http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v8i10.18

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Article

Comparison of Magnesium Sulphate with Clonidine and Magnesium Sulphate alone in terms of Motor & Sensory Blockade as an adjuvant to Hyperbaric Bupivacaine during Spinal Anaesthesia- A Prospective Randomised Clinical Trial

Authors
Dr Archana Gautam[1], Dr Reji S Varghese[2]
[1]Assistant Professor, Anesthesia, Krishna Institute of Medical Sciences Karad Maharashtra
[2]Associate Professor, Anesthesia, Pushpagiri Medical College and Hospital, Pathanamthitta Kerala

Abstract
Background: *The task of medicine is to preserve, restore health and to relieve pain. Understanding pain is essential to both these goals. This present study was designed to know the motor and sensory blockade when clonidine with MgSO4 was added as an adjunct to bupivacaine*
Objectives: *To evaluate the Sensory Block: onset, duration, time for maximal sensory block and Motor Block: onset and duration of motor block*
Methods: *A prospective randomized controlled trial was done in patients posted for elective lower abdominal and lower limb surgeries for 2 years. Two groups were decided Group M (n=35), received 3 ml of 0.5% hyperbaric bupivacaine, preservative free magnesium sulphate 50%, 0.1 ml(50 mg) and preservative free normal saline 0.5 ml. Group CM (n=35), received 3 ml of 0.5% hyperbaric bupivacaine, preservative free magnesium sulphate 50%, 0.1 ml(50 mg) and clonidine 0.5ml (75µg). SPSS (version 22.0) was used for analysis.*
Results: *In group M, there were 17 males and 18 females, and in group CM there were 18males and 17 females. The onset of sensory block was faster in group CM compared to group M. By using unpaired t-tests, p-value was <0.0001.The onset of motor block was faster in group CM compared to group M. By using unpaired t- tests, p-value was <0.0001.*
Conclusion: *Based on the present clinical comparative study, we conclude that the combination of clonidine (75µg) and magnesium sulphate (50 mg) as adjuvants with hyperbaric bupivacaine 0.5% (15 mg) for subarachanoid blockade results in earlieronset of action, prolonged duration of sensory blockade and extended postoperative analgesia.*
Keywords: *Spinal Anaesthesia, Intrathecal Bupivacaine, Sensory blockade, Randomization, Bromage scale, post-operative analgesia.*

Introduction

The task of medicine is to preserve, restore health and to relieve pain. Understanding pain is essential to both these goals.[1] Pain is derived from the Latin word poena which means penalty or punishment.[2] Relief of pain during operation is one of the mainstays of balanced anaesthesia. So, any experience acquired in this field should be

extended to the postoperative period also. In the pursuit of relief of pain, particularly pain during and after surgery, many attempts have been made since time immemorial. Postoperative pain relief is a growing concern for an anaesthesiologist as an uneventful postoperative period makes surgery a comfortable proposition for surgicalpatients.[3] Spinal anaesthesia was introduced into clinical practice by Karl August Bier in1898.[4] More than a century has passed and even today, it is one of the most popular techniques for both elective and emergency surgical procedures particularly caesarean sections, lower abdominal surgeries, orthopedic and urological surgeries just to name a few.[5] Other methods like epidural anaesthesia require technical expertise, larger amount of drug usage and sometimes even ending up with failed epidural analgesia. Further, Transcutaneous electrical nerve stimulator does not stand up against drug therapies as a sole treatment for anything other than mild postoperative pain. Therefore, it forms a challenging forefront in clinical and research advances, where if one can enhance sensory blockade into postoperative period by combining the lowest dose of the drugs with longer duration of action and least side effects, probably it may go a long way in alleviation of pain and suffering.[6] Adding Magnesium sulphate, on other hand, may improve the quality and increase the duration of spinal anaesthesia. Magnesium sulphate (MgSO4), which is the fourth most plentiful action in the body, proved to have antinociceptive effects in animal and human model of pain.[7] The intrathecal route of administration has been shown to be clinically safe in human. This present study was designed to know the motor and sensory blockade when clonidine with MgSO4 was added as an adjunct to bupivacaine in comparison withMgSO4 alone added as an adjunct to bupivacaine.

