International Journal of Research in Medical Sciences
Sur D et al. Int J Res Med Sci. 2017 May;5(5):2046-2052
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20171840

Original Research Article

A comparative study of different adjuncts to enhance the effects of intrathecal bupivacaine

Debajyoti Sur[1], Archana Agarwal[2], Ajay Kumar Chaudhary[3]*, Jaishri Bogra[2], Prithvi Kumar Singh[1], Rajni Gupta[1], Vinod Kumar Bhatia[1]

[1]Department of Anaesthesiology, Murshidabad Medical College and Hospital, West Bengal, India
[2]Department of Anaesthesiology, Hind Institute of Medical Sciences, Lucknow, Uttar Pradesh, India
[3]Department of Anaesthesiology, King George's Medical University, Lucknow, Uttar Pradesh, India

Received: 03 February 2017
Revised: 09 February 2017
Accepted: 08 March 2017

***Correspondence:**
Dr. Ajay Kumar Chaudhary,
E-mail: ajaychaudhary62@yahoo.com

ABSTRACT

Background: Spinal anaesthesia is the commonly used technique for lower abdominal surgeries. Adjuvants to bupivacaine have been used to provide good quality of perioperative and postoperative analgesia. The aim of the study was to evaluate the effects of subarachnoid administration of bupivacaine with clonidine, magnesium, dexmedetomidine and saline group.
Methods: The prospective, comparative single blind study included 120 patients in American society of anaesthesiologist (ASA) grade I and II, scheduled for lower abdominal surgeries were allocated in four groups. Each group included 15 mg bupivacaine with various adjuvants (30 µg clonidine, 50 mg magnesium sulphate and 3µg dexmedetomidine) were compared with saline group (group S).
Results: Time of onset was earlier in groups D and C but delayed in group M. The total power regains (B0) in group D (250.8±18.87), group M (235.23±24.66) and group C (242.70±25.98) were significantly delayed ($p<0.05$) as compare with group S (180.07±18.53). Demand of analgesia was significantly earlier in group S as compared with groups C, M and D. Similarly, the time of two segment regression was significantly earlier in group S as compared with groups C, M and D ($p<0.001$). Patients were hemodynamically stable in groups D, C and M as compared to Group S.
Conclusions: Dexmedetomidine and clonidine were equally effective and better as compared to magnesium as an adjunct to intrathecal bupivacaine.

Keywords: Bupivacaine, Clonidine, Dexmedetomidine, Intrathecal, Magnesium

INTRODUCTION

Spinal anaesthesia provides a safe technique for lower abdominal surgeries. Bupivacaine is routinely used in spinal anaesthesia with minimal side effects.[1,2] Clonidine is centrally acting partial α-2 adrenergic agonist and it potentiates intradural analgesia.[3,4] The safe dosage of intrathecal clonidine has been found to be 15 to 30 µg or 1µg/kg in different studies.[5,6] That's why the dosage of intrathecal clonidine in this study would be fixed to 30µg to minimize hypotension, bradycardia and sedation caused by higher dosages of it.

Magnesium is biological cation in our body and it counteracts pain in animal and human.[7,8] The role of magnesium in providing intraoperative analgesic effect is

promising.[9] The safety of intrathecal magnesium has been extensively evaluated in animals.[10-14] Studies in which intrathecal magnesium was given to various different groups of patients found that none had symptoms suggestive of neurotoxicity, nor did they exhibit signs of systemic toxicity such as hypotension, arrhythmias, somnolence or weakness, during the study.[15-17] Intrathecal magnesium (50mg) potentiated analgesic effect of fentanyl, this represented 10% of a dose shown to be safe dose in animals.[6] Various other clinical studies in human showed that intrathecal magnesium 50 mg was found to be safe and effective.[12,16,17] Dexmedetomidine is an alpha 2-adrenergic agonist, potentiate intradural analgesia in animals and human.[6,18] Low dose of dexmedetomidine (3µg) with bupivacaine for spinal anaesthesia produce a faster onset of good quality motor block, prolonged sensory block and maintain hemodynamic stability with minimal sedation.[6]

This clinical study has compared the effects of intrathecal magnesium sulphate, clonidine and dexmedetomidine as an adjunct to hyperbaric bupivacaine in lower abdominal surgery. Our primary outcomes are the hemodynamic, onset of sensory and motor blockade. Secondary outcomes are regression of sensory and motor blockade, duration of postoperative analgesia and side effects.

