Magnesium sulphate added as an adjuvant to intrathecal bupivacaine in patients with mild pregnancy induced hypertension undergoing caesarean section

Venkatesan K[1], Vijay Narayanan S[2,*], Iniya R[3], Rajalekshmi M[4]

[1]Senior Assistant Professor, Govt. Villupuram Medical College, Villupuram, [2]Associate Professor, [4]Assistant Professor, Saveetha Medical College, Chennai, [3]Senior Resident, Dept. of Anaesthesiology, K.A.P.V. Govt. Medical College, Tiruchirappalli

***Corresponding Author:**
Email: drvijay2000@gmail.com

Abstract

Background: Adequate analgesia following caesarean section decreases morbidity, ambulation, improves patient outcome and facilitates care of the newborn baby. Intrathecal Magnesium, an NMDA antagonist has been shown to prolong analgesia without significant side effect in healthy parturients. We therefore studied the effect of adding intrathecal Magnesium sulphate to Bupivacaine, Fentanyl in patient with mild pregnancy induced hypertension undergoing caesarean section.

Aim: To study and compare the effect of added Fentanyl 0.5cc (25 mcg) & Magnesium sulphate 0.1cc 50% (50mg) to 0.5% 2cc (10mg) Bupivacaine, in patients with pregnancy induced hypertension (PIH) undergoing elective Caesarean section under spinal anesthesia.

Materials and Methods: 60 patients undergoing elective caesarean section under spinal anaesthesia were randomly divided into three groups. Control group (N=20) received 0.5% 2cc (10mg) Inj.bupivacaine+0.6cc normal saline. Fentanyl group (N=20) received 0.5% 2cc (10mg) Inj.bupivacaine+0.5cc (25micgm) Inj.fentanyl+0.1cc normal saline. Magnesium sulphate group (N=20) received 0.5% 2cc (10mg) Inj.bupivacaine+0.5cc (25mcg) Inj.fentanyl+0.1cc 50% (50mg) magnesium sulphate. Onset, duration and recovery of sensory and motor block, duration of spinal anaesthesia, APGAR score and post operative analgesia duration were studied. Statistical analysis was done using univariate analysis, ANOVA and two group 'T' test. $p<0.05$ was taken as statistically signicant.

Results: Onset of sensory and motor blockade were delayed in the magnesium sulphate group which was significant. Duration of spinal anesthesia, motor block duration and post-operative analgesia were also significantly prolonged in Magnesium sulphate group.

Conclusion: Addition of magnesium sulphate to intrathecal bupivacaine is beneficial in antenatal women undergoing caesarean section, as it prolongs the motor blockade and duration of analgesia.

Key Words: Fentanyl, Magnesium sulphate, NMDA antagonist, Bupivacaine, Pregnancy induced hypertension

Access this article online	
Quick Response Code:	**Website:** www.innovativepublication.com
	DOI: 10.5958/2394-4994.2016.00045.7

Introduction

Spinal anaesthesia was first performed by August Bier on 16th August 1898 when he injected 3ml of 0.5% cocaine intrathecally. Spinal anaesthesia is simple, easy to perform and has got a definite endpoint. It requires a small dose of local anaesthetic drug to produce profound sensory and motor blockade. Ever since the introduction of local anaesthetic drugs, diverse classes of drugs such as epinephrine, opioids, clonidine, neostigmine, ketamine and benzodiazepines have been added as adjuvants to local anaesthetics in an attempt to prolong analgesia and reduce the incidence of side effects.

Glutamate and aspartate neurotransmitters are released due to noxious stimulation and they bind to NMDA receptors. Activation of these NMDA receptors facilitates calcium entry which leads to central sensitization and long term potentiation in spinal cord.[1] These NMDA receptors play an important role in the duration of acute pain.[2] Magnesium reduces NMDA induced currents by blocking calcium entry and thus antagonises the NMDA receptor channels non-competitively in a voltage dependent way.[3,4,5] Therefore magnesium has been called "Nature's physiological calcium channel Blocker". Parenteral magnesium has been used for many years on an empirical basis for intraoperative and postoperative analgesia. Although systemic magnesium decreases postoperative Opioid requirements, its intrathecal use has not been evaluated clinically. However, it has been safely used in humans and its safety profile has been documented in experimental studies.

