



Complication of regional anaesthesia in addition of midazolam with hyperbaric bupivacaine 0.5% in intrathecal block – A Comparative Study done in tertiary care centre

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Abstract

Introduction: Spinal anaesthesia with local anaesthetic agents and adjuvant is extensively used for lower abdominal surgery. Neuraxial opioids have effective postoperative analgesia without sensory or motor blockade. But in spite of ease of administration and patient comfort, worrisome adverse effects like potentially catastrophic respiratory depression, urinary retention, vomiting, pruritus, etc.

Material and Method: 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. 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.

Result: Ninety patients of physical status I and II as per American Society of Anaesthesiologists, of either sex, in age groups 18 to 60 years undergoing elective lower limb surgeries under SAB were subject of the study. Patients were randomly divided into three groups of thirty patients each to receive different doses of Midazolam (0, 1 and 2 mg with 15 mg bupivacaine) by adopting block randomization method. Statistical comparison that in control group patients there is no significant difference in complications rate and dose strength of Midazolam administered. Bradycardia and hypotension responded to treatment. Twenty tree patients from all groups had bradycardia that is pulse rate less than 60 bpm. All patients responded to intravenous atropine injection 0.6 mg.

Discussion: 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 were revealed that there were no significant changes present.

Keywords: Midazolam, Bupivacaine.

Introduction

Spinal anaesthesia with local anaesthetic agents and adjuvant is extensively used for lower

abdominal surgery.^{1,2} The used of regional anaesthesia like midazolam are more effective and many time reduces surgical stress..The analgesia

extends for variable duration in the postoperative period. It provides excellent pain relief as compared to intravenous or epidural route. Neuraxial opioids have effective postoperative analgesia without sensory or motor blockade. But in spite of ease of administration and patient comfort, worrisome adverse effects like potentially catastrophic respiratory depression, urinary retention, vomiting, pruritus, etc.

In order to prolong postoperative analgesia, a number of adjuvants have been added to spinal local anaesthetics including morphine, pethidine, ketamine, tramadol, clonidine, neostigmine, midazolam etc. Of them, midazolam holds a good promise for its analgesic efficacy when administered intrathecally in combination with local anaesthetics.

In 1976 Walser and colleagues first time used a water soluble benzodiazepine in which synthesized Midazolam³. Faull and Villiger in 1986 describe a high density of benzodiazepine (GABA-A) receptor in lamina II of spinal cord⁴. The present study conducted to evaluated complications and vital changes used to mixture of midazolam and bupivacaine.

Aims and Objectives

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

1. To study the associated hemodynamic changes.
2. To find out any adverse drug reaction to intrathecal Midazolam.

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 ethical committee this study was carried out on 90 patients admitted for lower limb surgery in Department of Orthopaedics, under intrathecal block. 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 by 25 gauge Quincke type spinal needle in lateral position by midline approach at L3-L4 intervertebral space under all aseptic precautions.

After performing lumbar 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 intraoperatively. 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.

Using multiparameter monitor, vital parameters Pulse, B.P, ECG, R.R and SpO₂ were observed

- Heart rate, NIBP, R.R & Spo2 were recorded before intrathecal injection and after intrathecal injection at 5, 10, 15, 20, 25 and 30 minute and then at every fifteen minutes till the end of the operation.
- Level of sedation was assessed using the sedation score described by chernik et al. (0= Wide awake, 1= sleeping comfortably, responding to verbal commands, 2= deep sleep, but arousable, 3=deep sleep, not arousable). It is assessed pre op than after 15 mins, 30 mins, 45 mins, 60 mins & 120 mins.

- Incidence of hypotension (M.A.P \leq 70 mmHg) treated with 500ml IV fluid push and incremental doses of ephedrine 6 mg and bradycardia (heart rate \leq 60/min) was treated with atropine 0.6 mg IV.

Data Type: The data on onset and offset character and on post operative pain free period, intraoperative hemodynamic parameters will be ordinal categorical type and shall be subjected to statistical calculations by Mean and standard deviation test. In situations of wider range of observations interquartile range was quoted because standard deviation provided clinically unacceptable data.

Age Distribution

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.

Result

The present study entitled “Complication of regional anaesthesia in addition of midazolam with hyperbaric bupivacaine 0.5% in intrathecal block – A Comparative Study done in tertiary label of central India”. This study had carried out in the Department of Anaesthesiology M. G. M. Medical College and M Y Hospital, Indore.

Ninety patients of physical status I and II as per American Society of Anaesthesiologists, of either sex, in age groups 18 to 60 years undergoing elective lower limb surgeries under SAB were subject of the study. Patients were randomly divided into three groups of thirty patients each to receive different doses of Midazolam (0, 1 and 2 mg with 15 mg bupivacaine) by adopting block randomization method.

