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Comparative Study of Intrathecal Hyperbaric Bupivacaine, Hyperbaric Bupivacaine with Clonidine and Hyperbaric Bupivacaine with Magnesium Sulphate for Perioperative Pain Relief in Lower Limb and Infraumblical Surgeries

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Abstract

Background: Spinal anaesthesia is the primary anaesthetic technique for many types of surgery. Limiting the dose of local anaesthetic used in spinal anaesthesia has been an aggressive topic of study as it will achieve rapid anaesthetic recovery as well as reduce the incidence and severity of its side effects. *Context:* In our study we compared clonidine and magnesium as adjuvants to hyperbaric bupivacaine in spinal anaesthesia in terms of duration of sensory and motor block, sedation, respiratory depression and haemodynamic parameters. *AIM:* To compare Clonidine and Magnesium sulphate as adjuvants to bupivacaine heavy 0.5% for spinal anaesthesia in patients undergoing infraumbilical surgeries in terms of analgesic efficacy, duration of sensory block and adverse effects. *Settings and Design:* Conducted in ASA I-II patients with age group 18-60 years undergoing infraumbilical surgical procedures. Patients were randomly divided into three groups each of 25 patients. Group 1 (B) received 14 mg (2.8ml of 0.5%) preservative free hyperbaric bupivacaine 0.2 ml NS; Group 2 (BC) received 14 mg (2.8ml of 0.5%) preservative free hyperbaric bupivacaine+0.2 ml clonidine (30µg); Group 3 (BM) received 14 mg (2.8ml of 0.5%) preservative free hyperbaric bupivacaine+0.2 ml MgSO4 (100mg. *Statistical analysis used:* The data of the study were recorded in the record chart and results were evaluated using statistical tests (ANOVA, student t-test, chi-square test and post hoc test, F-test whichever was applicable). *Results:* The onset of sensory block and motor block was significantly delayed in group BM as compared to group B and BC. The duration of motor block was significantly prolonged in the Group BM and BC as compared to Group B. *Conclusions:* Magnesium is superior to Clonidine as an adjuvant to bupivacaine for infraumbilical and lower limb surgeries.

Keywords: Hyperbaric Bupivacaine; Lower Limbs; Infraumblical Surgery; Clonidine; Magnesium Sulphate; Pain; Spinal Anesthesia.

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Introduction

Spinal anaesthesia, since its origin has been extensively used for lower abdominal and lower extremity surgeries with advantages over general anaesthesia like optimal operative conditions, minimal intraoperative blood loss, less incidence of post operative morbidity, intense analgesia and sufficient muscle relaxation for surgery[1]. Traditionally local anaesthetic solution of hyperbaric bupivacaine is most frequently used drug in spinal anaesthesia. After years of extensive research on different pharmacological agents studies are now being done with adjuvants like clonidine, fentanyl, dextomeditidine, magnesium and others. The focus of these studies is on increasing the duration of action of spinal

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anaesthesia, having better haemodynamic stability as well as using lesser amount of local anaesthetic agent.

Intrathecal clonidine is being extensively evaluated as an alternative to neuraxial opioids for control of pain and has proved to be potent analgesic, free from at least some of the opioid related side effects [2]. Intrathecal clonidine produces dose dependent analgesia and prolongs the duration of intrathecally administered local anaesthetics and has potent antinociceptive properties. Clonidine acts on alpha 2 adrenoceptors that are located on primary afferent terminals on neurons in the superficial laminae of the spinal cord and within several brainstem nuclei implicated in analgesia, supporting the possibility of analgesic action at peripheral, spinal and brainstem sites [3].

Magnesium sulphate was used intrathecally as early as 1906 by Meltzer and Haubold and was found to potentiate analgesia caused by other intrathecal agents. One of the important mechanisms for the persistence of postoperative pain is considered to be due to central sensitization which increases the excitability of spinal neurons [4]. This sensitization has been found dependent on N-Methyl D-Aspartate (NMDA) receptors activating excitatory aspartates and glutamates on dorsal horn. Magnesium sulphate is a noncompetitive antagonist of NMDA receptor. It has the potential to prevent central sensitization from peripheral nociceptive stimulation in a voltage dependant manner [5]. The analgesic effect is not due to direct action of magnesium but due to prevention of subsequent NMDA activation.

The aim of our study was to compare Clonidine and Magnesium sulphate as adjuvants to bupivacaine heavy 0.5% for spinal anaesthesia in patients undergoing infraumbilical surgeries in terms of analgesic efficacy, duration of sensory block and adverse effects.

