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A Study of Additional Medazolam with 0.5% Heavy Bupivacane in Subarachnoid Block in Central India

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Abstract
Regional anesthesia is much safer in lower abdominal & lower limb surgery in comparison to general anesthesia. The 0.5% hyperbaric bupivacaine is the most commonly used drugs. The study was conducted on 90 patients aged between 18 to 60 years admitted in MGM medical college Indore. The patients were randomly divided into three groups A,B and C of 30 each. All the observations were made before and at 2 minute interval after the induction of spinal block for first 20 minute and at10 minute interval till end of surgeries. Time for onset of sensory block in group A patients was 6.27 ± 2.88 minutes In-group B patients it was 5.03 ± 2.76 minutes. In-group C patients, the sensory block resulted in mean time of 3.00 ± 00 minutes. The time for onset of motor block in group A patients was 7.45 ± 3.25 minutes, in-group B patients it was 6.25 ± 2.85 minutes. In-group C patients, the motor block resulted in mean time of 2.93 ± 2.64 minutes. It can be concluded from the present study that preservative free Midazolam (1&2mg) out of them 2mg is optimum dose of midazolam increases duration of sensory block, motor block and postoperative pain free period no any significant side effects were seen.
Keywords: *Regional anesthesia, medazolam, bupivacaine, spinal block, motor block.*

Introduction

The anesthesia type of regional anesthesia is much safer in lower abdominal & lower limb surgery in comparison to general anesthesia because it avoids general anesthesia related problems such as complications of poly-pharmacy, airway manipulation, hypo or hyperventilation, vomiting and pulmonary aspiration. Regional anesthesia also reduces surgical stress and attenuates increase in plasma catecholamines and other hormones. Regional anesthesia gives intra and postoperative pain relief with full preservation of mental status and normal reflexes. It provides excellent pain relief as compared to intravenous or epidural route. The subarachnoid blockade is the common form of centrineuraxial blockade performed for lower abdomen & lower limb surgeries. The sensory block ensures the patient well being,

while motor block facilitates the surgeon's work. The 0.5% hyperbaric bupivacaine is the most commonly used drugs. It produces longer duration of anesthesia with good muscle relaxation.

Midazolam, synthesized by Walsar and colleagues in 1976[1], is the first clinically used water soluble benzodiazepine. It is also the first benzodiazepine that was produced primarily for use in anaesthesia. The subarachnoid midazolam was originally shown to have anti-nociceptive properties in studies performed in animals in early 1980's[2]. The subarachnoid midazolam has been used in humans since 1986 and doses up to 2 mg have been described[3]. It abolishes pain of somatic origin, produces selective sensory block and blocks somato sympathetic reflexes without any neurotoxicity. The subarachnoid midazolam potentiates the blocking actions of local anaesthetics.

It improves the quality of sensory and motor block, without prolonging the recovery. It also provides prolonged post-operative pain relief without producing sedation[4,5,6]. The subarachnoid midazolam is also devoid of complications such as, bradycardia, hypotension, post- operative nausea and vomiting, pruritus, urinary retention and neurotoxicity[4,5].

Aims and Objective

a) To study the effects of addition of different doses of Midazolam with
hyperbaric Bupivacaine 0.5% in Intrathecal block in terms of:

- Onset time of sensory and motor block.
- Quality of motor block.
- Duration of sensory and motor block.
- Highest dermatomal level of sensory block achieved.

b) To find out the optimum dose of Midazolam to be added to Bupivacaine
0.5% in intrathecal block that would offer maximum duration of postoperative analgesia with minimum side effects.

c) To find out post operative pain free period.

d) To study the associated hemodynamic changes.

Material and Methods

The present study entitled was carried out in the Department of Anaesthesiology M.G.M Medical College & M. Y. Hospital, Indore after approval of a hospital ethics committee this study was carried out on 90 patients admitted for lower limb surgery, under intrathecal block during the period of April 2015 to April 2016

The study was conducted on 90 patients aged between 18 to 60 years of ASA class I and II posted for lower limb surgeries. The patients were randomly divided into three groups of 30 each according to drug used for intrathecal block.

1. Group A– Inj. Bupivacaine 0.5% (H) – 3ml +0 .5ml 0.9 % NS (Control group)

2. Group B– Inj. Bupivacaine 0.5% (H) – 3.0 ml with Midazolam 1 mg.(0.2ml) + 0.3 ml 0.9 %NS

3. Group C– Inj. Bupivacaine 0.5% (H) – 3.0 ml with Midazolam 2mg(0.4ml) + 0.1 ml 0.9% NS

After assessing the base line vital parameters and securing IV line, 500ml of RL was given for preloading. Subarachnoid block was performed by25 gauge Quincke type spinal needle in latral position by midline approach at L3-L4 intervertibral space under all aseptic precations.