Gender Distribution

Table 2: Gender distribution of the patients

	Group A (n = 30)	Group B (n = 30)	Group C (n = 30)
Male	24	25	27
Female	6	5	3

Table No. 2 shows the gender distribution of the patients, of the 90 patients included in study; 76 patients were male and 14 patients were female.

Incidence of Side Effects during Intrathecal Block

Table no 3: Incidence of side effects during intrathecal block.

Side Effects	Group A (n=30)	Group B (n=30)	Group C (n=30)
Hypotension	10	8	5
Bradycardia	8	9	6
Shivering	4	4	2
Vomiting	4	3	3

Table No. 3 shows incidence of complications seen in control and study groups.

Complications seen were hypotension, bradycardia, shivering, nausea and vomiting.

Incidence of complications is shown in table No.8. Table no.4– 7 shows the statistical comparison that in control group patients there is no significant difference in complications rate and

dose strength of Midazolam administered. Bradycardia and hypotension responded to treatment.

Table no 4: Incidence of hypotension during intrathecal block.

Study group	No. of Patients	No. of Patients in Group A	Z –Test value	p value	Significance
Group B	8	10	0.5634	0.5748	(p>0.05) Not significant
Group C	5	10	1.490	0.1368	(p>0.05) Not significant

Table no 5: Incidence of bradycardia during intrathecal block

Study group	No. of Patients	No. of Patients in Group A	Z –Test value	p value	Significance
Group B	9	8	0.286	0.771	(p>0.05) Not significant
Group C	6	8	0.61	0.541	(p>0.05) Not significant

Table no 6: Incidence of vomiting during intrathecal block.

Study group	No. of Patients	No. of Patients in Group A	Z –Test value	p value	Significance
Group B	3	4	0.40	0.684	(p>0.05) Not significant
Group C	3	4	0.40	0.684	(p>0.05) Not significant

Table no 7: Incidence of shivering during intrathecal block.

Study group	No. of Patients	No. of Patients in Group A	Z –Test value	p value	Significance
Group B	4	4	0.00	1	(p>0.05) Not significant
Group C	2	4	0.86	0.389	(p>0.05) Not significant

Changes in Heart Rate

Table No 8: Changes in heart rate.

GROUPS	PreOp	5min	10min	15min	20min	25 min	30min	45min	60min	90 Min	120 Min
GroupA (n=30)	86.83±10.99	86.77±12.23	86.17±14.20	86.03±16.39	84.00±14.75	81.07±12.34	78.63±12.19	80.5±10.93	81.43±11.21	84.10±10.78	86.80±9.03
GroupB (n=30)	84.60±8.26	81.70±10.37	81.10±11.94	78.50±13.20	74.3±11.17	72.43±12.81	69.03±9.07	67.37±9.53	70.23±9.49	76.47±11.61	82.87±9.99
GroupC (n=30)	92.1±10.15	91.6±11.75	87.87±13.69	87.07±17.15	80.47±13.6	77.07±15.02	72.6±11.67	72.73±12.31	74.37±10.07	79.13±12.01	88.00±11.10

Table No.8 shows changes in mean heart rate at different time of observations in control and study group patients. In all patients mean heart rate did not change significantly. Twenty tree patients

from all groups had bradycardia that is pulse rate less than 60 bpm. All patients responded to intravenous atropine injection 0. 6 mg.

Changes in Mean Arterial Pressure

Table no 9: Changes in mean arterial pressure

GROUPS	PreOp	5min	10min	15min	20min	25 min	30min	45min	60min	90 min	120 Min
GroupA (n=30)	89.97±7.45	80.63±11.76	72.83±10.97	67.37±11.02	66.80±13.88	65.80±10.80	69.23±10.72	72.03±8.72	76.90±8.26	80.60±8.10	86.73±7.8
GroupB (n=30)	91.0±6.31	84.37±7.33	77.63±8.37	71.23±9.04	67.80±10.97	67.27±9.7	68.43±7.73	70.53±6.76	72.9±7.8	78.3±7.66	83.5±7.81
GroupC (n=30)	89.67±6.01	80.77±7.16	73.5±8.05	69.63±8.17	65.70±8.33	64.53±7.34	65.6±6.26	68.67±8.1	73.83±7.39	78.1±8.00	86.40±7.491

Table no. 9 shows changes observed in mean arterial pressure in control and study group patients. In 23 patients hypotension was observed. It was treated when the mean arterial pressure

value was lower than 60. Patients responded to intravenous fluid bolus and injection ephedrine 6-12 mg given intravenously.

Changes in Respiratory Rate

Table No 10: Changes in respiratory rate.