METHODS

Design of study

After approval from institutional ethical committee, the study was conducted in the patients aged 18-60 years within ASA grade I or II being admitted for lower abdominal surgeries under spinal anaesthesia after taking written informed consent. Patients were excluded from the study groups who had contraindications to central neuraxial block, allergy to drug, chronic pain syndrome and patients of heart block and hypertension. Spinal pencil point needles (23 or 25) gauge used at L3-4 or L4-5 interspace in sitting position. Patients randomised by using computer generated random number table to receive one of the following into the subarachnoid block: group S (control group): spinal anaesthesia with hyperbaric bupivacaine 15 mg (3ml of 0.5%) + 1ml of normal saline (NS), group C: spinal anaesthesia with hyperbaric bupivacaine 15mg (3ml of 0.5%) + intrathecal clonidine 30µg in 1ml of NS, group M: spinal anaesthesia with hyperbaric bupivacaine 15mg (3ml of 0.5%) + intrathecal magnesium sulphate 50mg in 1ml of NS, group D: spinal anaesthesia with hyperbaric bupivacaine 15 mg (3ml of 0.5%) + intrathecal dexmedetomidine 3µg in 1 ml of NS.

All patients were premedicated with ranitidine 150mg, metoclopramide 10mg and alprazolam 0.25mg orally at night before surgery. All of them were properly made aware regarding the process of giving spinal anaesthesia and were preloaded with 10-15ml/kg of Ringer Lactate. After the patients had been given spinal anaesthesia, heart rate and noninvasive arterial blood pressure were monitored in three groups preoperatively, intraoperatively and during shifting. Hypotension has been defined as systolic blood pressure <90 mmHg or >30% decrease in baseline values.

Tachycardia has been defined as heart rate >100/min and bradycardia has been defined as heart rate <60/min. Sensory block was assessed bilaterally by pin prick in midclavicular line. The time to reach the maximum level of sensory block and time for regression of two segments in the maximum block height was noted. Motor blockade was assessed by using Bromage scale (0: no motor block; 1: inability to raise extended legs; 2: inability to flex knees; 3: inability to flex ankle joints).[19] The time for first analgesic requirement postoperatively or the time when the patient perceives pain for the first time following spinal anaesthesia was noted. VAS (visual analogue scale) was also monitored hourly for 24 hours. Total number of rescue analgesic given was also noted for 24 hours. Rescue analgesia was given with i.v. tramadol 50mg. Sedation was assessed hourly for 24 hours on a four-point scale (grade 0, awake and alert; 1, mildly sedated, easily aroused; 2, moderately sedated, aroused by shaking; 3, deeply sedated, difficult to be aroused by physical stimulation).[14] Single blinding was done i.e. patients included in the study were not aware of the drug combination they received for spinal anaesthesia and results obtained were subjected to statistical analysis.

Statistical analysis

Continuous data were summarized as Mean ± SD while discrete (categorical) data in percentage. The outcome measures (pulse rate, systolic BP, diastolic BP, sedation score and VAS score) of four groups over the periods (time) were compared by repeated measures two factor (groups x periods) analysis of variance (ANOVA). Groups were also compared by one way ANOVA followed by Tukey's post hoc test. The categorical variables were compared by chi-square (χ^2) test. A two-sided (α=2) $p<0.05$ was considered statistically significant.

RESULTS

Observations were made from total 120 patients, 30 in each group. Demographic profile (age, height, weight and ASA physical status) was similar in all four groups (Table 1).