In 1906, Haubold and Meltzer showed that intrathecal administration of Magnesium Sulphate produces spinal anaesthesia that includes profound motor and sensory blockade without any permanent untoward effects.

In this prospective randomized double blind controlled study, we evaluated the effect of adding intrathecal Magnesium Sulphate to Bupivacaine and Fentanyl in patients undergoing elective Caesarean section.

Aim of the study

To study and compare the effect of added Fentanyl 25 (micro gm) & MgSO4 0.1cc 50% (50mg) to 0.5% 2cc (10mg) Bupivacaine, in patients with mild gestational hypertension(PIH) undergoing elective Caesarean section under spinal anaesthesia.

To evaluate:

- Onset time of Sensory block
- Onset time of Motor block
- Upper level of analgesia
- Duration of postoperative analgesia

Materials and Methods

After obtaining ethical committee approval from Govt. Kilpauk Medical College. 60 Pregnant women with mild PIH undergoing elective Caesarean section ASA I and II between the age group of 18-35 under spinal anaesthesia were randomly divided into three groups.

Control group: Control group (N=20) recieved patients 0.5% 2cc (10mg) Inj.bupivacaine + 0.6cc normal saline.

Fentanyl group: Fentanyl group (N= 20) patients received 0.5% 2cc Inj.bupivacaine +0.5cc (25mic gm) Inj.fentanyl +0.1cc NS.

$MgSO_4$ group: MgSO4 group (N=20) received 0.5% 2cc Inj.bupivacaine + 0.5cc Inj.fentanyl + 0.1cc 50% (50mg) Inj.MgSO4.

Minimal fasting period was 8hrs and IV line was secured with 18G IV cannula. All patients received premedication with Inj. Ranitidine 50mg IV and Inj. Metoclopramide 10 mg IV, 10 min before surgery and preloaded with RL 10-12ml /kg. All patients received 5L of O2/ min through mask throughout procedure Patients were treated with titrated doses of

- Inj. Ephedrine 6mg I.V if systolic BP<90mmhg
- Inj. Atropine 0.6mg I.V if heart rate <60/min

After the delivery of baby Inj. Oxytocin 10 IU in drip and 10 IU IM was given.

Inclusion Criteria	Exclusion Criteria
ASA I and II	Patient refusal for spinal anaesthesia
Age between 18-35 years	Heart disease
Mild PIH (BP<160/110mmHg)	Foetal distress
Planned for Elective Caesarean Section	Eclampsia
	Allergy to local anaesthetic drugs
	Seizure disorders
	Patient with coagulation disorders

All patients were monitored with ECG, NIBP, Pulse Oximetry. Respiratory rate, urinary output and knee jerk were also monitored. Under aseptic precaution with patient in right lateral decubitus position by mid line approach, spinal anaesthesia was performed according to the study groups. Wedge was placed to prevent decreased venous return due to aortocaval compression.

The local anaesthetic drug was prepared by the assistant according to the group and given to the performer who injected drug by spinal anesthesia without knowing the content of the drug and he records his findings needed for the study.

Parameters monitored

The onset of sensory blockade, motor blockade, upper level of analgesia, intensity of motor block, two segment regression time, APGAR Score, Postoperative analgesia duration and hemodynamic parameters were observed.

Motor block was assessed by Bromage motor score and sedation by Ramsay sedation score.