After performing lumber puncture, hyperbaric Bupivacaine 0.5% in a dose of 3ml combined with or without Midazolam was administered according to assigned study group. The syringe along with the needle was withdrawn; the wound was dressed with sterile gauze soaked in Tincture Benzoin. The patient was made supine and oxygen was given via a venturi - mask @ 4 L / min. Then vital parameter (Spo2, PR, NIBP, ECG) were recorded intraoperativly. Assessment of level of sensory block was done by pinprick method, assessment of motor block was done by modified Bromage scale on 3-point scale.

Results

All the observation were made before and at 2 minute interval after the induction of spinal block for first 20 minute and at10 minute interval till

end of surgeries. Sedation score was assessed by scoring system of chernik et al the score range from 0 to 3. Total duration of analgesia was also recorded during the period of study. Statistical analysis was done by various methods like Z-score, p value. Mean, median and SD were recorded for all data based on normality. Parametric and non-parametric tests were declared statistically significant for p-value< 0.05, highly significant on p-value 0.00 to <0.05 & not significant if p-value >0.05.

Age Distribution

The age of patients included in the study was from 18 years to 60 years with a mean age of 36.41 years. Majority of patients (52/90) included in the study were between age group 21 – 40 years.

Table No. 1: Age distribution of the patients

Age group (yrs)	Group A (n = 30)	Group B (n = 30)	Group C (n = 30)
10-20	2	3	5
21-30	6	7	10
31-40	10	9	10
41-50	6	7	1
51-60	6	4	4

Table No. 1 shows age distribution of the patients included in the study. The age of patients included in the study was from 18 years to 60 years with a mean age of 36.41 years. Majority of patients (52/90) included in the study were between age group 21 – 40 years. The gender distribution of the patients, of the 90 patients included in study; 76 patients were male and 14 patients were female.

Onset time of sensory block

Table No. 2 shows the mean onset time of sensory block in each group tested by pinprick method and defined as time interval between the injection of local anesthetic solution with or without study drug

• Time for onset of sensory block in group A patients was 6.27 ± 2.88 minutes, median value of 6 minute. In-group B patients it was 5.03 ± 2.76 minutes, median value of 4 minutes. In-group C patients, the sensory block resulted in mean time of 3.00 ± 00 minutes, median value of The time for onset of sensory block in-group B was found statically insignificant (p value >0.05) while in-group C was found statistically highly significant (p value < 0.05).

Table No. 2: Onset Time Of Sensory Block

OSB	Mean Time (minutes)	S.D	t	P	Significance
Group a (n=30)	6.27	2.88	-	-	-
Group b (n=30)	5.03	2.76	1.69	0.096	(p>0.05) Not significant
Group c (n=30)	3.00	00	6.02	0.00	(p<0.05) Highly significant

Table No. 3 shows the mean onset time of motor block in each group. • The time for onset of motor block in group A patients was 7.45 ± 3.25 minutes and median value was 7.5 minutes; in-group B patients it was 6.25 ± 2.85 minutes and median value 6 minutes. In-group C patients, the motor block resulted in mean time of 2.93 ± 2.64 minutes and median value was 2 minutes. The time for onset of motor block was found statistically insignificant (p-value >0.05) in-group B and statically highly significant (p value < 0.05) in-group C.

Table No. 3: Onset Time Motor of Block

OMB	Mean-Time (Min)	S.D	T	P	Significance
Group a (n=30)	7.45	3.25	-	-	-
Group b (n=30)	6.25	2.85	1.499	0.139	(p>0.05) Not significant
Group c (n=30)	2.93	2.64	5.91	0.00	(p<0.05) Highly significant

Highest Dermatomal Level of Sensory Block Achieved

• The highest dermatomal levels of sensory block between T4 and T5 was observed 2 out of 30 patients in group A and one out of 30 & 5 out of 30 patients in-group B and group C respectively. Maximum number of patients had highest dermatomal level of sensory block at level T6-T7 in group A 14 out of 30 and 16 out of 30 & 19 out of 30 respectively in group B and group C. The level of T8 –T9 was found 9 out of 30 patients in group A and 10 out of 30 & 5 out of 30 respectively group B and group C. The lower dermatomal levels of sensory block at T10 was found only 5 out of 30 patients in group A and group B & group C found 3 out of 30, 1 out of 30. In group A patient's intrathecal block regressed in 153.0 ± 30.43 minutes that is much lower than that observed in study group patients. Mean duration of sensory block in-group B, and C had found to be 178.93 ± 32.55 and 189.00 ± 39.88 minutes respectively. The changes in mean duration of sensory block was significant in group B (p-value =0.002) and highly significant in group C (p-value =0.00).