Type of surgeries and duration was similar in all patients. Comparing the proportion of sensory blockade level between the four groups were significantly ($p<0.001$) different sensory blockade level ($p<0.001$) respectively among the groups (Table 2).

Time of onset was earlier in group D but delayed in group M. Time needed for maximum height of sensory blockade in group D (6.50±1.50) and group C

(5.93±0.78) were significantly lower as compare with group S (10.10±3.64) and group M (8.00±1.81) (Table 2). Time to achieved maximum block of height was delayed in group M as compared to groups C and D.

Table 1: Basic characteristics (Mean ± SD) of four groups.

Characteristics	Group S (n=30)	Group C (n=30)	Group M (n=30)	Group D (n=30)
Age (yrs)	38.00±15.15	43.05±15.22	42.10±10.71	34.35±10.43
Gender				
Males	18 (65.0%)	19 (70.0%)	20 (75.0%)	19 (70.0%)
Females	12 (35.0%)	11 (30.0%)	10 (25.0%)	11 (30.0%)
ASA				
I	14	13	15	14
II	16	17	15	16

Table 2: Sensory blockade of four groups.

Sensory blockade	Group S (n=30)	Group C (n=30)	Group M (n=30)	Group D (n=30)	p-value
Level:					
T4	6	5	0	4	
T6	4	18	12	18	
T7	2	1	2	1	<0.001**
T8	2	1	12	5	
T10	16	5	4	2	
Time for maximum block					<0.001**
Height (Min.) (Mean±SD)	10.10 ± 2.41	5.93±0.78	8.10±1.16	6.50±1.50	

** Significance at p < 0.001.

Mean time to achieve motor blockade (Bromage I, Bromage II and Bromage III) in group D was (2.16±0.80, 3.83±1.78, 5.56±1.14) group M (1.73±0.74, 4.20±0.99, 7.60±1.10) and group C (2.07±0.69, 3.73±1.17, 5.60±1.61) were significantly faster (p<0.001) as compare with group S (2.87±0.90, 5.13±1.41, 7.70±2.60) and non-significant within group (Table 3). The total power regain (B0) in group D (250.8±18.87), group M (235.23±24.66) and group C (242.70±25.98) were significantly delayed (p<0.05) as compare with group S (180.07±18.53) (Table 3).

Table 3: Motor blockade (Mean ± SD) of four groups.

	Group S (n=30)	Group C (n=30)	Group M (n=30)	Group D (n=30)	p-value
Motor Block (min)					
B1	2.87±0.90	2.07±0.69	1.73±0.74	2.16±0.80	0.001**
B2	5.13±1.41	3.73±1.17	4.20±0.99	3.83±1.78	0.001**
B3	7.70±2.60	5.60±1.61	7.60±1.10	5.56±1.14	<0.001**
Total power regains (min) B0	180.07±18.53	242.70±25.98	235.23±24.66	250.8±18.87	<0.05*
Demand of analgesia (min)	141.90±18.94	220.73±31.21	215.57±26.41	235.73±34.01	<0.001**
Time of two segment regression	100.83±12.81	130.03±18.51	110.83±15.56	136.53±20.46	<0.001**

* Significance at p<0.05, ** Significance at p < 0.001.

Table 4: Postoperative pain managements.

Requirements	Group S (n=30)	Group C (n=30)	Group M (n=30)	Group D (n=30)	p-value
Request for first analgesia	198.30±45.88	396.00±70.81	216.00±45.24	314.35±56.49	<0.001**
No. of rescue analgesia	3.35±0.67	2.00±0.65	3.30±0.57	2.80±0.62	<0.001**

** Significance at p < 0.001.

Table 5: Adverse effects of four groups.