Sensory Score:

Score	Response
0	normal sensation
1	analgesia (loss of pin prick sensation)
2	anaesthesia (loss of touch sensation)

Bromage Motor score:

Grade	Response	Degree of block
0	no motor block	Nil (0%)
1	unable to do straight leg raise	Partial (33%)
2	unable to flex knee against resistance	Almost complete (66%)
3	unable to flex ankle	Complete

Ramsay Sedation Score:

Score	Response
1	Anxious or restless or both
2	Co-operative, oriented and tranquilised
3	Responds to commands
4	Brisk response to stimulus
5	Sluggish response to stimulus
6	No response to stimulus

Sensory block onset time: Time interval between end of anaesthetic injection and appearance of cutaneous analgesia in dermatomes T-12, T-10, T-8, T-6.

Duration of motor block: Time interval between administration of anaesthetic and attainment of grade 0 in Bromage motor scale.

Duration of analgesia: Time interval between administration of anaesthetic and disappearance of cutaneous level of sensation at each dermatomal level.

Post-op analgesia duration: Time interval between administration of anaesthetic and time of analgesic requirement in PACU.

Results

Table 1: Sensory block onset time in min

	Participants	Mean	Std. deviation	Std. error	p value
Fentanyl group	20	0.62	0.204	0.046	<0.001
Control group	20	0.54	0.123	0.028	
$MgSO_4$ group	20	1.03	0.424	0.097	
Total	60	0.73	0.345	0.045	

Onset time of sensory block was highly significant with p<0.001

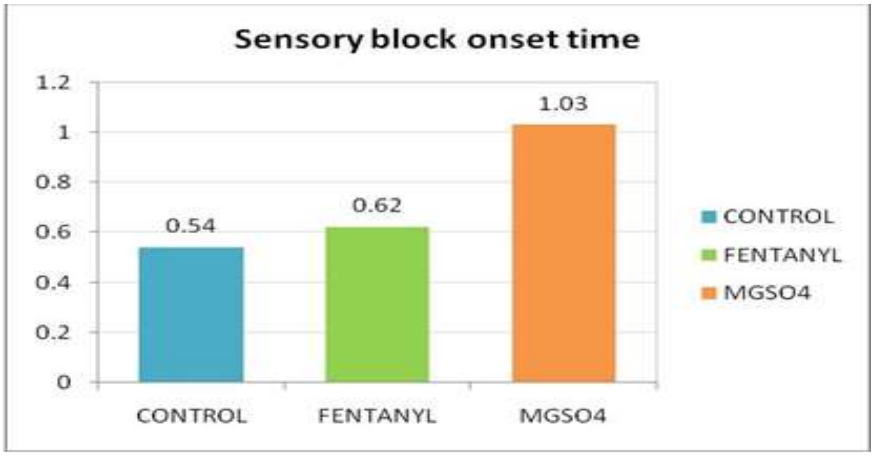

Fig. 1

Table 2: Motor Block onset time in min

	Participants	Mean	Std. deviation	Std. error	p value
Fentanyl group	20	5.350	1.3387	0.2993	<0.001
Control group	20	3.315	0.8707	0.1947	
$MgSO_4$ group	20	9.150	1.6230	0.3629	
Total	60	5.938	2.7598	0.3563	

