on the onset of sensory and motor blockade as well as its maximum level and the time taken to achieve it and the total duration of analgesia. **Methods:** A prospective randomized control study involving 80 adult patients of ASA 1 and 2, satisfying inclusion and exclusion criteria scheduled for elective infra umbilical oncosurgeries was carried out after obtaining institutional ethical Committee approval at Kidwai Memorial Institute of Oncology, Bangalore. Forty patients of Group A received Inj. Magnesium Sulphate 50 mg (0.1ml) +inj 0.5% bupivacaine heavy15mg (3ml)+Inj Fentanyl 20 mcg (0.4ml) intrathecally. 40 patients of Group B received 0.1ml of Normal saline + inj 0.5% bupivacaine Heavy 15mg (3ml)+Inj Fentanyl 20 mcg (0.4ml) intrathecally. Then Sensory and motor blockade assessed, hemodynamic parameters were recorded. Statistical analysis was performed by descriptive statistics to calculate the mean and standard deviation, the t-test, χ^2 tests for calculating the materiality for establishing the results. **Results:** the mean onset time (mins) of both sensory and motor blockade as well as the time to attain highest dermatomal levels were more in Group A compared to Group B and was statistically significant. ($p<0.001$). There was significant difference in the maximum level of sensory block attained between the two groups with Group A attaining mean level of T_7-T_6 and Group B attaining mean level of T_8-T_7 with p value 0.025. The mean duration (mins) of effective analgesia was found to be higher in Group A compared to Group B and the difference between them was statistically significant (p 0.011). **Conclusion:** Though the addition of Magnesium sulphate to Bupivacaine and fentanyl intrathecally delays the onset of sensory and motor blockade, it achieves a higher dermatomal blockade and prolongs the duration of blockade hence is a promising non-opioid adjuvant for prolonged analgesia.

Keywords: Magnesium Sulphate,Non-opioid Intrathecal Adjuvants.

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INTRODUCTION

Subarachnoid block results in temporary interruption of nerve transmission in the affected nerves leaving the spinal cord produced by injection of local anaesthetic into the CSF. Bupivacaine has been used since 1963; Bupivacaine is more potent and has longer duration of action. Though the duration of action of Bupivacaine is prolonged, it will not produce prolonged postoperative

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analgesia. Hence, another adjuvant is required for producing prolonged postoperative analgesia. Since the discovery of opioid receptors and endorphins in spinal and supra spinal regions soon led to the use of spinal opiates. Local anaesthetics supplemented with opioids are found to have synergistic effect.[1,2] Morphine was the first opioid to be used intrathecally in combination with local anaesthetics[1,2] but was associated with slower onset of action and risk of delayed respiratory depression because of its hydrophilic nature. The use of intrathecal fentanyl, a lipophilic opioid, with bupivacaine was described by Hunt *et al* in 1989.[11] It is found to reduce the dose of bupivacaine and there by the incidence of hypotension and nausea, it increases the duration of bupivacaine induced sensory block by 28% and reduces the postoperative analgesic requirement.[3] Techniques involving the smaller doses of opioid in combination with non-opioid adjuvant drugs are becoming increasingly popular approaches for perioperative pain management. Magnesium blocks NMDA channels in a voltage-dependent way, and the addition of magnesium produces a reduction of NMDA-induced currents.[4] By modulating not only ion channels and ion pumps but also receptor signaling, magnesium affects numerous cellular processes. Magnesium inhibits calcium entry into neuronal cell at a variety of calcium channels including as NMDA antagonist.[5] On Peripheral nervous system, it Causes reduced excitability of nerves and prolongs the actions of non depolarising muscle relaxants and local anaesthetics. On Autonomic nervous system it progressively inhibits the release of catecholamines from both adrenergic nerve terminals and adrenal medulla. Thus it has anti-nociceptive effect and has application in anaesthesia**.** The safety of intrathecal magnesium administration has been evaluated and established.[6,7] Fentanyl citrate is a synthetic phenylpiperdine opioid agonist that is structurally related to meperidine.[8,9] Fentanyl is primarily a μ receptor agonist with an analgesic potency greater than morphine. Analgesia is produced principally through interaction with μ receptor at supraspinal site. It also binds to a lesser degree to Kappa receptor, substantia gelatinosa of spinal cord. It is worthwhile to study the role of supplemental magnesium in providing perioperative analgesia**,** because this is a relatively harmless molecule**,** economical and also because the biological basis for its potential anti-nociceptive effect is promising.[10]

MATERIALS AND METHODS

A study was conducted on 80 patients and divided in two groups A and B (40 patients in each group) of physical status ASA I and II, aged between 18 to 55 years, scheduled to undergo elective surgery below the level of umbilicus and who satisfied all the inclusion criteria during period of December 2012 to December 2013 at Kidwai Memorial Institute of Oncology, Bangalore.