Complications	Group S (n=30)	Group C (n=30)	Group M (n=30)	Group D (n=30)
Hypotension	1 (3.33%)	4 (13.33%)	1 (3.33%)	6 (20.0%)
Bradycardia	3 (10.0%)	4 (13.33%)	4 (13.33%)	7 (23.33%)
Nausea	2 (6.67%)	4 (13.33%)	2 (6.67%)	5 (16.67%)
Vomiting	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Persistent neurological deficit	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Shivering	2 (6.67%)	1 (3.33%)	3 (10.0%)	3 (10.0%)

VAS score was significant lower in groups C, D and M as compare to group S. Demand of analgesia was significantly earlier in group S as compared with groups C, M and D ($p<0.001$) (Table 3). Similarly, the time of two segment regression was significantly earlier in group S as compared with groups C, M and D ($p<0.001$) (Table 3).

Patients were hemodynamically (Heart rate (HR) and Blood Pressured (BP)) stable in groups C, M and D and lower as compared to Group S (Figure 1). Comparing the mean HR of four groups, ANOVA revealed significant effect of both groups (treatments) ($p=0.001$) and time (period) ($p<0.001$) on HR. However, the interaction (groups x time) effect of both on HR was insignificant ($p=0.188$).

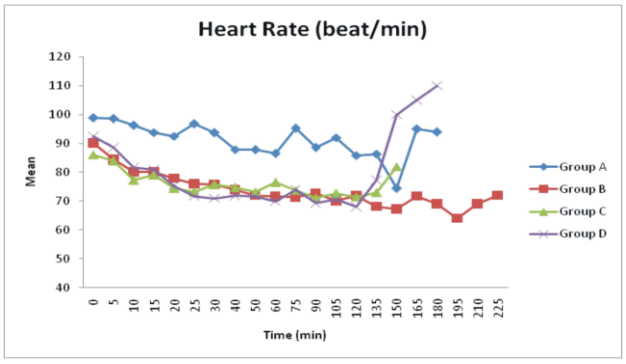

Figure 1: Heart rate.

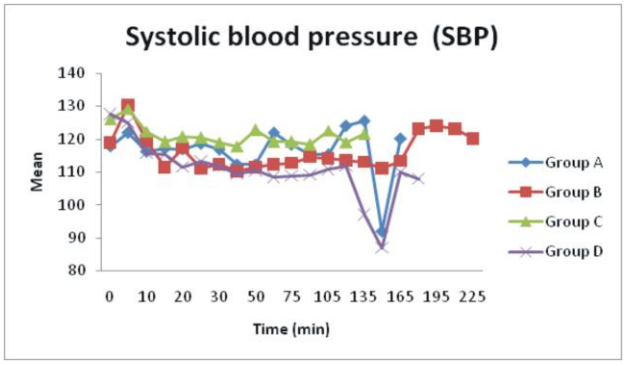

Figure 2: Systolic blood pressure.

The systolic blood pressure (SBP) and diastolic blood pressure (DBP) in all four groups remains similar but comparatively lower in groups C and D as compared to group M (Figure 2 and 3).

Comparing the mean SBP and DBP of four groups were no significant effect of all groups ($p=0.742$) while significant effect of time (periods) ($p<0.001$) on SBP.

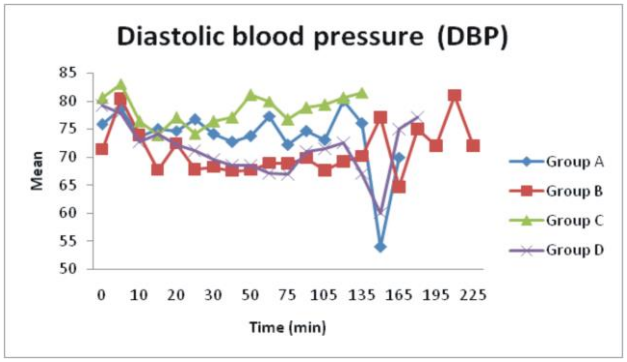

Figure 3: Diastolic blood pressure.

Intra operative, sedation scores were shows the similar pattern at periods (1 hr. to 24 hrs) except initially (at 1 hr.) high in group D. The overall sedation (average of all periods) remains similar among the groups though it was comparatively low in group M as compared to group D (Figure 4).