Table No. 4: Dermatomal level of sensory block achieved.

Dermatomal level	No. of patients		
	Group A (n= 30)	Group B (n= 30)	Group C (n= 30)
T4 – T5	2	1	5
T6 – T7	14	16	19
T8 – T9	9	10	5
T10	5	3	1

Table No.4 shows the highest dermatomal level of sensory block achieved after intrathecal injection in control and study groups. A tilt of 10 degree was given, the resulting height varied from T-4 to T-10 dermatomes. In 8/90, patient's highest level of block was between T 4 and T 5, whereas in 49/90 patients highest block level, was between T 6 to T 7 and 24/90 patient's level up to T-8 to T-9 was observed. In 9/90, patient has observed highest level up to T-10.

Duration of Sensory Block

Table No. 5 shows the duration of sensory block. It is defined as the interval from intrathecal administration to the point of a regression of sensory blockade from T10 to S1, recorded in minutes. In control group patient's intrathecal block regressed in 153.0 ± 30.43 minutes that is much lower than that observed in study group patients. Mean duration of sensory block in-group B, and C had found to be 178.93 ± 32.55 and 189.00 ± 39.88 minutes respectively. Statistical analysis revealed that the changes observed are significant in-group B and statically highly significant in- group C.

Table No 5: Duration of sensory block.

Groups	Mean Time (minutes)	S.D	t	P	Significance
Group A (n=30)	153.00	30.43	-	-	-
Group B (n=30)	178.93	32.55	3.18	0.002	(p<0.05) Significant
Group C (n=30)	189.00	39.88	3.93	0.00	(p<0.05) Highly significant

Duration of Motor Block

Table No. 6 shows the duration of motor block defined as the interval from intrathecal administration to the point in which the Bromage score was back to one or zero, recorded in minutes. The mean duration of motor block was found to be 137.37 ± 25.00 minutes in control group; it was significantly prolonged in study group patients and was found to be 155.00 ± 23.26 minutes and 151.93 ± 46.30 minutes in-group B and C respectively. Statistical analysis revealed that the changes observed are significant in- group B and insignificant in-group C.

Table No. 6: Duration of Motor Block

GROUPS	P	Significance	Mean Time (minutes)	S.D	t
Group a (n=30)	-	-	137.37	25.00	-
Group b (n=30)	0.006	(p<0.05) Significant	155.00	23.26	2.82
Group c (n=30)	0.137	(p>0.05) Not significant	151.93	46.30	1.51

Discussion

The present study correlate with the previous studies done by Batra et al[7], M. H. Kim and Y. M. Lee[8]. Bharti et al, Agarwal et al. Batra et al in 1999 showed that the duration of sensory blockade was increased from 229.8 ± 41.4 minutes in bupivacaine group to 267.6 ± 67.38 minutes in midazolam group with p value < 0.05, thus being statistically significant. M. H. Kim and Y. M. Lee in year 2001 found that the analgesic effect of intrathecal bupivacaine was potentiated by intrathecal midazolam. The addition of 1 or 2 mg of intrathecal midazolam prolonged the postoperative analgesic effect of bupivacaine after hemorrhoidectomy by approximately 2 h and 4.5 h, respectively, compared with controls . Bharti et al in 2003[8] showed that the duration of sensory block was significantly longer in the midazolam group than the bupivacaine group (218min versus 165min, p < 0.001). Agarwal et al[9] in 2005 conducted a study on postoperative pain relief following intrathecal administration of 1mg preservative free midazolam with bupivacaine in patients scheduled for elective lower abdominal, lower limb,and endoscopic urological surgeries. Time to first rescue analgesic in patients who received bupivacaine alone was significantly earlier than in patients who received bupivacaine and midazolam combination (4 ± 3.5 hours versus 17.6 ± 8.87 hours, p < 0.0001). In the study conducted by Shadangi et al. in 2011 the time for onset of motor block in control patients was 5.9 ± 0.4 minutes where as in Midazolam group patients it was 6.0 ± 0.8 minutes. The time for onset of motor block was similar in both groups and found statistically insignificant (p>0.05).