Materials and Methods

Study Design- Prospective, Randomized double blind, controlled trial

Study Settings- Krishna institute of medical sciences and hospital, Karad

Study Duration- 2 years between 2012-2014

Study Population- those patients posted for elective lower abdominal and lower limb surgeries.

Sampling Technique- Purposive sampling technique

Inclusion Criteria

1. ASA physical status I and II
2. Valid informed consent

Exclusion Criteria

1. ASA III and IV
2. Contraindication to regional anaesthesia.
3. Significant coexisting systemic disorders like neuromuscular diseases, neuronal degenerative disorders, bleeding and hematological disorders, cardiac disorders or gestational diabetes.
4. History of allergy to bupivacaine or clonidine.
5. History of opioid, clonidine medication or magnesium treatment prior to surgery
6. Parturients
7. Patient refusal
8. History of seizures

Sample Size- Sample size was calculated based on onset of sensory block to detect that onset will be earlier by 3.1 min (SD ±0.6) and duration of analgesia will be prolonged by at least 50 min (SD ±35) more, with α value of 0.05,power >95%. So, the required sample size was 70.

Ethical Consideration- The study was approved by Institutional ethics committee.

Consent Type- Written informed consent

Methodology

70 adult patients of each gender, randomly divided into two groups of 35 each were included in the study:

Group M (n=35), received 3 ml of 0.5% hyperbaric bupivacaine, preservative free magnesium sulphate 50%, 0.1 ml (50 mg) and preservative free normal saline 0.5 ml.

Group CM (n=35), received 3 ml of 0.5% hyperbaric bupivacaine, preservative free magnesium sulphate 50%, 0.1 ml(50 mg) and clonidine 0.5ml (75µg).

The procedure of double blinding was done by 2 separate anaesthetist and patient underwent thorough preoperative evaluation which includes history taking, general physical examination, investigation etc.

Patient was shifted to the operation table; intravenous access was obtained on the forearm with 20 Gauge intravenous cannula and Lactated Ringer's solution 500mL was infused intravenously before the block. The monitors connected to the patient included non-invasive blood pressure, oxygen saturation using pulse oximeter and electrocardiogram. Baseline PR and MAP was recorded.

A lumbar subarachnoid block was performed under strict aseptic precautions with the patients in the left lateral position with a 25-gauge Quincke needle at L2-3 orL3-4 using a midline approach. After free flow of cerebrospinal fluid (CSF), the premixed solution was injected over 10 sec with the needle orifice directed cephalad, making sure of negative aspiration for blood. Patients were made to lie supine immediately after the completion of injection. The time of injection of the drug was recorded as 0 minute.

Following parameters were studied:

Sensory Blockade:

a. Onset of sensory block (min): defined as~loss of pin prick at T10.

b. Time taken for maximal level of sensory block.

c. Duration of sensory block (min): defined as~Time to 2-segment regression. ~Time to regression of sensory block to S1.

Motor Blockade:

a. Time of onset of motor block

b. Total duration of motor block (min)

Sensory block was assessed every minute by pinprick. This was assessed by Bromage scale.

Bromage Scale[8]:

- ✓ Grade 0 - Full flexion of hip, knees and feet.
- ✓ Grade 1 - Unable to flex hip, full flexion of knees & feet.
- ✓ Grade 2 - Unable to flex hip, knees, but flexion of feet possible.
- ✓ Grade 3 - Unable to move legs or feet.

Statistical Analysis-Patients were allocated to the two insertion techniques randomly by computer generated random numbers. Parametric data were expressed as mean and standard deviation (S.D) and analysed using the independent t test using SPSS (version 22.0). $P<0.05$ is considered statistically significant.

Results and Observations

Table 1 Comparison of gender wise distribution of patients in group M and group CM

Gender	Group M		Group CM	
	No. of patients	Percentage (%)	No. of patients	Percentage (%)
Male	17	48.57	18	51.43
Female	18	51.43	17	48.57
Total	**35**	**100**	**35**	**100**

According to table 1 in group M, there were 17 males and 18 females, and in group CM there were 18males and 17 females.

Table 2 Comparison of weight (kilogram) wise distribution of patients in groupM and group CM

Weight (kgs)	Group M		Group CM	
	No. of patients	Percentage (%)	No. of patients	Percentage (%)
40 - 49	02	5.72	00	00
50 – 59	16	45.71	14	40
60 – 69	11	31.43	08	22.86
70 - 79	06	17.14	13	37.14
Total	35	100	35	100
Mean ± SD	59.02±8.57		62.54±7.19	
P- value	0.067			

Table 2 shows weight wise comparison of demographic parameters in group M and group CM. By using independent sample t-tests, p-value was 0.06. so, no significant difference was seen.