Statistical Analysis: Descriptive and inferential statistical analysis was used in our study. Results on continuous measurements were presented on Mean±SD (Min-Max) and results on categorical measurements were presented in Number (%). Student t test (two tailed, dependent) was used to find the significance of study parameters on continuous scale within each group. Chi-square/ Fisher Exact test was used to find the significance of study parameters on categorical scale between two or more groups. Significance was assessed at 5 % level of significance. (P<0.05) and P<0.001 highly significant.

The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, Med Calc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel was used to generate graphs, tables etc**.**

RESULTS

Table 1: Sample distribution according to age group (in years)

	Group A	Group B
Mean ± SD	49.62±9.20	48.67±11.05
p value	0.669	

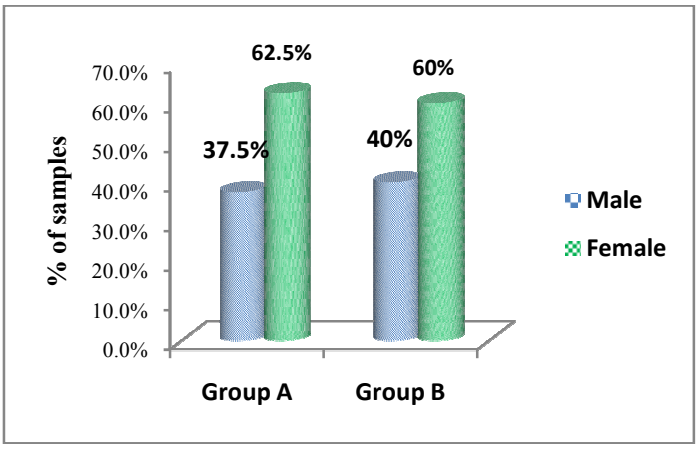

Figure 1: Gender distribution in the groups

Table 2: Time for sensory onset (mins)

Groups	Mean±SD	p value
Group A	6.53±0.80	<0.001*
Group B	4.03±0.94	

Table 3: Mean of maximum sensory level

Groups	Mean±SD	p value
Group A	6.93±1.02	0.025*
Group B	7.55±1.40	

Table 4: Mean time to attain maximum sensory level (mins)

Groups	Mean±SD	p value
Group A	8.83±1.42	<0.001*
Group B	6.09±0.84	

Table 5: Time for motor onset (mins)

Groups	Mean±SD	p value
Group A	6.55±1.39	<0.001*
Group B	4.47±1.01	

Table 6: Duration of effective analgesia (mins)

Groups	Mean±SD	p value
Group A	416.75±72.52	<0.001*
Group B	376.88±64.51	

Table 7: Adverse effects

Adverse effects	Group A		Group B		Total
	#	%	#	%	
Hypotension	2	22.2	1	12.5	3
Bradycardia	3	33.3	1	12.5	4
Nausea	1	11.1	2	25.0	3
Vomiting	0	0.0	0	0.0	0
Shivering	3	33.3	3	37.5	6
Pruritis	0	0.0	1	12.5	1
Total adverse effects	9	22.5	8	20.0	17
p-Value	0.7334				

DISCUSSION

Subarachnoid block is a commonly employed anaesthetic technique for performing lower abdominal and lower limb surgeries. It is a safe, simple, inexpensive, easy-to-administer technique and has rapid onset and is reliable.This technique also offers a high level of post–anaesthesia satisfaction for patients. One of the limitations of spinal anaesthesia is the relative short duration of postoperative analgesia. To increase the duration of anaesthesia and analgesia, many adjuvants like opioids, clonidine, ketamine and neostigmine are added to bupivacaine spinal anaesthesia. But noted side effects such as pruritis, nausea, vomiting and respiratory depression may limit their use. Buvanendran A *et al* (2002) did a randomized controlled trial on 52 patients requesting labour analgesia randomized into one of two study groups: 25mcg of fentanyl citrate (0.5 mL) + 3.0 mL of preservative-free 0.9% sodium chloride injection (Group F) or 25mcg of fentanyl citrate (0.5 mL)+ 50 mg of magnesium sulphate (3.0 mL) (Group F + MAG). The median duration of analgesia after the IT drug administration was significantly longer for Group F +MAG, 75 min (range, 30–140 min), compared with Group F, 60 min (range, 25–133 min).[12] Lee JW *et al* (2007) did a study on 60 patients enrolled for Total Knee Replacement surgery receiving single dose 100mg of intrathecal magnesium sulphate with 0.5% tetracaine showed that intrathecal magnesium can be used as a local anaesthetic adjuvant to strengthen the analgesic effect of spinal local anaesthetic and to intensify the analgesic effect of epidural local anaesthetic for postoperative pain.[13] Arcioni R *et al* (2007) did a trial on 120 patients undergoing major lower limb orthopedic surgery supplementation of spinal anaesthesia with combined intrathecal and epidural magnesium sulphate patients were randomly assigned to receive intrathecal $MgSO_4$(94.5mg,6.3%), epidural $MgSO_4$(2%, 100 mg/h), intrathecal and epidural $MgSO_4$ combined or spinal anesthesia alone. It significantly reduced patients' postoperative analgesic requirements compared to intrathecal magnesium sulphate, epidural magnesium sulphate and spinal anaesthesia alone.[14] Kerdawy HE (2008) studied the analgesic requirements for patients undergoing lower extremity surgery using magnesium sulphate as an adjuvant in spinal and epidural anaesthesia was studied. 2ml of 0.5% bupivacaine heavy, 25microgram fentanyl with 50mg magnesium sulphate was used intrathecally and epidural infusion of 2% magnesium sulphate at the rate of 100mg per hour. It was concluded that the usage of magnesium sulphate for combined spinal epidural technique would reduce the intra and postoperative analgesic requirements and improve the quality of analgesia.[15] Dayioglu H *et al* (2009) did a randomized, double blind study on 60 ASA 1 / 2 patients who received intrathecal magnesium as magnesium sulphate 50mg with low dose bupivacaine (6mg, 0.5%) and fentanyl (10mcg) combination for knee arthroscopy revealed prolonged time for regression of two segments of maximum block height and prolonged time to first analgesic requirement.[16] Nath MP *et al* (2012) had studied efficacy of intrathecal magnesium sulphate for hysterectomy under subarachnoid block with bupivacaine and fentanyl was evaluated. Group S received 2.5 ml (12.5 mg) of hyperbaric bupivacaine + 0.5 ml (25 mcg) of fentanyl + 0.5 ml of normal saline and Group M received 2.5 ml (12.5 mg) of hyperbaric bupivacaine + 0.5 ml (25 mcg) of fentanyl + 0.5 ml (100 mg) of magnesium sulphate. Addition of 100 mg intrathecal magnesium led to prolonged duration of analgesia significantly without increasing the incidence of side-effects.[17]