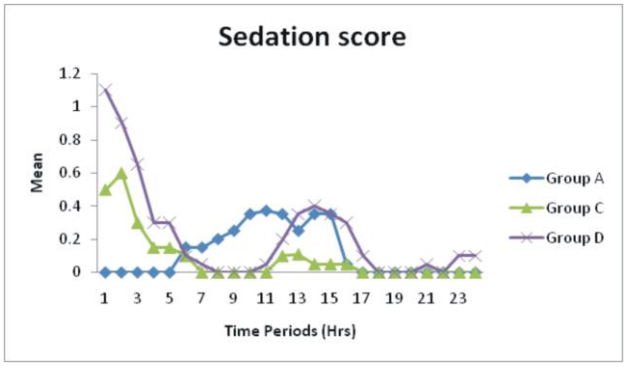

Figure 4: Sedation (score).

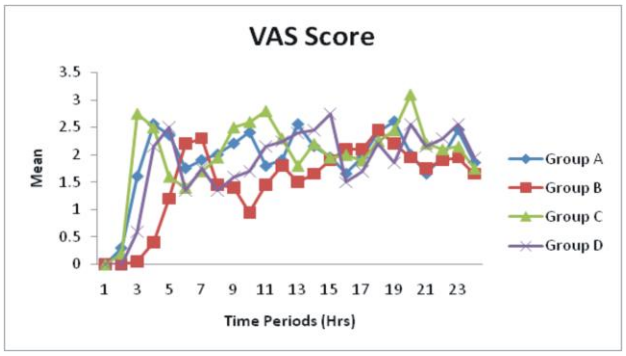

Figure 5: VAS (score).

The pain levels (VAS score) of all four groups showed similar pattern at periods; initially (1 hr.) low and gradual increase thereafter and remains higher till end (24 hrs). The overall pain (average of all periods) differed significantly among the groups and lowered significantly in group C as compared to rest of the groups (Figure 5).

Analgesic usage viz. Request for first analgesia ($p<0.001$) differed significantly among the groups and was significantly delayed in group C than the rest of the groups (Table 4). In contrast, No. of rescue analgesia also differed significantly among the groups ($p<0.001$) but lowered significantly in group C than the other groups (Table 4).

The treatment related complications such as hypotension, bradycardia, nausea, vomiting, persistent neurological deficit and shivering were not significant ($p>0.05$) in all groups (Table 5). Intra operative mephentramine requirement was comparatively more in groups D and C as compared to groups M and S.

DISCUSSION

Bupivacaine acts by blocking sodium channels, whereas the dexmedetomidine and clonidine acts by binding to pre-synaptic C-fibers and post-synaptic dorsal horn neurons. It produces analgesia by depressing the release of C-fiber transmitters and by hyperpolarization of post-synaptic dorsal horn neurons.[20,21] This antinociceptive effect may explain the prolongation of the sensory block when added to spinal anesthetics. The prolongation of the motor block of spinal anesthetics may result from the binding of α2-adrenoceptor agonists to motor neurons in the dorsal horn.[22] Magnesium occur naturally in spinal cord, blocks the N-methyl D-aspartate (NMDA) channels, and improves analgesia with no side effects with reduced postoperative shivering.[10]

Present results indicate that the clonidine (30µg), dexmedetomidine (3µg) or magnesium sulphate (50mg) when added to intrathecal bupivacaine, produces a significant prolongation in the duration of the motor and sensory block with preserved hemodynamic stability and lack of sedation as compared to alone. Spinal adjunct dexmedetomidine (3µg) or clonidine (30µg), with bupivacaine, produces a similar prolongation of the motor and sensory block.[6]

Dobrydnjov et al showed that spinal anesthesia bupivacaine 15mg and clonidine 30µm produced similar spinal anesthesia, because it did not prolong the motor block. Dexmedetomidine as an adjuvant with bupivacaine has dose dependent effects on the onset of sensory and motor block.[19] Dexmedetomidine and magnesium with bupivacaine shows similar effects except onset was delayed with magnesium.[23]