Materials and Methods

The design of the study was prospective randomized control study. After obtaining informed consent from the patients and approval from the ethical committee of Indira Gandhi Medical College, Shimla, this study was conducted in ASA I-II patients with age group 18-60 years undergoing infraumbilical and lower limb surgical procedures within the time period extending from 1st July 2015 to 30th June 2016. Patients were randomly divided into three groups each of 25 patients.

- Group 1(B) received 14 mg (2.8ml of 0.5%) preservative free hyperbaric bupivacaine + 0.2 ml normal saline.
- Group 2(BC) received 14 mg (2.8ml of 0.5%) preservative free hyperbaric bupivacaine + 0.2 ml clonidine (30μg).
- Group 3(BM) received 14 mg (2.8ml of 0.5%) preservative free hyperbaric

All patients were premedicated with tablet alprazolam 0.50 mg per orally night before surgery and 3 hours prior to surgery with a sip of water.

Monitoring was started with heart rate, non invasive blood pressure, pulse oximeter and electrocardiogram. Intravenous line was secured with 18 gauge cannula and intravenous infusion was started with crystalloid fluids. Spinal anaesthesia was given using 26 gauge Quincke's needle under all aseptic conditions at L_3– L_4 interspace in sitting position. Drugs were given slowly intrathecally at the rate of 0.2ml/second. Immediately after injecting the drug patients were kept in supine position.

Blood pressure (systolic blood pressure, diastolic blood pressure, mean arterial pressure), heart rate and peripheral oxygen saturation (SpO_2) were measured every 5 minutes for first 60 minutes, than every 10 minutes for next 1 hour. Vitals of all the patients were monitored for 2 hours after giving spinal anaesthesia.

The Following Parameters were Observed

- Onset of sensory block: from the time of injecting drug into subarachnoid space till complete analgesia at the level of T_{10}.
- Onset of motor block: assessed every 2 minutes till complete motor block will be achieved as per Modified Bromage Scale. (Score 1)

Modified Bromage Scale

Score	Definition
1	Total motor block
2	Total motor block, patient can only move his/her feet
3	Partial motor block, patient can move his/her knees
4	Patient can lift his/ her leg but cannot hold the position
5	No hip function, patient can lift and hold his/her leg for 10 seconds
6	No motor block

- Duration of sensory block: the time taken for two segment regression of the block from the maximum sensory block level.
- Duration of motor block: taken as the time from complete motor block (Modified Bromage 1) to time when lower limb can be moved freely (Modified Bromage 6).
- Sedation assessment: using Ramsay Sedation Scale.
- Side effects like Hypotenstion(mean blood pressure recording less than 20% of baseline), Bradycardia(heart rate less than 50/min), Respiratory depression(RR< 8 breath/min or SpO_2 < 90%), nausea, vomiting.

Analysis of data among groups was performed using appropriate statistical tests.

Inclusion Criteria

ASA physical status I or II with normal coagulation profile with age between 18 to 60 years, undergoing infraumbilical and lower limb surgical procedures within the time period extending from 1st July 2015 to 30th June 2016

Exclusion Criteria

Patients with history of allergy to amide local anaesthetics or clonidine or magnesium, bleeding or coagulation abnormalities, peripheral neuropathy, raised intracranial pressure, demyelinating central nervous disorders, local sepsis, spinal deformities, psychiatric diseases, valvular heart diseases and pregnant patients .

Study plan

All patients were premedicated with tablet alprazolam 0.50 mg per orally night before surgery and 3 hours prior to surgery with a sip of water.

Monitoring was started with heart rate, non invasive blood pressure, pulse oximeter and electrocardiogram. Intravenous line was secured with 18 gauge cannula and intravenous infusion was started with crystalloid fluids. Spinal anaesthesia was given using 26 gauge Quincke's needle under all aseptic conditions at L_3–L_4 interspace in sitting position. Drugs were given slowly intrathecally at the rate of 0.2ml/second. Immediately after injecting the drug patients were kept in supine position.

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Statistical Analysis

Statistical analysis of data among groups was performed by using appropriate tests (ANOVA, Student t test, post hoc test).