Table 3 Comparison of duration (seconds) for onset of sensory block in group M and group CM

Time in Seconds	Group M	Group CM
Minimum	124 (2.06mins)	85 (1.41 mins)
Maximum	396 (6.6 mins)	169 (2.81 mins)
Mean ± SD	289.57±61.94 (4.8±1 mins)	108.42±14.82 (1.8±0.2 mins)
P- value	<0.0001	

According to table 3 shows comparison of duration (seconds) for onset of sensory block in group M and group CM during induction of spinal block. The onset of sensory block was faster in group CM compared to group M. By using unpaired t-tests, p-value was <0.0001. Since the p-value is < 0.05, hence the difference is statistically significant. 95% confidence interval of the difference: -202.62 to -159.66

Table 4- Comparison of duration (seconds) for onset of motor block in group Mand group CM

Time in Seconds	Group M	Group CM
Minimum	204 (3.4 mins)	117 (1.95 mins)
Maximum	476 (7.9 mins)	195 (3.25 mins)
Mean ± SD	349.74±66.89 (5.8±1.1 mins)	151.82±18.38 (2.5±0.3 mins)
P- value	<0.0001	

Table 4 shows comparison of duration (seconds) for onset of motor block in group M and group CM during induction of spinal block. The onset of motor block was faster in group CM compared to group M. By using unpaired t- tests, p-value was <0.0001. Since the p-value is < 0.05, hence the difference is extremely significant. 95% confidence interval of the difference: -221.31 to -174.52.

Table 5 Comparison of duration (seconds) to reach highest level of sensoryblock in group M and group CM

Time in Seconds	Group M	Group CM
Minimum	246 (4.1 mins)	225 (3.75 mins)
Maximum	541 (9.01 mins)	350 (5.83 mins)
Mean ± SD	411.82±82.95 (6.86±1.3 mins)	301.74±29.77 (5.03±0.4 mins)
P- value	<0.0001	

According to table 5 comparison of duration (seconds) to reach highest level of sensory block in group M and group CM during induction of spinal block. The duration (seconds) to reach highest level of sensory block was faster in group CM compared to group M. By using unpaired t-tests, p-value was <0.0001.Since the p-value is < 0.05, hence the difference is statistically significant. 95%confidence interval of the difference: -139.81 to -80.358.

Table 6 Comparison of duration (minutes) for 2 Segment Regression of sensory block in group M and group CM

Time in Minutes	Group M	Group CM
Minimum	95	170
Maximum	160	210
Mean ± SD	115.57±12.93	192±10.79
P- value	<0.0001	

In table 6 the duration (minutes) of 2 Segment Regression of sensory block was delayed in group CM compared to group M. By using unpaired t-tests, p-value was <0.0001. Since the p-value is < 0.05, hence the difference is statistically significant. 95% confidence interval of the difference: 70.747 to 82.110.

Table 7- Comparison of duration (minutes) for recovery of sensory block ingroup M and group CM

Time in Minutes	Group M	Group CM
Minimum	170	310
Maximum	250	385
Mean ± SD	197±18.07	350.42±19.15
P- value	<0.0001	

In table 7 shows comparison of duration (minutes) for recovery of sensory block in group M and group CM. The duration (minutes) for recovery of sensory block was delayed in group CM compared to group M. By using unpaired t-tests, p-value was <0.0001. Since the p-value is < 0.05, hence the difference is statistically significant. 95% confidence interval of the difference: 144.55 to 162.31.

Table 8- Comparison of duration (minutes) for recovery of motor block in group M and group CM

Time in Minutes	Group M	Group CM
Minimum	140	250
Maximum	210	320
Mean ± SD	164.14±15.31	297±17.91
P- value	<0.0001	

According to table 8 comparison of duration (minutes) for recovery of motor block in group M and group CM. The duration (minutes) for recovery of motor block was delayed in group CM compared to group M. By using unpaired t-tests, p-value was <0.0001. Since the p-value is < 0.05, hence the difference is statistically significant. 95% confidence interval of the difference: 124.91 to 140.81.