In the present study, the clonidine (group C), magnesium (group M) and dexmedetomidine (group D) all provide a faster motor blockade up to bromage II in comparison to control group while being used as an adjuvant to intrathecal bupivacaine. Clonidine and dexmedetomidine also elicit faster motor blockade up to bromage III in comparison to control group and magnesium. Previously also, other studies found that onset of motor block a significantly shorter in bupivacaine (12mg) supplemented with clonidine (30µg) with dexmedetomidine (3µg).[6] The effects of dexmedetomidine and magnesium sulphate given similar spinal effect except onset of block was delayed in magnesium group.[24] In present study magnesium and dexmedetomidine similar effect with reference to onset of analgesia.

The present study shows that the heart rate (HR) was similar in clonidine, magnesium and dexmedetomidine with bupivacaine and lower as compared to control group, systolic blood pressure (SBP) and diastolic blood pressure (DBP) in all four groups remain similar over a period except a slight decrease in DBP bupivacaine alone and with dexmedetomidine. Heart rate and MBP were significantly low in clonidine group.[25] Larsen et al showed long lasting reduction in heart rate and mean arterial pressure in both clonidine groups (75 and 150µg).[26] Clonidine added to spinal isobaric bupivacaine improves quality of spinal anaesthesia without significant deleterious hemodynamic effects.[5] Intrathecal dexmedetomidine is associated with hemodynamic stability and prolong duration of anaesthesia.[27] Magnesium sulphate and dexmedetomidine group were similar with respect to hemodynamic variables when given intrathecally with hyperbaric bupivacaine.[24]

In the present study, the sedation scores of all four groups showed similar pattern at periods (1 hr to 24 hrs) except initially (at 1 hr) high in group D. The overall sedation (average of all periods) remains similar among the groups though it was comparatively low in group M as compared to group D i.e. dexmedetomidine has better sedative effects than magnesium when given intrathecally. Dexmedetomidine produces intrathecal analgesia, circulatory uptake of the drug leads to a sedation.[12]

In present study, the VAS scores of all four groups showed a similar pattern at periods; initially (1 hr) low and gradual increase thereafter and remains higher till

end (24 hrs). The overall pain (average of all periods) differed significantly among the groups and lowered significantly in group C (1.51) as compared to rest of the groups. Request for first analgesia differed significantly among the groups and was significantly delayed in group C than the rest of the groups. Number of rescue analgesia also differed significantly among the groups but lowered significantly in group C than the other groups. Overall clonidine is more efficacious for postoperative analgesia than the rest of the adjuvant drugs in this study. There are similar evidences found in previous studies also. Dexmedetomidine and clonidine in intradural dose produced responsible analgesia.[28] The addition of clonidine 75µg to prilocaine 75mg for subarachnoid anaesthesia reduced the need for additional postoperative analgesics for about 8 hours during recovery from transurethral resection of bladder tumors.[29] The addition of clonidine (15µg and 30µg) to bupivacaine prolonged time to first analgesic request. We have found similar evidence in present study.[17] The intrathecal combination of bupivacaine with magnesium (50mg) to provide postoperative pain relief.[9,30,31] Bupivacaine with dexmedetomidine (1µg/kg), prolongs pain relief.[32] Dexmedetomidine is associated with VAS score less than 3 in 24 hours.[27]

The treatment related complications (hypotension, bradycardia, nausea, vomiting, persistent neurological deficit, shivering) did not differ among the groups i.e. found to be statistically the same except dexmedetomidine and clonidine has increased incidence of hypotension in comparison with magnesium and control groups.