Results

1. All the three groups were comparable in demographic variables like age and sex distribution. (p-value > 0.05)
2. The baseline parameters like heart rate, mean arterial blood pressure, and SpO_2 were comparable in three groups. (p-value > 0.05)
3. The onset of sensory block was significantly delayed in group BM as compared to group B and BC (Table 1).
4. The onset of motor block was significantly delayed in group BM as compared to group B and BC (Table 3).
5. The maximum sensory block level reached was significantly higher when we added Magnesium and Clonidine as an intrathecal adjuvants to Bupivacaine respectively (more with Magnesium than clonidine) (Table 2).
6. The time required to reach the maximum sensory level was significantly delayed in Group BM as compared to Group B and BC (Table 1).
7. The time for two segment regression was significantly more in Group BM and BC as compared to Group B (Table 3).
8. The duration of motor block was significantly prolonged in the Group BM and BC as compared to Group B (Table 3).
9. The sedation scores were more in the Group BC as compared to Group BM which were more than those in Group B which had least sedation scores (Table 4).

Table 1: Sensory assessment

Sr. No.	Group of Patients	TOS Mean	TOS S.D.	TOS p-value	Tmax Mean	Tmax S.D.	Tmax p-value
1	B	4.08	0.64	.607 (B Vs BC)	5.88	0.72	.267 (B Vs BC)
2	BC	4.40	1.53	.000** (BC Vs BM)	6.36	1.29	.000** (BC Vs BM)
3	BM	7.04	1.20	.000** (B Vs BM)	9.44	1.16	.000** (B Vs BM)

p > 0.05= not significant, p <0.05=significant (*), p < 0.001=highly significant (**)

Group 1 (B group) received 14 mg (2.8ml of 0.5%) preservative free hyperbaric bupivacaine + 0.2 ml normal saline. Group 2 (BC) received 14 mg (2.8ml of 0.5%) preservative free hyperbaric bupivacaine + 0.2 ml clonidine (30μg). Group 3(BM) received 14 mg (2.8ml of 0.5%) preservative free hyperbaric bupivacaine + 0.2 ml $MgSO_4$ (100mg).

Table 2: Maximum level of sensory block achieved

Sr. No.	HS Level	B No.	B % age	BC No.	BC % age	BM No.	BM % age	p- value
1.	T_4	0	0	6	24	9	36	
2.	T_5	3	12	9	36	10	40	
3.	T_6	10	40	6	24	5	20	0.000
4.	T_7	5	20	1	4	1	4	
5.	T_8	7	28	3	12	0	0	

p > 0.05= not significant, p <0.05=significant (*), p < 0.001=highly significant (**)

Table 3: Time for two segment regression and motor assessment

Sr. No.	Group of Patients	T_2seg reg Mean	T_2seg reg S.D.	T_2seg reg p-value	TOM Mean	TOM S.D.	TOM p-value	Motor duration Mean	Motor duration S.D.	Motor duration p-value
1	B	129.48	15.30	.000** (B Vs BC)	7.08	0.81	.888 (B Vs BC)	226.42	29.83	.000** (B Vs BC)
2	BC	169.72	11.85	.000** (BC Vs BM	6.96	1.13	.000** (BC Vs BM)	335.88	42.74	.000** (BC Vs BM)
3	BM	216.44	14.94	.000** (B Vs BM)	8.32	0.75	.000** (B Vs BM)	401.92	26.67	.000** (B Vs BM)

p > 0.05= not significant, p <0.05=significant (*), p < 0.001=highly significant (**)
T_2seg reg (Time for 2 segment Regression), **TOM** (time of onset of motar block)

Table 4: Assessment of sedation score

Sedation score	B		BC		BM		p-value
	Number of patients	%age	Number of patients	%age	Number of patients	%age	
1	3	12	0	0	1	4	
2	19	76	6	24	15	60	
3	3	12	11	44	9	36	
4	0	0	8	32	0	0	.000**
5	0	0	0	0	0	0	
6	0	0	0	0	0	0	

p > 0.05= not significant, p <0.05=significant (*), p < 0.001=highly significant (**)

Table 5: Assessment of side effects

Parameter	Group B		Group BC		Group BM		p-value
	Number	% age	number	% age	Number	% age	
Nausea	0	0	0	0	0	0	NS
Bradycardia	1	4	3	12	1	4	.435
Shivering	0	0	0	0	0	0	NS
Respiratory depression	0	0	3	12	2	8	.132

Table 6: Comparison of hypotension given in group B, BC and BM

Incidence of Hypotension	B		BC		BM		p-value
	Number of patients	%age	Number of patients	%age	Number of patients	%age	
Absent	20	80	13	52	18	72	
Present	5	20	12	48	7	28	0.004

10. None of the patients in any group experienced nausea, vomiting or shivering (Table 5).
11. 20% patients in group B, 48% patients in group BC and 28% patients in group BM had hypotension (Table 6).
12. 4% patients in group B, 12% patients in group BC and 4% patients in group BM had bradycardia (Table 5).
13. 12% patients in group BC and 8% patients in group BM had respiratory depression (Table 5).

