Original research article

A Comparative Study on Effect of Intravenous $MGSO_4$ on Spinal Anaesthesia with Bupivacaine and Buprenorphine

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Abstract

Background: Present clinical study was conducted to study the effects of intravenous Magnesiun Sulphate on spinal anesthesia with Bupivacaine and Buprenorphine,

Methods: After thorough pre anaesthetic evaluation , Pre operative vitals para meters in the form of baseline pulse, blood pressure pulse were recorded. A good venous access was taken. Patient connected to ecg, pulse oximetry, non invasive blood pressure monitoring. Patients randomly allocated into two groups: Group M-50 received 50mg/kg intravenous $MgSO_4$ in 500ml Ringer lactate over 20 mins. Group C-50 received intravenous 500ml Ringerlactate over 20 mins. Both the groups received intrathecal 15mg of Inj.Bupivacaine (0.5%) and 30 mcg of Inj. Buprenorphine.

Conclusion: We conclude that IV bolus dose of magnesium sulfate of 50mg·kg−1 in 500mL of Ringer Lactate solution dose not prolongs the duration of anaesthesia and analgesiawhen given in combination with intrathecal bupivacaine5% and Buprenorphine 30mcg. but itreduces the analgesic consumption and incidence of nausea and vomiting associated with intrathecal Buprenorphine.

Keywords: Buprenorphine, Bupivacaine, Intravenous Ringer Lactate, Magnesium Sulphate.

Introduction

Spinal anaesthesia is the most preferred regional anaesthesia technique as it is easy to perform, produces rapid onset of anaesthesia and complete relaxation and it is also economical. These advantages are sometimes offset by relatively short duration of action andlack of sedation. The aim of intrathecal local anaesthetic is to provide adequate sensory and motor block necessary for infraumbilical surgeries. hyperbaric bupivacaine is the most commonly used intrathecal local anaesthetic. Adjuvants have been used most commonly to shorten the onset of block, prolong the duration of block and provide sedation. Postsurgical pain is one of the most important issues that could impress on postoperative peace and comfort .The major goal in postoperative pain management is to minimize the doseof medications to lessen side effects, while still providing adequate analgesia. Postoperative pain relief leads to earlier mobilization, shortened hospital staying, reduced hospital costs, andincreased patient satisfaction. Narcotics and NSAIDS are the most common analgesics which are used in the post-operative period, but are associated with side effects. Magnesium sulfate is a antiarrhythmic agent for torsades de pointes in cardiac arrest under the ECC guidelines and for managing quinidine-induced arrhythmias. As a bronchodilator after beta-agonist and anticholinergic agents have been tried,

e.g. in severe exacerbations of asthma, magnesium sulfate can be nebulized to reduce the symptoms of acute asthma. It is commonly administered via the intravenous route for the management ofsevere asthma attacks. Magnesium sulfate is effective in decreasing the pre-eclampsia progression to eclampsia. IV magnesium sulfate is used to prevent and treat seizures of eclampsia. It reduces the systolic blood pressure but doesn't alter the diastolic blood pressure, so the blood perfusion to the fetusisn't compromised. It is also commonly used for eclampsia where compared to diazepam or phenytoin it results in better outcomes.Magnesium (Mg) is a non-competitive N-methylD- aspartate (NMDA) receptor antagonist with antinociceptive effects. Preemptive analgesia is a innovative method initiated before surgical injury in order to reducethe physiological consequences of nociceptive stimulation and there adverse effects. It has been defined as an antinociceptive treatment that prevents establishment of altered central processing of afferent input from injuries. One of the intravenous adjuvant that has been shown potential in pre-emptive analgesia is magnesium sulfate, could be administered with multiple routes or methods. One of those ispre-emptive single low dose IV Mg. Mg has been used for many years in anesthesia and cardiology as an anticonvulsant or antiarrhythmic drug. Mechanism of the analgesic effect ofMg is not clear but interference with calcium channels and N-methyl-D-aspartate (NMDA) receptor seem to play an important role. It seems that analgesic mechanism of NMDA- antagonists is made by preventing nociceptive central sensitization. Another suggesting mechanism is the role of it on reduction of catecholamine release with sympathetic stimulation, thereby decreasing peripheral nociception or the stress response to the surgery.

Objectives

To study the effect of intravenous magnesium sulphate 50 mg/kg with intrathecal 0.5%hyperbaric Bupivacaine and buprenorphine 30µg.