CONCLUSION

In conclusion, present study showed that addition of bupivacaine spinal block with clonidine, magnesium sulphate and dexmedetomidine as an adjunct produces shorter onset of motor block and significant longer sensory and motor block than bupivacaine alone. Dexmedetomidine and clonidine have similar effects and better drugs as compared to and magnesium (50mg) in lower abdominal surgeries.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Meyer RA, Macarthur AJ, Downey K. Study of equivalence: spinal bupivacaine 15 mg versus bupivacaine 12 mg with fentanyl 15 µg for cesarean delivery. Int J Obstet Anesth. 2012;21:17-23.
2. Sirvinskas E, Laurinaitis R. Use of magnesium sulphate in anesthesiology. Medicine. 2002;38:147-50.
3. Bischoff P, Kochs E. Alpha 2-agonists in anaesthesia and intensive medicine. Anasthesiol Intensivmed Notfallmed Schmerzther 1993;28:2-12.
4. Yaksh TL, Reddy SV. Studies in the primate on the analgesic effects association with intrathecal actions of opiates, alpha-adrenergic agonists and baclofen. Anesthesiology. 1981;54:451-67.
5. Dobrydnjov I, Axelsson K, Thörn S E, Matthiesen P, Klockhoff H, Holmström B, Gupta A. Clonidine Combined with small-dose bupivacaine during spinal anaesthesia for inguinal herniorrhaphy: a randomized double-blinded study. Anesth Analg. 2003;96:1496-503.
6. Kanazi GE, Aouad MT, Jabbour-Khoury SI. Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anaesthesiol Scand. 2006;50:222-7.
7. Begon S, Pickering G, Dubray C. Magnesium increases morphine analgesic effect in different experimental models of pain. Anesthesiology. 2002;96:627-32.
8. Lysakowsi C, Dumont L, Czarnetzki C, Trame MR. Magnesium as an adjuvant to postoperative analgesia: A systematic review of randomized trials. Anesth Analg. 2007;104:1532-9.
9. Arcioni R, Palmisoni S, Tigano S. Combined intrathecal and epidural magnesium sulfate supplementation of spinal anaesthesia to reduce post-operative analgesic requirements: a prospective, randomized, double blind, controlled trial in patients undergoing major orthopedic surgery. Acta Anaesthesiol Scand. 2007;51:482-9.
10. Chanimov M, Cohen ML, Grinspun Y, Herbert M, Reif R, Kaufman I, et al. Neurotoxicity after spinal anaesthesia induced by serial injections of magnesium sulphate: an experimental study in a rat model. Anaesthesia. 1997;52:223-8.
11. Mageed Nabil A, El-Ghoniemy Yasser F. Intrathecal fentanyl magnesium for fast-track cardiac anaesthesia. Eg J Anaesth. 2005;21:289-93.
12. Sabbe MB, Penning JP, Ozaki GT, Yaksh TL. Spinal and systemic action of the alpha 2 receptor agonist dexmedetomidine in dogs. Antinociception and carbon dioxide response. Anesthesiology 1994;80:1057-72.
13. Virtanen R, Savola JM, Saano V, Nyman L. Characterization of the selectivity, specificity and potency of medetomidine as an alpha 2-adrenoceptor agonist. Eur J Pharmacol 1988;150:9-14.
14. Buvanendran A, McCarthy RJ, Kroin JS, Leong W, Perry P, Tuman KJ. Intrathecal magnesium prolongs fentanyl analgesia: a prospective, randomized, controlled trial. Anesth Analg. 2002;95:661-6.
15. Ozalevli M, Cetin TO, Unlugenc H, Guler T, Isik G. The effect of adding intrathecal magnesium sulphate to bupivacaine-fentanyl spinal anaesthesia. Acta Anaesthesiol Scand. 2005;49:1514-9.
16. Shoebi G, Sadegi M, Firazian A, Tabassomi F. The additional effect of magnesium to lidocaine in