GROUPS	PreOp	5min	10min	15min	20min	25 min	30min	45min	60min	90 min	120 Min
GroupA (n=30)	13.80± 0.925	13.40±0. 81	13.23 ±1.00	13.17± 0.95	13.30± 0.95	13.30± 0.87	13.17± 1.05	13.23± 0.89	13.30 ±0.87	13.20± 0.96	13.07 ±0.97
GroupB (n=30)	13.77± 0.89	13.53±0. 86	13.50 ±1.14	13.30± 1.39	13.30± 1.02	13.37± 0.93	13.30± 1.02	13.23± 0.82	13.43 ±1.22	13.43± 1.07	13.27 ±0.87
GroupC (n=30)	13.6±0. 89	13.13±1. 31	13.23 ±1.43	13.27± 1.28	13.23± 1.16	13.13± 0.97	13.33± 0.75	13.47± 0.77	13.43 ±0.93	13.57± 0.89	13.50 ±0.77

Table No.10 shows changes in Respiratory rate at different time of observations in control and study group patients. In all patients, mean respiratory rate did not change significantly and remained close to pre-operative mean value

Discussion

The subarachnoid blockade is the common form of centrineuraxial blockade performed for lower limb surgeries. The ensuing nerve block ensures the patient well being, while motor block facilitates the surgeon's work. 0.5% hyperbaric bupivacaine produces longer duration of anaesthesia with good muscle relaxation. It provides effective pain relief during initial post-operative period.

In order to maximize postoperative analgesia, a number of adjuvants have been added to spinal local anaesthetics. Midazolam is a water-soluble imidazo-benzodiazepine derivative which has been tried since early 1980's³. It had tried widely and antinociceptive effect with neurological safety of midazolam well established in animals and humans.

A study conduct by Batra et al.⁵ in year 1999 included 30 healthy patients scheduled for knee arthroscopy were divided into two groups to receive either midazolam-bupivacaine mixture (group M; n = 15) or bupivacaine alone (group B; n = 15) intrathecally. Level of sensory block, sedation score, assessment of pain using visual analogue score recorded in both groups at regular

time intervals. Blood pressure, heart rate, oxygen saturation and sedation score showed no differences between the groups. Neither motor block nor times to void prolonged with the addition of midazolam to bupivacaine. They conclude that addition of midazolam to bupivacaine intrathecally provided better post-operative analgesia without any adverse effects. In the present study, patients randomly divided into three groups by adopting block randomization method. That was showed significantly increased the pain free duration in adjuvant of midazolam without any significant adverse effect.

In 2003, Bharti et al.⁶ reported in their study that intrathecal midazolam added to bupivacaine improves the duration and quality of spinal anaesthesia in patients undergoing lower abdominal surgery. They concluded in their study that the addition of intrathecal midazolam to bupivacaine significantly improves the duration and quality of spinal anesthesia and provides prolonged preoperative analgesia without any significant side effects. In the present study also added bupivacaine adjuvant with 0.2 ml and 0.4 ml midazolam respective in study group B and C we also found improve the duration and quality of spinal anesthesia without any significant side effects.

In 2005, Agrawal et al.⁷ 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. The authors reported no episodes of bradycardia, hypotension, pruritus, urinary retention, and sedation related to midazolam.

In 2007, Gupta et al.⁹ also found that intrathecal midazolam 2.5mg provided moderate prolongation of postoperative analgesia when used as an adjunct to bupivacaine without significant complications.

Conclusions

On the basis of observations made in the present study we concluded 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 were revealed that there were no significant changes present.

References

1. Mauermann WJ, Shilling AM, Zuo Z. A comparison of neuraxial block versus general anesthesia for elective total hip replacement: a meta-analysis. *Anesth Analg.* 2006;103(4):1018–25. doi: 10.1213/01.ane.0000237267.75543.59. [PubMed] [CrossRef] [Google Scholar]
2. Valentin N, Lomholt B, Jensen JS, Hejgaard N, Kreiner S. Spinal or general anaesthesia for surgery of the fractured hip? A prospective study of mortality in 578 patients. *Br J Anaesth.* 1986;58(3):284–91. [PubMed] [Google Scholar]
3. A. 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.
4. Faull RL, Villiger JW. Benzodiazepine receptor in the human spinal cord: a detailed anatomical and pharmacological study. *Neuroscience* 1986;17:791-802.
5. 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.
6. N. Bharti, R. Madan, P. R. Mohanty, and H. L. kaul, “Intrathecal midazolam added to bupivacaine improves the duration and quality of spinal anaesthesia,” *Acta Anaesthesiologica Scandinavica*, vol. 47, no. 9, pp. 1101–1105, 2003.
7. 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.
8. Kim MH, Lee YM. Intrathecal midazolam increased the analgesic effect of spinal blockade with bupivacaine in patients undergoing haemorrhoidectomy. *Br J Anaesth.* 2001;86:77–9. [PubMed].
9. A. Gupta, S. Prakash, S. Deshpande, and K. S. Kale, “The effect of intrathecal midazolam 2.5mg with bupivacaine on postoperative pain relief in patients undergoing orthopaedic surgery,” *The Internet Journal of Anesthesiology*, vol. 14, no. 2, 2007.