Review of Literature

Ko SH et al conducted a study 60 patients undergoing abdominal hysterectomy received 50 mg/kg intravenous magnesium sulfate as a bolus dose followed by a continuous infusion of 15 mg x kg(-1) x h(-1) for 6 h (magnesium group) or the same volume of isotonic saline (control group). They found that despite significantly higher serum magnesium concentrations in the magnesium group, there was no significant difference in magnesium concentration measured in postoperative CSF. Cumulative postoperative analgesic doses were similar in both groups. However, they observed an inverse relation between cumulative postoperative analgesic consumption and the CSF magnesium concentration in both groups. Visual analog pain scores at rest and during forced expiration were similar and less than 4 inboth groups. Concluded that Perioperative intravenous administration of magnesium sulfate did not increase CSF magnesium concentration and had no effects on postoperative pain.

However, an inverse relation between cumulative postoperative analgesic consumption and the CSF magnesium concentration was observed. These results suggest that perioperative intravenous magnesium infusion may not be useful for preventing postoperative pain**.** Apan et al studied Postoperative magnesium sulphate infusion reduces analgesic requirements in spinal anaesthesia they included Fifty ASA I–II patients in the randomized double blind study. Patients received a 5 mg kg−1 bolus of magnesium sulphate followed bya 500 mg h−1 infusion or saline in the same volumes for 24 h. Concluded that Magnesium sulphate infusion may be used as an adjunct for reducing analgesic consumption after spinalanaesthesia. Ozalevli et al conducted a study The effect of adding intrathecal magnesium sulphate tobupivacaine fentanyl spinal anaesthesia 102 ASA I or II adult patients undergoing lowerextremity surgery were recruited and were randomly allocated to receive 1.0 ml of preservative-free 0.9% sodium

chloride (group S) or 50 mg of magnesium sulphate 5% (1.0 ml) (group M) following 10 mg of bupivacaine 0.5% plus 25 µg of fentanyl intrathecally, 24 patients undergoing elective hysterectomy in general anaesthesia receiveda 5 h infusion of either placebo or magnesium laevulinate (initial bolus 8 mmol: then 8 mmol/h) starting with induction of anaesthesia. Results of this study were overall pain scores were similar with magnesium and placebo infusion, although patients in the magnesium groupexperienced more episodes of severe or unbearable pain, Median pain scores were higher in the magnesium group only at 3 h postoperatively (P = 0.04): afterwards there were no significant differences. Except for the first postoperative hour (placebo = 12.8 +/- 4.7 mg, magnesium = 9.3 +/- 3.2 mg, P = 0.04), cumulative morphine consumption was similar. **Bilir et al** conducted a study in which Fifty patients undergoing hip surgery were enrolled toreceive either fentanyl (Group F) or fentanyl plus magnesium sulphate (Group FM) for 24 h for epidural analgesia. All patients were equipped with a patient-controlled epidural analgesiadevice and the initial settings of a demand bolus dose of fentanyl 25 µg. In Group FM, patients received 50 mg magnesium sulphate epidurally as an initial bolus dose followed by a continuous infusion of 100 mg day^{-}. J.-H. Ryu et al, conducted a randomized, double-blind, prospective study to evaluate the effects of magnesium sulphate on anaesthetic requirements and postoperative analgesia in patients undergoing total i.v. anaesthesia (TIVA). They randomly divided Fifty patients who underwent gynecological surgery were into two groups. Before induction of anaesthesia, the magnesium group (Group M) received magnesium sulphate 50 mg kg 2 1 i.v. as a bolus and then 15 mg kg 2 1 h 2 1 i.v. by continuous infusion. Muhammet Gozdemir et al, Magnesium sulfate infusion prevents shivering during transurethral prostatectomy with spinal anesthesia conducted a, double-blind study in 60 patients, aged 40 to 70 years, scheduled for elective transurethral resection of the prostate (TURP) during spinal anesthesia. Subarachnoid anesthesia consisting of hyperbaric bupivacaine three mL 0.5% was injected using a 25-G Quincke spinal needle. Tanmoy Ghatak et al**,** conducted a prospective randomised double-blind study was undertaken to establish the effect of addition of magnesium or clonidine, as adjuvant, to epidural bupivacaine in lower abdominal and lower limb surgeries. 90(ASA) grade I and II patients undergoing lower abdominal and lower limb surgeries were enrolled to receive either magnesium sulphate (Group B) or clonidine (Group C) along with epidural bupivacaine for surgical anaesthesia.