Onset time of motor block was highly significant between the groups with p<0.001

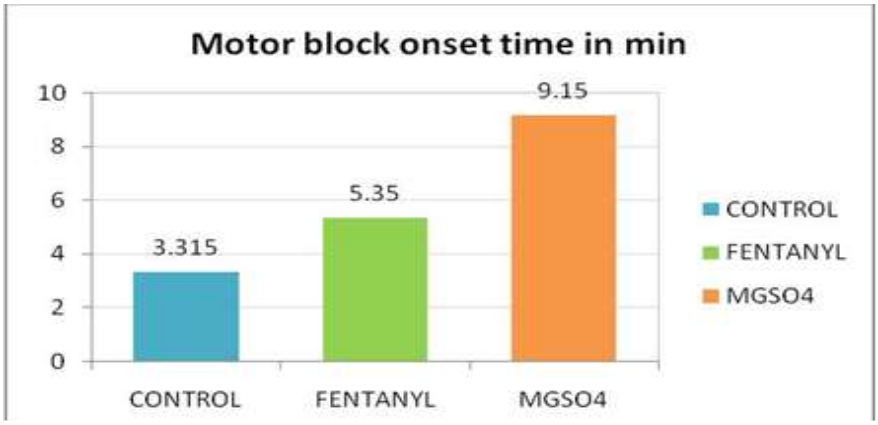

Fig. 2

Table 3: Analgesic and motor block duration in min

	Participants	Mean	Std. deviation	Std. error	p value
Fentanyl group	20	131.90	11.634	2.602	<0.001
Control group	20	127.60	14.065	3.145	
$MgSO_4$ group	20	189.40	19.329	4.322	
Total	60	149.63	32.169	4.153	

The analgesic and the motor block duration was also highly significant with p<0.001

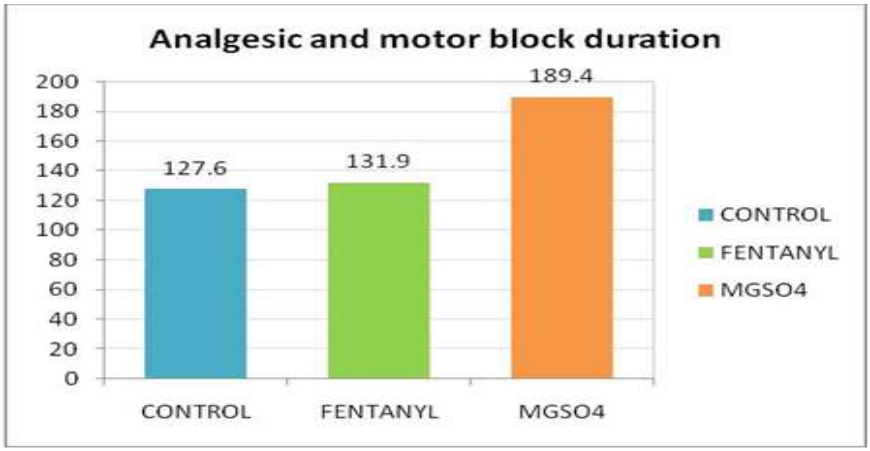

Fig. 3

Table 4: Duration of Post-operative analgesia in min

	Participants	Mean	Std. deviation	Std. error	p value
Fentanyl group	20	310.80	25.548	5.713	<0.001
Control group	20	222.45	13.942	3.117	
$MgSO_4$ group	20	403.65	27.186	6.079	
Total	60	312.30	77.955	10.064	

The duration of post-operative analgesia was highly significant with p<0.001.

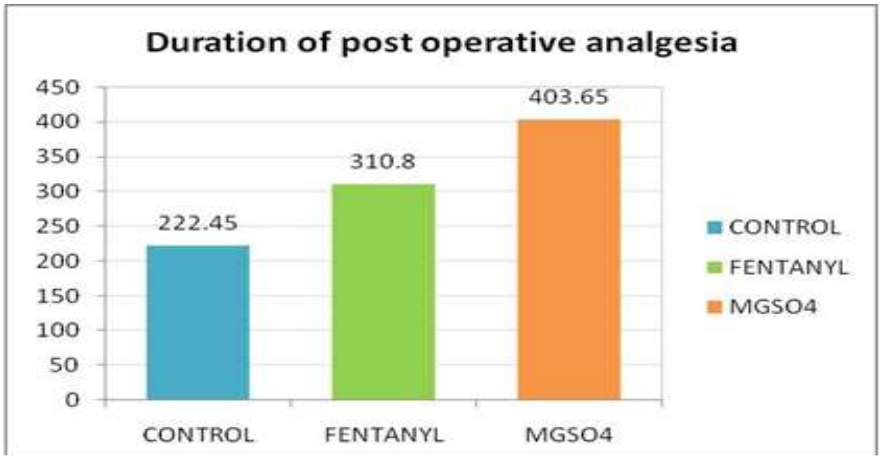

Fig. 4

Table 5: BP (Systolic) in mmHg in 5th min

	Participants	Mean	Std. deviation	Std. error	p value
Fentanyl group	20	115.65	13.647	3.052	0.226
Control group	20	119.15	14.376	3.215	
$MgSO_4$ group	20	122.80	10.476	2.343	
Total	60	119.20	13.059	1.686	

There was no statistical significance in the systolic BP between the groups.