In the present study mean duration of motor block was found to be 137.37 ± 25.00 minutes in control group; it was significantly prolonged in study group patients and was found to be 155.00 ± 23.26 minutes and 151.93 ± 46.30 minutes in-group B and C respectively. Statistical analysis revealed that the changes observed were significant between- group B p<0.05 (p value= 0.06 and insignificant p>0.05(p value= 0.137) in-group C. The results of present study are consistent with that of Shadangi et al.[10] about onset of motor block. The mean time for onset of sensory block did not change significantly after adding of Midazolam 1mg but it significantly changed after the addition of 2mg midazolam. Similarly, the mean time for onset of motor block did not change significantly after adding of Midazolam 1mg but it significantly changed after adding of 2mg. Statistical analysis revealed this difference to be insignificant in-group B and highly significant in-group C. Incidences of various complications – nausea, vomiting, bradycardia, hypotension and shivering, noticed in patients receiving Midazolam were not significant when compared with control group patients. Statically data analysis was revealed that there were no significant changes present. The addition of Midazolam increased the duration of sensory block; the change was statistically significant for all doses of Midazolam (1mg &2mg) but highly significant in group C (2mg). The addition of Midazolam increased the duration of motor block; the change was statistically significant for group B (1mg) doses of Midazolam but insignificant in group C (1mg) employed in the study group patients. Dose related enhancement in postoperative pain free period was observed in all patients who received Midazolam in combination with bupivacaine. The mean duration of the postoperative pain free period with 1 and 2 mg Midazolam was increased Statistical analysis revealed that the changes observed were

significant in both groups, but highly significant in-group C.

Also, sedation score was observed 0 in group A (control group), 0 to one in group B & 0 to 2 in group C. Most of the patient in the study group was calm, sleeping & comfortably, whereas most of the patients in the control group were awake & alert.

Conclusion

It can be concluded from the study that among preservative free Midazolam (1&2mg) out of them 2mg is an optimum dose of midazolam increases duration of sensory block, motor block and postoperative pain free period no any significant side effects were seen. Therefore, drug 2mg Midazolam can be safely used as an adjuvant to bupivacaine for subarachnoid block.

References

1. Walser, L. E. Benjamin Sr., T. Flynn, C. Mason, R. Schwartz, and R. I. Fryer, "Quinazolines and 1,4-benzodiazepines. 84. Synthesis and reactions of imidazo[1,5 a][1,4]benzodiazepines," *Journal of Organic Chemistry*, vol. 43, no. 5, pp. 936–944, 1978.
2. D. Niv, J. G. Whitwam, and L. Loh, "Depression of nociceptive sympathetic reflexes by the intrathecal administration of midazolam," *The British Journal of Anaesthesia*, vol. 55,no. 6, pp. 541– 547, 1983.
3. C. S. Goodchild and J. Noble, "The effects of intrathecal midazolam on sympathetic nervous system reflexes in man—a pilot study," *The British Journal of Clinical Pharmacology*, vol. 23, no. 3, pp. 279–285, 1987.
4. Y. K. Batra, K. Jain, P. Chari, M. S. Dhillon, B. Shaheen, and G. M. Reddy, "Addition of intrathecal midazolam to bupivacaine produces better post-operative analgesia without prolonging recovery," *International Journal of Clinical Pharmacology and Therapeutics*, vol. 37, no. 10, pp. 519–523, 1999.
5. M. H. Kim and Y. M. Lee, "Intrathecal midazolam increases the analgesic effects of spinal blockade with bupivacaine in patients undergoing haemorrhoidectomy," *The British Journal of Anaesthesia*, vol. 86, no. 1, pp. 77–79, 2001
6. A. Sen, A. Rudra, S. K. Sarkar, and B. Biswas, "Intrathecal midazolam for postoperative pain relief in caesarean section delivery," *Journal of the Indian Medical Association*, vol. 99, no. 12, pp. 683–686, 2001.
7. R. Mahajan, Y. K. Batra, V. K. Grover, and J. Kajal, "A comparative study of caudal bupivacaine and midazolam-bupivacaine mixture for post-operative analgesia in children undergoing genitourinary surgery," *International Journal of Clinical Pharmacology And Therapeutics*, vol. 39, no. 3, pp. 116–120, 2001.
8. N. Bharti, R. Madan, P. R. Mohanty, andH. L. kaul, "Intrathecal midazolam added to bupivacaine improves the duration andquality of spinal anaesthesia," *Acta Anaesthesiologica Scandinavica*, vol. 47, no. 9, pp. 1101–1105, 2003.
9. N. Agrawal, A. Usmani, R. Sehgal, R. Kumar, and P. Bhadoria, "Effect of intrathecal midazolam bupivacaine on post-operative analgesia," *Indian Journal of Anaesthesia*, vol. 49,no. 1, pp. 37–39, 2005.
10. B. K. Shadangi, R. Garg, R. Pandey, and T. Das, "Effects of intrathecal midazolam in spinal anaesthesia a prospective randomized case control study," *Singapore Medical Journal*, vol. 52, no. 6, pp. 432–435, 2011.