All patients received 19 ml of epidural bupivacaine 0.5% along with 50 mg magnesium in group B, 150 mcg clonidine in Group C, whereas in control group (Group A), patients received same volume of normal saline ,and concluded that co-administration of epidural magnesium with bupivacaine produces predictable rapid onset of surgical anaesthesiawithout any side-effects, and addition of clonidine to epidural bupivacaine produces, Shukla et al conducted a comparative study of intrathecal dexmedetomidine with intrathecal magnesium sulfate used as adjuvants to bupivacaine A total of 90 patients of ASAstatus I andII scheduled for lower abdominal and lower limb procedures were prospectively studied they randomly allocated Patients to receive intrathecally either 15 mg hyperbaric bupivacaine plus 0.1 ml (10 µg) dexmedetomidine (group D, *n*=30) or 15 mg hyperbaric bupivacaine plus 0.1 ml (50 mg) magnesium sulfate (group M, *n*=30) or 15 mg hyperbaric bupivacaine plus 0.1 mlsaline (group C, *n*=30) as control. Concluded that it was found that onset of anesthesia was rapid and of prolonged duration in the dexmedetomidine group (D). In 1764, Cotungo described the presence of a collection of water around the brain and inside the spinal column. In 1825, Magendie was credited with appreciating that this fluid circulated around the brain and spinal column.

Material and methods

The Patients admitted to Nalanda medical college and Hospital Patna, Bihar. Study duration of two years. undergoing infraumbilicalsurgeries under subarachnoid block, After thorough pre anaesthetic evaluation , Pre operative vitals para meters in the form of baseline pulse, blood pressure pulse were recorded. A good venous access was taken. Patient connected to ecg, pulse oximetry, non invasive blood pressure monitoring. Patients randomly allocated into two groups: Group M-50 received 50mg/kg intravenous $MgSO_4$ in 500ml Ringer lactate over 20 mins. Group C-50 received intravenous 500ml Ringerlactate over 20 mins. Both the groups received intrathecal 15mg of Inj.Bupivacaine (0.5%) and 30 mcg of Inj. Buprenorphine.

Inclusion criteria:

ASA physical status I and II, Patients weighing 50-70kg,measuring 150-170cm height with body mass index18-35/m2, Age less than 60 years of either sex.

Exclusion criteria*:*

History of allergy to the local anaesthetic or any of the study drug Spinal deformities, Contraindication to spinal anesthesia

A preanaesthetic check up was done. Patients of ASA I&II with normal laboratory findingsand normal radiological findings such as chest x-ray were accepted for the study. Informedand written consent was obtained after thoroughly explaining the procedure and drug to thepatients. On arrival to preoperative room patient connect ,Routine monitors such as non-invasive blood pressure, Pulse oximeter (SpO_2),Electrocardiogram were attached ,baseline parameters such as systolic and diastolic Non invasive Blood Pressure, Oxygen saturation and Electrocardiogram and Body temperature recorded in supine position. Intravenous accesswas established .Patients fulfilling inclusion criteria were randomized by computer generated randomization into two groups. Group M (study) received magnesium sulfate 50 mg/kg in500 ml Ringer Lactate over 20min. Group C (control) received 500ml Ringer Lactate over 20min. After painting and draping under strict aseptic precautions L3-L4 intervertebral space identified, Lumbar puncture was done by using 25G Quincke's needle. After free flow of Cerebrospinal fluid , 15mg of injection Bupivacaine 0.5%(Heavy) mixed with 30µg injection Buprenorphine was administered in both groups thenthe patients were turned to supine position. Onset of spinal block, level of sensory and motor blockade was evaluated by pin prick method and modified Bromage scale respectively.

Results

Demographic Parameters between Group M and Group C for Age, Height and Weight were comparable, there was no statistically significant difference seen between the groups.

Table 1:

Demographic Parameters	**Study**		**Control**		P Value
	Mean	SD	Mean	SD	
AGE(in yrs)	45.52	7.61	45.08	8.97	0.7919
HEIGHT(in cms)	147.24	7.13	153.28	10.11	0.0008
WEIGHT (in kgs)	56.34	8.75	57.96	6.74	0.3022

Table 2:

Baseline	**Study**		**Control**		P Value
	Mean	SD	Mean	SD	
SBP_baseline	128.7600	5.3930	128.7600	5.3930	1.0000
DBP_baseline	78.0600	7.0809	78.0600	7.0809	1.0000
HR_baseline	83.0200	6.1295	83.0200	6.1295	1.0000
SPO_2_baseline	97.8800	0.9179	97.8800	0.9179	1.0000

Baseline Noninvasive Blood pressure systolic and diastolic (SBP and DBP), Heart rate (HR), oxygen saturation (SPO_2) were comparable in both the groups. No statistically significant difference was found between the groups. Noninvasive Blood pressure diastolic (DBP) was lower in study group compared to controlgroup which was statistically significant.