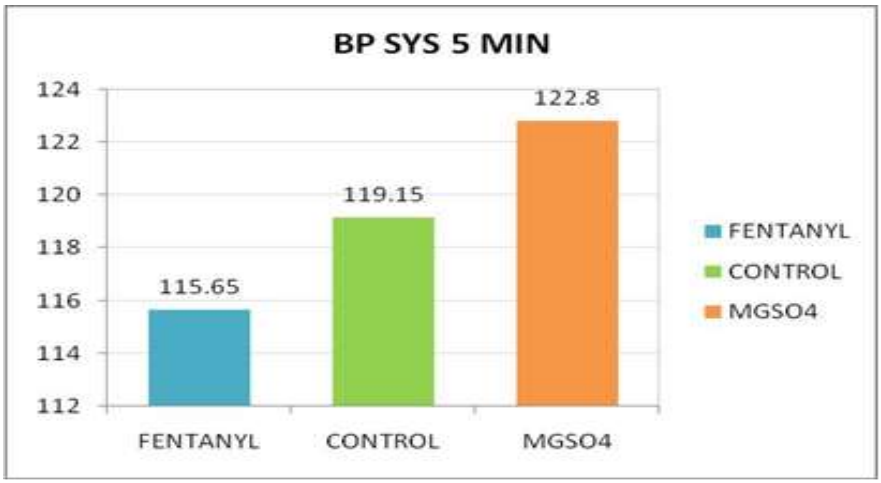

Fig. 5

Table 6: BP (Diastolic) in mmHg in 5th min

	Participants	Mean	Std. deviation	Std. error	p value
Fentanyl group	20	71.70	9.804	2.192	0.059
Control group	20	74.90	8.955	2.002	
$MgSO_4$ group	20	78.85	9.115	2.038	
Total	60	75.15	9.604	1.240	

There was no statistical significance in the diastolic BP between the groups.

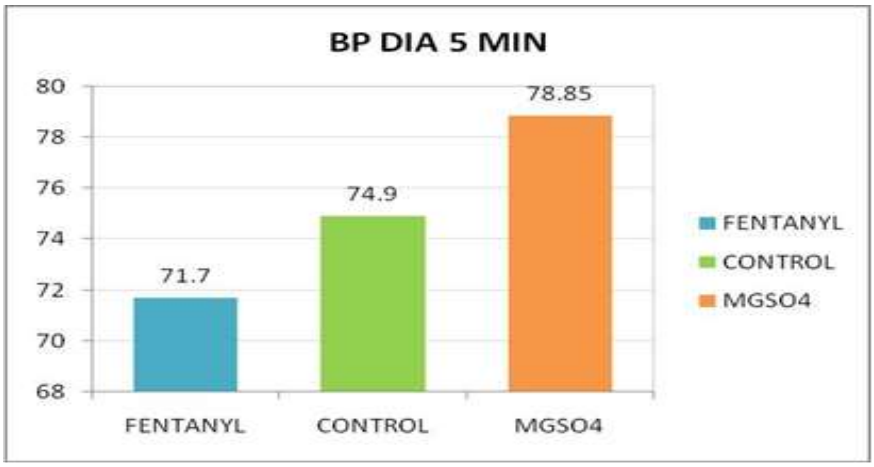

Fig. 6

Table 7: Ephedrine requirement in mg

	Participants	Mean	Std. deviation	Std. error	p value
Fentanyl group	20	11.15	3.297	0.737	<0.001
Control group	20	17.35	3.407	0.762	
$MgSO_4$ group	20	8.55	2.438	0.545	
Total	60	12.35	4.797	0.619	

Ephedrine requirement was highly significant ($p<0.001$) between the groups.