Discussion

Our study design consisted of 70 patients, ASA physical status I, II undergoing elective lower abdominal and lower limb surgeries under spinal anesthesia were randomly divided into two groups after taking informed consent. In our study we have evaluated the effects of intrathecal magnesium sulphate with clonidine as ato bupivacaine in comparison with intrathecal magnesium sulphate alone as an adjunct to bupivacaine under following:

- ✓ Sensory Block: onset, duration, time for maximal sensory block
- ✓ Motor Block: onset and duration of motor block

In the present study the onset of sensory blockade in group M was289.57±61.94 seconds (4.8±1 mins) compared to 108.42±14.82 seconds (1.8±0.2mins) in group CM which was statistically significant (P< 0.0001). Similarly, the onset of motor blockade in group M was 349.74±66.89 seconds (5.8±1.1 mins) compared to151.82±18.38 seconds (2.5±0.3 mins) in group CM which was also statistically significant (P< 0.0001). This shows that there is an early onset of both sensory and motor block when clonidine with magnesium sulphate is added to bupivacaine compared to addition of magnesium sulphate alone as adjunct to bupivacaine. S.J. Bajwa et al[9] conducted a randomized clinical study, carried out among 100pregnant females showed that onset of sensory analgesia was significantly shorter ingroup receiving clonidine and bupivacaine (2.10±0.64 minutes vs 3.58±0.92 minutes) compared to group receiving bupivacaine alone. Onset of motor block was shorter in group receiving clonidine and bupivacaine (4.02±1.98 min vs 5.14±2.98 min) compared to group receiving bupivacaine alone. Another study conducted by Gurudatta et al[10] on 50 patients concluded that the mean time for onset of sensory blockade was faster in group BC (bupivacaine and clonidine group) 1.62±0.85 min compared to group B (bupivacaine group) 2.24±1.04 min which was highly significant with p value 0.000.Shukla D et al[11] conducted a study on 90 patients showed that the onset time of block, both sensory up to T10 dermatome and motor to Bromage 3 scale, was delayed in the group M (receiving bupivacaine with magnesium sulphate) (6.46 ± 1.33 and 7.18 ± 1.38) in comparison with the group C(receiving bupivacaine alone) (4.14 ± 1.06 and 4.81 ± 1.03). The difference between the groups was statistically significant in both sensory (P <0.0001) and motor (P<0.0001).Kothari N etAl[12] conducted a randomized single blind study for patients undergoing emergency caesarean section showing that the time to maximum

sensory block was faster in group receiving clonidine and bupivacaine (5.6±0.28 min vs 5.5±0.66 min) compared to group receiving bupivacaine alone. In a study conducted by Malleeswaran S et al[13] on sixty women with mild preeclampsia undergoing caesarean section showed that the time to reach maximum sensory block was delayed in group receiving bupivacaine, fentanyl and magnesium (8.7±0.9 min vs 7.7±0.8 min)compared to group receiving bupivacaine and fentanyl. In our study the time for two segment regression was considerably prolonged in group CM with 192±10.79 minutes and in group M it was 115.57±12.93 minutes which was statistically significant ($p<0.0001$). D.J. Fogarty, et al[14] conducted a comparative study on 90 patients showing that the time to two segment regression was prolonged by 216±97.1 minutes in group receiving bupivacaine and clonidine vs138±59.9 minutes in group receiving bupivacaine alone. In a study conducted by M Ozalevli, et al[15] on 100 patients showed the time to reach two segment regression ingroup receiving bupivacaine, fentanyl and magnesium was (84.1± 8.4 min vs 85.9±8.4 min) in group receiving bupivacaine and fentanyl which was not statistically significant. In our study, the time for complete sensory recovery was prolonged in group CM with 350.42±19.15 minutes and in group M it was 197±18.07 minutes which was statistically highly significant ($p<0.0001$). Gurudutta C.L et al[10]found in his study conducted on 50 patients that the sensory recovery (327 minutes vs207 minutes) and motor recovery (290.8minutes vs 150.0 minutes) was prolonged ingroup receiving clonidine and bupivacaine compared to group receiving bupivacaine alone. Shashni, et al[16] showed the sensory recovery (153.54±19.76 minutes vs138.87±12.55 minutes) and motor recovery (133.06±14.21 minutes vs 127.33±10.39 minutes) was prolonged in group receiving bupivacaine and magnesium compared togroup receiving bupivacaine and midazolam.