Discussion

Not many studies have compared clonidine and magnesium as adjuvants to hyperbaric bupivacaine in spinal anaesthesia for infraumblical surgeries. Hence a study was undertaken to find out the effectiveness of hyperbaric 0.5% bupivacaine in subarachnoid block in infraumblical surgeries and also to compare clonidine and magnesium sulphate as adjuvants to hyperbaric 0.5% bupivacaine for spinal anaesthesia in patients undergoing infraumbilical surgeries in terms of analgesic efficacy, duration of sensory block, quality of sensory block and adverse effects.

- In our study, the mean time for onset of sensory block in group B was 4.08 minutes, in group BC was 4.40 minutes and group BM was 7.04 minutes. Our study compared with the study conducted by Shende et al. [6] who found no significant difference regarding the onset of sensory block at T10 level in both the clonidine groups and control group. Our study also compared with the study conducted by Khalili et al. [7] who had evaluated the effect of adding Mg to intrathecal hyperbaric bupivacaine and found that the onset of the sensory block was slower in the $MgSO_4$ group than in the control group.

  Our study does not compare with the study done by Tabdar et al. [8] who found early onset of sensory block in the Magnesium 100 mg group as compared to the control (hyperbaric bupivacaine 0.5%) group. The delay in onset of sensory blockade in our study is most probably caused by Mg causing an adverse change in the pH of the cerebrospinal fluid leading to delay in the onset.
- In our study, time for 2 segment sensory regression in control group B, BC and BM groups were

129.48 minutes, 169.72 minutes and 216.44 minutes respectively which was statistically significant. Our study corresponds to the study conducted by Shende et al. [6], Sethi et al. [9] , Saxena et al. [10], Agarwal et al. [12], Prabha et al. [13] who found that the regression of the level of sensory analgesia by two segments was significantly longer in the the clonidine group as compared to the control group ($p<0.001$). Our study corresponds to the study conducted by Tabdar et al. [8], Nath et al. [11] who found that the regression of the level of sensory analgesia by two segments was significantly longer in the the Magnesium group as compared to the control group ($P<0.001$).

- In our study, the duration of motor block was 226.42 min, 335.88 min and 401.92 min in control group B, group BC and group BM respectively which was highly significant statistically with a p-value of 0.000.Similar observations were made with the studies conducted by Shende et al. [6], Sethi et al. [9], Saxena et al. [10] and Prabha et al. [13] where they have found longer duration of motor blockade in clonidine groups compared to control group.Similar observations were made with the studies conducted by Khalili et al. [7] , Tabdar et al. [8] and Nath et al. [11] where they have found longer duration of motor blockade in Magnesium groups compared to control group.
- Our study showed that the patients receiving bupivacaine and bupivacaine with Magnesium had minimal sedation but when we added clonidine in bupivacaine, the sedation scores were more. Similar observations have been made in studies conducted by Shende et al. [6], Sethi et al. [9], Saxena et al. [10], Nath et al. [11]. Clonidine acting directly on the locus ceruleus produces increased incidence of sedation.
- In our study, heart changes can be explained by the fact that clonidine at dose of 30 micrograms does not cause stastically significant decrease in heart rate. The changes in systolic and mean arterial blood pressure readings are attributed to clonidine. Magnesium as adjuvant to bupivacaine doesnot cause stastically significant changes in any of the haemodynamic parameters. Similar hemodynamic changes were observed in the studies conducted by Tabdar et al. [8], Nath et al. [11], Agarwal et al. [12] and Prabha et al. [13] , Clonidine reduces sympathetic drive in the nucleus tractus solitarius and locus ceruleus of the brainstem, by activation of postsynaptic alpha2-adrenoceptors. In the periphery, activation of presynaptic alpha-2 adrenoceptors by clonidine at sympathetic terminals reduces their release of norepinephrine, which could cause vasorelaxation and reduced chronotropic drive.

Conclusion

In conclusion, both 30 µg clonidine and 100 mg Magnesium are an attractive alternative as an adjuvant with bupivacaine in subarachnoid block for infraumblical surgical procedures especially in those that need quite long time with minimal side effects and excellent quality of spinal analgesia. But on account of greater duration of sensory and motor block and lesser incidence of side effects like hypotension, on the basis of our study Magnesium is superior to Clonidine as an adjuvant to bupivacaine for infraumbilical and lower limb surgeries.

Acknowledgement

None

Conflict of Interest: Nil

Key Messages

Magnesium is superior to Clonidine as an adjuvant to bupivacaine for infraumbilical and lower limb surgeries.

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