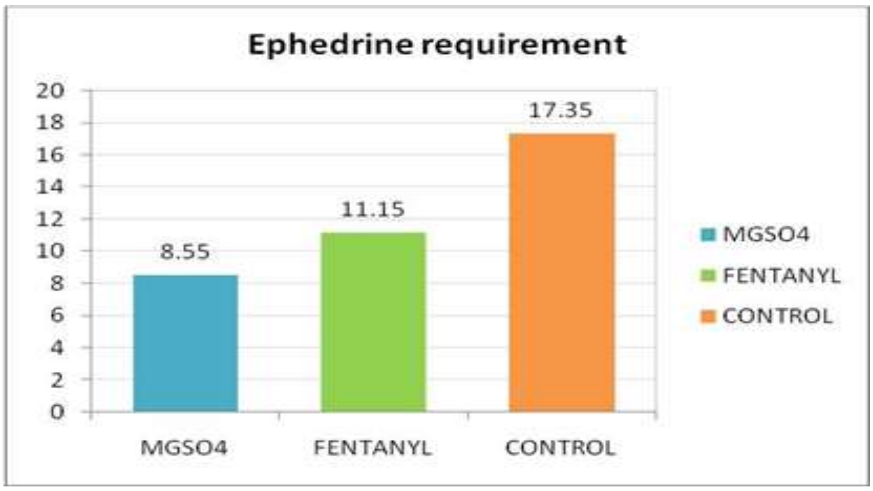

Fig. 7

Table 8: APGAR 5min

	Participants	Mean	Std. deviation	Std. error	p value
Fentanyl group	20	8.20	0.951	0.213	0.073
Control group	20	8.20	0.768	0.172	
$MgSO_4$ group	20	8.70	0.571	0.128	
Total	60	8.37	0.802	0.104	

There was no statistical significance in the APGAR score between the groups.

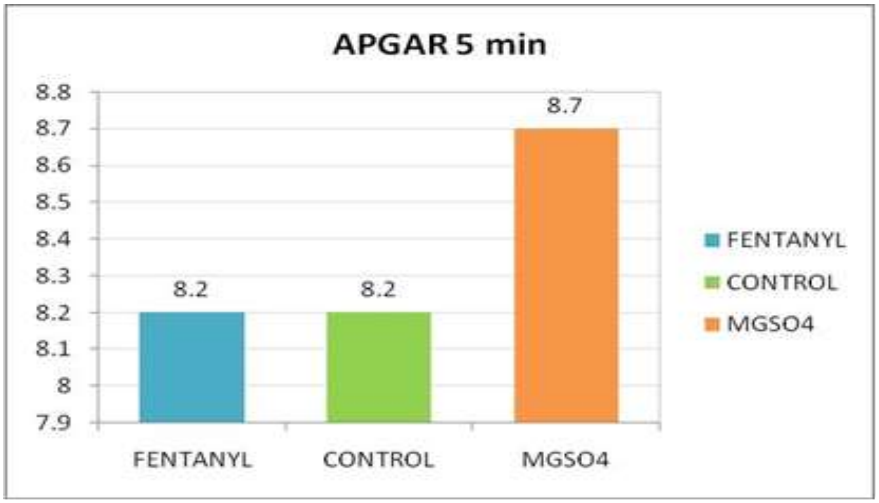

Fig. 8

Discussion

The study was conducted at Govt. Kilpauk Medical College on 60 pregnant patient with mild PIH ASA I and II undergoing elective Caesarean Section under spinal anaesthesia after obtaining informed consent. Sensory and motor block onset time, upper level of analgesia, Duration of analgesia and motor blockade and APGAR score hemodynamics between the groups were evaluated.