Conclusion

Based on the present clinical comparative study, we conclude that the combination of clonidine (75µg) and magnesium sulphate (50 mg) as adjuvants with hyperbaric bupivacaine 0.5% (15 mg) for subarachanoid blockade results in earlier onset of action, prolonged duration of sensory blockade and extended postoperative analgesia. The duration of sensory blockade and postoperative analgesia seems to be augmented by the combination since these are more prolonged than what is expected with either of the drugs used alone as adjuvants. It is an attractive alternative to opioids for prolonging spinal anesthesia.

Source of Funding- none
Conflict of Interest- None declared

References-

1. Howard LF, Joseph BM. Pain-Pathophysiology and Management In Harrison_s Principles of Internal Medicine, 15th Edition, Mc Grawhill, 2001.
2. Ronald DM editor. Miller‘s anesthesia. 7th ed. Churchill Livingstone; 2009; p3-54. 2767, 2758, 2760-7, 782-807, 1544, 1343, 2228
3. Vaswani RK, Raiger LK, Purohit R, Bajaj P. The effect of intrathecal midazolam on postoperative pain relief in orthopaedic surgery. Hospital Today2002;7(4):150-153.
4. Parameshwara G. Spinal, epidural to combined spinal epidural analgesia, thehistory of central neuraxial block. Indian J Anaesth 2001; 45(6):406- 412.
5. Dureja GP, Jayalaxmi TS. Colloid preloading before spinal and epidural anaesthesia. Hospital today 2000: V (11):601-603.
6. Buvanendran A, Mccarthy RJ, Kroin JS, et al. Intrathecal magnesium prolongsfentanyl analgesia: a prospective

randomized controlled trial. Anesth Analgl,2002; 95:661-6.
7. Begon S, Pickering G, Eschalier A, Dubray C. Magnesium increase morphineanalgesia effect in different experimental models of pain. Anesthesiology,2002; 96:627-32
8. Sethi BS, Samuel M, Sreevastava D. Efficacy of Analgesic Effects of Low Dose Intrathecal Clonidine as Adjuvant to Bupivacaine. Indian Journal of Anaesthesia, 2007;51(5):415-419.
9. Bajwa SS, Bajwa SK, et al. Prevention of hypotension and prolongation of postoperative analgesia in emergency cesarean sections: A randomized study with intrathecal clonidine. Int J CritIllnInj Sci, 2012; 2(2): 63–69.
10. Gurudatta CL, Svenkatesh G et al. A Prospective randomized controlled study of the effect of intrathecal clonidine with hyperbaric bupivacaine 0.5% forlower abdominal surgeries. Karnataka Anesthesia J, 2008; 9(2).
11. Shukla D, Verma A, Agarwal A, Pandey HD, Tyagi C. Comparative study ofintrathecal dexmedetomidine with intrathecal magnesium sulfate used asadjuvants to bupivacaine. J Anaesth Clin Pharmacol, 2011;27:495-9.
12. Kothari N, Bogra J, Chaudhary AK. Evaluation of analgesic effects ofintrathecal clonidine along with bupivacaine in cesarean section. Saudi JAnaesth, 2011; 5(1): 31–35.
13. Malleeswaran S, Panda N, Mathew P, Bagga R. A randomised study ofmagnesium sulphate as an adjuvant to intrathecal bupivacaine in patients withmild preeclampsia undergoing caesarean section. International Journal of Obstetric Anesthesia, 2010; 19:161–166.
14. Fogarty DJ, Carabine UA, Milligan KR. Comparison of the analgesic effects of intrathecal clonidine and intrathecal morphine after spinal anaesthesia in patients undergoing total hip replacement. Br J Anaesth,1993;71:661-664.
15. Ozaleli M, Cetin TO, Unlugenc H, et al. The effect of adding intrathecal magnesium sulphate to bupivacaine-fentanyl spinal anesthesia. Acta Anesthesiol Scand, 2005; 49:1514-9.
16. Shashni S, Nair AS, Gopal T. Clinical effects of intrathecal midazolam versusintrathecal magnesium sulfate as adjuncts to hyperbaric bupivacaine: acomparative study. Indian j pain, 2013;27:175-81.