Table 3:

VAS	Study		Control		P Value
	Mean	SD	Mean	SD	
VAS 2HRS	1.2400	0.4314	1.7400	0.9435	0.0010
VAS 4HRS	1.1600	0.4219	3.7800	0.5067	0.0000
VAS 6hrs	1.9796	0.8537	2.4694	1.0429	0.0126
VAS 8 HRS	3.3400	0.9392	3.1000	1.0926	0.2417
vas 10hr	2.1600	1.1132	2.9000	1.1294	0.0014
VAS_12hrs	1.2653	0.7005	3.0400	1.1058	0.0000

There was a significant difference in Visual analogue score in study and control group.
Vas scores at 4 hrs(P value 0.0000)to 6 hrs were significantly high in control group compared to study group.Vas s score at (P value 0.2417) 8 hrs doesn't show significant difference in both the groups.Vas scores at 10 hrs (P0.0014)and12 hours (0.0000) show significant difference with highervalues in control group.

Table 4:

Duraion of Analgesia in hrs	Study		Control		P Value
	Mean	SD	Mean	SD	
	4.43	1.48	4.26	0.54	0.45

The duration of analgesia in study group is 4.43±1.48 hrs and in control group 4.26±0.54 hrs There was a no significant difference in duration of analgesia in two groups (with p value of 0.45)

Table 5:

Rescue analgesia	Study		Control		P Value
	Mean	SD	Mean	SD	
	1.12	0.52	2.62	0.63	0.0000

This bar diagram shows the total no. of inj Diclofenac consumed by both the groups as a rescue analgesics in 12 hrs. There was a significant difference in analgesia requirements inboth the groups with analgesic request more in control group.

Table 6:

SIDE EFFECTS	Study(N=50)	Control(N=50)
NAUSEA/VOMITING	4	15
HYPOTENSION	12	2
PRURITIS	1	10

Frequency of nausea and vomiting was more pronounced in control group compared to study group. There was significant difference in frequency of hypotension in two groups hypotension washigher in study group.

Discussion

The major goal in postoperative pain management is to minimize the dose of medications and lessen side effects, while still providing adequate analgesia. Pain after infraumbilical surgeries can be multifactorial, incisional pain and pain from deeper (visceral) structures. Dynamic pain during straining, coughing, or mobilizing, can be quite severe. Postsurgical pain is one of the most important issues that could impress on postoperative peace and comfort. Abdominal hysterectomy associated with intense inflammatory response, resulting in moderate to severe postoperative pain perception. Opioids remain the common analgesic drugs after abdominal surgeries but their adverse effects such as respiratory depression, nausea and vomiting make this category of drugs undesirable. So we are always looking for replaceable methods with fewer side effects and cost. Adjuvant analgesics are the desirable replacements in prevention of severity of postoperative pain. Preventive analgesia is a method initiated before surgical procedure in order to reduce the physiological consequences of nociceptive stimulation and its adverse effects and has been defined as an antinociceptive treatment or pre-emptive analgesia that prevents establishment of altered central processing because of afferent input from injuries. One of the intravenous adjuvant that has been shown potential in pre-emptive analgesia is magnesium sulfate that could be administered with multiple routes or methods and one of those is single low dose. Mg has been used for many years in anesthesia and cardiology as an anticonvulsant or antiarrhythmic drug. Mechanism of the analgesic effect of Mg is not clear but interference with calcium channels and N-methyl-D-aspartate (NMDA) receptor seem to play an important role. The analgesic mechanism of NMDA-antagonists is by preventing nociceptive central sensitization. Another suggesting mechanism is the role of iton reduction of catecholamine release with sympathetic stimulation, thereby decreasing peripheral nociception or the stress response to the surgery. Spinal anesthesia is the most commonly used technique for lower abdominal and lower limb surgeries. Opioids and local anesthetics administered together intrathecally are known to havesynergistic analgesic effects, Buprenorphine is one of the opioid which increases sensory block without affecting motor block and haemodynamic significantly, it also has high lipid solubility and highest affinity for opiate receptors. using different doses of Buprenorphine, upto 150 mcg ofBuprenorphine has been used intrathecally. Increase in Buprenorphine dose is associated with prolonged duration of analgesia but it also increases the side effects. Although Buprenorphine has a high affinity for various opioid receptors, its effect at the mu receptor is associated with analgesia and respiratory depression. Administration of lipophilic opioids may be associated with significant, respiratory depression. Risk factors for respiratory depression with neuraxial opioids include increasing dose, increasing age, concomitant use of systemic opioids or sedatives, possibly prolonged or extensive surgery, the presence of co morbid conditions, and thoracic surgery. we wanted to prolong the duration of analgesia without increasing the side effect profile hence we used low doses of intrathecal Buprenorphine and studied the effect of intravenous Magnesium sulphate as a adjuvant to prolong the duration of analgesia without increasing the side effect profile of