The safety of intrathecal magnesium sulphate administration in humans and animals have been established. Simpson et al and Kroin et al demonstrated in animals by their study that intrathecal magnesium sulphate has a safety profile.[6,7]

Ozalevli et al and Buvendran et al demonstrated no deleterious effects in humans on administration of intrathecal magnesium sulphate in their study they used 50mg of MgSO4.[8,9] The dose of magnesium sulphate was based on data from a rat model of postoperative pain in which 188 micrograms of intrathecal magnesium sulphate potentiated morphine anti-nociception done by Kroin et al.[7] Based on the relative differences between human and rat CSF volume and body weight, the 188 microgram dose was conservatively extrapolated to 50 mg for humans.

In our study sensory block onset time was delayed in magnesium sulphate group which was 1.03 min in comparison to control group which was 0.54 min and it

is statistically significant (P value 0.000). Tanmoy Ghatak et al in their study concluded that addition of magnesium sulphate as an adjuvant to epidural bupivacaine reduces the onset time of sensory and motor block.[10]

In our study onset of motor block was delayed in magnesium sulphate group (9.15 min) when compared to control group (3.31 min) which was statistically significant (P value 0.000). My study was similar to the study by Buvanendran et al where the onset time in the magnesium sulphate group was delayed than the control group.[9]

Unlugenc and Ozalevli et al in their study concluded that in patients undergoing caesarean section with spinal anaesthesia, the addition of magnesium sulfate (50 mg) intrathecally to 10 mg of spinal bupivacaine (0.5%) did not shorten the onset time of sensory and motor blockade or prolong the duration of spinal anaesthesia, as seen with fentanyl.[8]

Analgesic and motor block duration is prolonged in magnesium sulphate group (189.40 min) when compared to control group which is statistically highly significant (p Value < 0.001). Buvanendran et al and Malleswaran S et al in their studies noted that there was prolongation in analgesic and motor blockade duration in magnesium sulphate group.[9,11] Tramer MR et al and Kara H concluded that the perioperative infusion of magnesium sulphate is associated with smaller analgesic requirement, less discomfort, and a better quality of sleep in the postoperative period without any adverse effects.[12,13] Vaibhav Shahi et al in their study have concluded that magnesium sulphate administered epidurally prolongs the duration of analgesia but lesser than that compared to dexmedetomidine.[14]

In our study the fall in blood pressure and requirement of ephedrine is more in the control group (17.35 mg) compared to Magnesium sulphate groups (8.55 mg) due to high level of blockade. The p value was <0.001 showing that it was highly significant. Malleeswaran S et al in their study also noted a similar trend in the haemodynamic changes in the magnesium sulphate group.[11]

In our study duration of post-operative analgesia was prolonged in Magnesium sulphate group (403.65 min) when compared to control group (222.45 min) being statistically highly significant (p value <0.001). M. Ozalevli and T.O. Cetin et al in their study substantiated that duration of post-operative analgesia was prolonged in the magnesium sulphate group.[15] Arcioni et al in his study concluded that supplementation of spinal anaesthesia with combined intrathecal and epidural magnesium significantly reduces the post-operative analgesic requirements.[16] Buvanendran et al concluded that intrathecal magnesium prolongs spinal opioid analgesia in humans and suggest that the availability of an intrathecal *N*methyl-D-aspartate antagonist could be of clinical importance for pain management.[9] Khemakhem K et al in comparison found that the addition of intrathecal magnesium sulphate 100 mg to morphine improved quality and duration of the postoperative analgesia with a better maternal satisfaction without additional side effects.[17]

There was no difference in APGAR score in 5 min between the groups and also was statistically insignificant (p value 0.073).

3 patients in fentanyl groups complained of prurities. 2 patients due to inadequate blockade converted to GA were excluded from the study. Sahar M et al concluded that supplementation of spinal bupivacaine anaesthesia for caesarean delivery with intrathecal fentanyl provides a better quality of anaesthesia and is associated with a decreased incidence of side effects as compared with supplementation with the same dose of IV fentanyl.[18]

Conclusion

There is a delay in the onset of sensory and motor blockade with the use magnesium sulphate group. However there is prolonged motor blockade and duration of analgesia which overlaps well into the postoperative period. Therefore magnesium sulphate added as an adjuvant to intrathecal bupivacaine is beneficial for the patient for post-operative analgesia without affecting the APGAR score.