spinal anaesthesia for caesarean section. Int J Pharmacol. 2007;3:425-7.
17. Woolf CJ, Thompson SW. The induction and maintenance of central sensitization is dependent on N-methyl-D-aspartic acid receptor activation; implications for the treatment of post-injury pain hypersensitivity states. Pain. 1991;44:293-9.
18. Eisenach JC, De Kock M, Klimscha W. Alpha2-adrenergic agonists for regional anaesthesia: A clinical review of clonidine (1984-1995). Anesthesiology. 1996;85:655-74.
19. Al-Mustafa M, Harawel S, Aloweidi A, Murshidi M, Ammari B, Awwad Z, Al-Edwan G, Ramsay M. Effect of dexmedetomidine added to spinal bupivacaine for urological procedures. Saudi Med J. 2009;30:365-70.
20. Rochette A, Raux O, Trocin R. Clonidine prolongs spinal anaesthesia in newborns: a prospective dose-ranging study. Anesth Analg. 2004;98:56-9.
21. Gupta R, Verma R, Bogra J, Kohli M, Raman R, Kushwaha JK. A Comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to Bupivacaine. J Anaesthesiol Clin Pharmacol. 2011;27:339-43.
22. Saadawy I, Boker A, Elshahawy MA. Effect of dexmedetomidine on the characteristics of bupivacaine in a caudal block in pediatrics. Acta Anaesthesiol Scand. 2009;53:251-6.
23. Dayiog˘ Lu H, Baykara N Z, Salbes A, Solak M, Toker K. Effects of adding magnesium to bupivacaine and fentanyl for spinal anaesthesia in knee arthroscopy. J Anesth. 2009;23:19-25.
24. Shukla D, Verma A, Agarwal A, Pandey HD, Tyagi C. Comparative study of intrathecal dexmedetomidine with intrathecal magnesium sulfate used as adjuvants to bupivacaine. J Anaesthesiol Clin Pharmacol. 2011;27:495-9.
25. Niemi L. Effects of intrathecal clonidine on duration of bupivacaine spinal anaesthesia, haemodynamics, and postoperative analgesia in patients undergoing knee arthroscopy. Acta Anaesthesiol Scand. 1994;38:724-8.
26. Larsen B, Dorscheid E, Macher-Hanselmann F, Buch U. Does intrathecal clonidine prolong the effect of spinal anaesthesia with spinal mepivacaine? A randomized double-blind study. Anaesthesist. 1998;47:741-6.
27. Bahar M, Chanimov M, Grinspun E, Koifman I, Cohen ML. Spinal anaesthesia induced by intrathecal magnesium sulphate: An experimental study in a rat model. Anaesthesia. 1996;51:627-33.
28. Bouaziz H, Hewitt C, Eisenach JC. Subarachnoid neostigmine potentiation of alpha 2-adrenergic agonist analgesia. Dexmedetomidine versus Clonidine. Reg Anesth. 1995;20:121-7.
29. Santiveri X, Arxer A , Plaja I, Metje M T, Villalonga A, López M. Anaesthetic and postoperative analgesic effects of spinal clonidine as an additive to prilocaine in the transurethral resection of urinary bladder tumours. Eur J Anaesthesiol. 2002;19:589-93.
30. Malleeswaran S, Panda N, Mathew P, Bagga R. A randomised study of magnesium sulphate as an adjuvant to intrathecal bupivacaine in patients with mild preeclampsia undergoing caesarean section. Int J Obstet Anesth. 2010;19:161-6.
31. Nath MP, Garg R, Talukdar T, Choudhary D, Chakrabarty A. To evaluate the efficacy of intrathecal magnesium sulphate for hysterectomy under subarachnoid block with bupivacaine and fentanyl: A prospective randomized double blind clinical trial. Saudi J Anaesth. 2012l;6:254-8.
32. Saadawy I, Boker A, Elshahawy MA. Effect of dexmedetomidine on the characteristics of bupivacaine in a caudal block in pediatrics. Acta Anaesthesiol Scand. 2009;53:251-6.

Cite this article as: Sur D, Agarwal A, Chaudhary AK, Bogra J, Singh PK, Gupta R, et al. A comparative study of different adjuncts to enhance the effects of intrathecal bupivacaine. Int J Res Med Sci 2017;5:2046-52.