Khezri MB *et al* (2012) in a study which compared the postoperative analgesic effect of intrathecal magnesium (100mg) and fentanyl (25µg) added to bupivacaine in patients undergoing lower limb orthopaedic surgery, it was concluded that although magnesium failed to prolong the time to first analgesic requirement as seen with fentanyl, it reduced the total consumption of opioids in

the first 12 hours postoperatively compared with the control group.[18] The present study was intended to know the synergistic effects of Intrathecal magnesium sulphate (50 mg) to a combination of Bupivacaine Heavy and Fentanyl in elective lower abdominal oncosurgeries. There are no statistically significant differences in terms of demographic properties as age, weight, height, gender, type of surgeries, duration of surgery and ASA grading. The mean are comparable in both the groups among demographic parameters and were statistically not significant. The mean onset of sensory blockade was significantly delayed in group A (6.53±0.80) when compared to Group B (4.03±0.94) with p <0.001. These observations concur similar findings in studies by Shukla *et al*[19].(6.46±1.33 vs 4.14±1.06), Nath *et al*[17] (10.1±2.0 vs 5.2±1.1), and Sanad *et al*[20] (4±0.5 vs 3.2±0.8). Significant difference in the maximum level of sensory block attained was noted between Group A (T7-T6) and Group B attaining mean level of T_8-T_7 with p value 0.025. However no such differences were observed in studies conducted by Jong Wha Lee [13] *et al*, Dayioglu *et al*,[16] Sanad *et al*[20]. It was observed that in Group A the time to attain highest dermatomal level was 8.83±1.42 and in Group B it was 6.09±0.84 which shows significant difference in time taken to reach highest dermatomal levels (p value of <0.001). Similar observations were made by Malleeswaran S *et al*[10] Shukla *et al*[19] (7.18±1.38 vs 4.81±1.03), Nath *et al*[17] (16.18 vs 14.3), Malleeswaran S *et al*[10] (5.7±0.7vs 5.1±1.0) studies noted delay in mean onset of motor block in the study group. Similar observations were noted in our study with group A - 6.55±1.39 and group B with 4.47±1.01 which was statistically significant p<0.001. The mean time to rescue analgesia in our study is 416.73±72.52 in Group A and 376.88±64.51 in Group B with p value of 0.011 which is statistically significant which is similar to the findings in studies by Hala el Kerdaway[15](182.8±19.1 vs 164±16.9), Malleeswaran S *et al*[10] (229.3±15.1 vs 187.7±11), Nath *et al*[17] (291.4±18.6 vs 263.9±23.3). However the lesser duration of analgesia in the above mentioned studies when compared to ours can be attributed to less dose of bupivacaine used (6mg, 0.5% bupivacaine) in these studies. Very few postoperative complications were reported total of 9 adverse effects in Group A and total of 8 adverse effects in Group B and were statistically insignificant (p value 0.7334) and were comparable between the two groups and were treated successfully. Similar findings were noted in studies by Malleeswaran *et al*[10] and Sanad *et al.*[20]

CONCLUSION

Addition of non-opiod adjuvants like Magnesium Sulphate to intrathecal Bupivacaine or Bupivacaine and fentanyl combination facilitates attainment of higher dermatomal levels and prolongs the duration of analgesia significantly however it delays the onset of the block. Larger studies involving general population of ASA III and IV may be required to validate its effect.

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