intrathecal Buprenorphine, Magnesium sulfate has been used as adjuvant in various anaesthetic procedures. It can be used in various routes such as intramuscular, intravenous, intrathecal, epidural, and for peripheral nerve blocks. It has been used in general anaesthesia to reduce perioperative opioidconsumption and to reduce muscle relaxant requirements, J H Ryu et al showed that I.V. magnesium sulphate during TIVA reduced rocuronium requirement and improved the quality of postoperative analgesia . Arman taheri et al Concluded that Single dose of magnesium sulfate during balanced general anesthesia could be considered as effective and safe method toreduce postoperative pain and opioid consumption after TAH. Dabbagh et al concluded that Intravenous magnesium sulfate can serve as a supplementary analgesic therapy to suppress theacute post-operative pain, leading to less morphine requirements in the first 24 h. It has been used intrathecally as an adjuvant to bupivacaine anaesthesia, Arcioni et al concluded that supplementation of spinal anesthesia with combined intrathecal and epidural MgSO4 significantly reduces patients post-operative analgesic requirements . Rihan et al concluded that Magnesium sulfate added to bupivacaine and fentanyl for labor epidural analgesia resulted in faster onset, longer duration of action and reduced the break through pain.It has been used for peripheral nerve blocks such as brachial plexus block, femoral block etc. Buprenorphine has been used intrathecally not only for postoperative anaelgesia, but also forintractable pain and phantom pain conditions, in the doses of 30 – 150 microgram (mcg). It was found to be safe even in elderly patients at 30 to 60 µgs Although the respiratory depression to intrathecal opioids is well established. Buprenorphine is also associated with respiratory depression nausea and vomiting at higher dosage. Most of the studies report minimal or no respiratory depression following the dose of 30µg. Khan et al demonstrated Buprenorphine 30mcg in combination with 2ml of 0.75% Bupivacaine provided analgesia for longer Duration clinically increased incidence of nauseaand vomiting. Rabee et al concluded that intrathecal Buprenorphine prolongs duration of analgesia without any significant side effects. Prerana et al showed in their study the duration of analgesia was 128.04±14.97 mins in study (magnesium) group compared to control group 103.89±12.27 mins the difference in duration between the two groups was 25min. In our study the duration of analgesia was 4.43±1.48 hrs in study (magnesium) and 4.26±0.54 hrs in control group and the difference between two groups was approximately 15 minutes compared to Prerana et al study. We haveused a single bolus dose of $MgSO_4$ 50mg/kg and prerna et al used bolus dose 250 mg of intravenous magnesium sulfate followed by an infusion of 500 mg magnesium sulfate (25 mg/ml) at the rate of 20 ml/hour. But in our study the duration of analgesia was prolonged compared to Prerana et al due to addition of intrathecal Buprenorphine to bupivacaine.Mustafa et al selected four groups which were divided in, group 1 and 2 of normal term pregnancy patients ,and group 3 and 4 of preeclampsia patients , 2 and 4 received intravenousmagnesium sulfate, group 1 and 3 were control. Duration of analgesia in group1 was 105±39min, group 2 - 98.3±27.2min,group 3-100.7±22.4min and group 4- 85.3 ±24.9min.

Conclusion

We conclude that pre-operative IV bolus dose of magnesium sulfate with dosage of 50mg·kg−1 in 500mL of Ringer Lactate solution, does not prolongs the duration of anaesthesia and analgesia when given in combination with spinal anaesthesia with bupivacaine 0-5% + Buprenorphine 30µg. But it reduces the post operative analgesicsconsumption and also reduces the frequency of nausea and vomiting associated with intrathecal Buprenorphine.

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