References

1. Pockett S. Spinal cord synaptic plasticity and chronic pain. Anesth Analg. 1995; 80:173–9.
2. Woolf CJ, Thompson SW. The induction and maintenance of central sensitization is dependent on N-methyl-o-aspartic acid receptor activation; Implications for the treatment of post-injury pain hypersensitivity states. Pain. 1991; 44:293–9.
3. Srivinskas E, Laurinaitis R. Use of magnesium in anesthesiology. Medicine 2002; 38:147-50.
4. Liu HT, Hollmann MW, Liu WH, Hoenemann CW, Durieux ME. Modulation of NMDA receptor function by ketamin and magnesium: Part 1. Anesth Analg. 2001; 92:1173–81.
5. Fawcett WJ, Haxby EJ, Male DA. Magnesium: Physiology and pharmacology. Br J Anaesth.1999; 83:302–20.
6. Simpson Thomas. Intrathecal magnesium sulphate protects the spinal cord from ischaemic injury during thoracic aortic cross clamping. Anaesthesiology.1994; 81(6);1493-98.
7. Kroin JS, McCarthy RJ, Von Roenn N, Schwab B, Tuman KJ, Ivankovich AD. Magnesium sulphate potentiates morphine anti-nociception at spinal level. Anaesth Analg 2000; 90:913-7.
8. Unlugenc H, Ozalevli M et al. Comparison of intrathecal magnesium, fentanyl, or placebo combined with bupivacaine 0.5% for parturients undergoing elective cesarean delivery. Acta Anaes Scandi 2009; 53(3):346-53.
9. Buvanendran A et al. Intrathecal magnesium prolongs fentanyl analgesia: a prospective randomized controlled trial. Anaesth Analg 2002; 95:661-7.
10. Tanmoy Ghatak et al. Evaluation of the effect of magnesium sulphate vs clonidine as adjunct to epidural

bupivacaine. Indian J Anaesth 2010 Jul-Aug; 54(4):308-313

11. Malleeswaran S, Panda N, Mathew P, Bagga R. A randomized study of magnesium sulphate as an adjuvant to intrathecal bupivacaine in patients with mild pre-eclampsia undergoing caesarean section. International Journal of Obstetric Anesthesia (2010); 19:161-166.
12. Tramer MR, Scheneider J, Marti RA, Kaplan R. Role of magnesium sulphate in postoperative analgesia. Anaesthesiology 1996; 84:340-7.
13. Kara H, Sahin N, Ulusan V, Aydogdu T. Magnesium infusion reduces postoperative pain. Eur J Anaesthesiol. 2002 Jan; 19(1):52-6.
14. Vaibhav Shahi et al. A comparative study of magnesium sulfate vs dexmedetomidine as an adjunct to epidural bupivacaine. J Anaesthesiol Clin Pharmacol. 2014 Oct-Dec; 30(4):538–542.
15. Ozalevli M, Cetin TO, Guler T. The effect of adding intrathecal magnesium sulphate to bupivacaine and fentanyl spinal anesthesia. Acta anesthesiol scand 2005; 49:1514-19.
16. Arcioni R, Palmisani S, Tigano S et al. Combined intrathecal and epidural magnesium sulphate supplementation of spinal anesthesia to reduce postoperative analgesic requirement. Acta Anaes Scandi 2007; 51(4):482-9.
17. Khemakhem K, Smaoui M, Ghrab, B et al .The effect of adding intrathecal magnesium sulphate to morphine for postoperative analgesia after caesarean section. Eur J Anaesth 2006; 23:183-84.
18. Sahar M. Siddik-Sayyid, Marie T. Aouad, et al. Intrathecal versus intravenous fentanyl for supplementation of subarachnoid block during cesarean delivery. Anesth Analg 2002;95:209-213.