Section: General Surgery

Original Research Article

A HOSPITAL BASED OBSERVATIONAL STUDY TO COMPARE THE INTRATHECAL BUPIVACAINE & MIDAZOLAM MIXTURE AS POST OPERATIVE ANALGESIA IN PATIENTS UNDERGOING ELECTIVE CAESAREAN DELIVERY

Ashish Sharma[1], Ankita Kumari Meghvanshi[2], Deepti Sharma[3]

[1]*Associate Professor, Department of General Surgery, Government Medical College & Attached Hospitals, Dholpur, Rajasthan, India.*
[2]*Assistant Professor, Department of Obstetrics & Gynaecology, Government Medical College & Attached Hospitals, Dholpur, Rajasthan, India.*
[3]*Senior Specialist, Assistant Professor, Department of Anaesthesiology, Government Medical College & Attached Hospitals, Dholpur, Rajasthan, India.*

Received *: 28/03/2025*
Received in revised form *: 19/04/2025*
Accepted *: 11/05/2025*

Corresponding Author:
Dr. Ankita Kumari Meghvanshi, Assistant Professor, Department of Obstetrics & Gynaecology, Government Medical College & Attached Hospitals, Dholpur, Rajasthan, India.
Email: ankitameghvanshi17@gmail.com

DOI: 10.70034/ijmedph.2025.3.109

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (3); 593-596

ABSTRACT

Background: Spinal anesthesia for caesarean delivery is the best anesthetic technique, as it is simple to perform with rapid onset of anesthesia, complete muscle relaxation, lower incidence of failed block, less drug doses, minimal neonatal depression and decreased incidence of aspiration pneumonitis are advantages of spinal anesthesia. The present study is to compare the efficacy and practicability of using the midazolam-bupivacaine mixture and bupivacaine intrathecally in patients undergoing elective caesarean delivery.

Materials and Methods: The present study was conducted on 50 patients belonging to ASA grade I and II between 18 to 35 years of age who were scheduled for caesarean delivery in Govt. Medical College & Attached Hospitals, Dholpur, Rajasthan, India during the one-year period. The patients were randomly allocated into 2 groups of 25 each. Effectiveness of pain relief in the postoperative period was assessed by Visual Analogue Score.

Results: The mean onset time for sensory blockade & maximum motor blockade was no statistical significance between the two groups. The duration of sensory blockade is increased from 90.5 minutes in group I to 116.4 minutes in group II and P value is < 0.001 which is highly significant. Here, the duration of analgesia has been increased considerably from 120.7 minutes in group I to 220.9 minutes in group II which is statistically highly significant with the p value being < 0.001. The visual analogue score for effectiveness of pain relief was no statistical significance between the two groups.

Conclusion: Postoperative pain relief is a growing concern to an anaesthesiologist since no single analgesic is free from side effects. Moreover, intrathecally administered midazolam improves quality of anaesthesia during the spinal procedure.

Keywords: Midazolam, Intrathecal, Sensory blockade, Motor blockade, VAS Score.

INTRODUCTION

Pain is defined, according to the international association for the study of pain, as “an unpleasant, sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage”. The role of an anaesthesiologist is to render patient pain free during surgical procedures. However, patient’s problem with pain does not end with surgical procedure. Pain during postoperative period is a cause of concern not only for the patient, but also for the surgeon and the anaesthesiologist.[1] Postoperative pain control is generally best managed by anaesthesiologist because

they offer regional techniques of anaesthesia as well as pharmacological expertise in analgesics.[1]

Apart from obvious humanitarian reasons, effective postoperative analgesia results in decreased incidence of respiratory and cardiovascular complications early ambulation and discharge from hospital.[1]

In this era of modern technology and facilities, caesarean delivery is remarkably safe, which is mainly due to availability of antibiotics, safe anaesthesia, blood transfusion facilities and recent improvement in surgical techniques. Spinal anesthesia for caesarean delivery is the best anesthetic technique, as it is simple to perform with rapid onset of anesthesia, complete muscle relaxation, lower incidence of failed block, less drug doses, minimal neonatal depression and decreased incidence of aspiration pneumonitis are advantages of spinal anesthesia.[2]

Spinal anaesthesia by 0.5% Hyperbaric bupivacaine is characterised by a relatively rapid onset of action, duration of anaesthesia at approximately 2-3 hours and profound motor blockade. In these patients, rescue analgesia is necessary after 2-3 hours, even though it provides effective pain relief in the initial postoperative period. In order to maximize postoperative analgesia, a number of adjuvants have been added to spinal local anesthetics.[3]

One of them is midazolam, a water-soluble benzodiazepine, used for induction of anaesthesia and sedation. Midazolam has been reported to have a spinally mediated analgesic effect. Clinically, single shot epidural or spinal administration of midazolam has been shown to have added analgesic effect on postoperative pain.[3] Recent literatures have reported the usefulness of intrathecal midazolam-bupivacaine mixture for relief of postoperative pain.

The present study is to compare the efficacy and practicability of using the midazolam-bupivacaine mixture and bupivacaine intrathecally in patients undergoing elective caesarean delivery.

MATERIALS AND METHODS

The present study was conducted on 50 patients belonging to ASA grade I and II between 18 to 35 years of age who were scheduled for caesarean delivery in Govt. Medical College & Attached Hospitals, Dholpur, Rajasthan, India during the one-year period.

Exclusion Criteria

1. Patients belonging to ASA grade III and IV.
2. Patients on chronic analgesic therapy.
3. Patients with medical complications like Diabetes, cardiovascular disease and cerebrovascular disease.
4. Patients with obstetric complications like. PIH, cord prolapse, placenta previa and placental abruption.
5. Patients with autonomic neuropathy, spinal deformities, infections in lumbar area, hemorrhagic diathesis.

Pre-anesthetic Evaluation: Pre-operatively a detailed history was carried out in all patients. Sex, weight, hospital registration number and baseline data i.e., of pulse rate, blood pressure and general condition was noted. The spinal column and back of the patient were examined to rule out any spinal deformity. Cardiovascular, respiratory and central nervous system were thoroughly examined.

The procedure of subarachnoid block was explained and the patient was informed to communicate to the anaesthesiologist about the perception of any pain or discomfort during surgery.

Procedure

The patients were randomly allocated into 2 groups of 25 each, namely

A) Group I –intrathecal bupivacaine 2 ml 0.5%hyperbaric+ 0.4 ml of normal saline

B) Group II –intrathecal bupivacaine 2 ml 0.5% hyperbaric+ 0.4 ml (2mg) of midazolam (preservative free).

Baseline pulse rate and blood pressure were recorded immediately before spinal anaesthesia. A suitable intravenous line was secured and 500 ml of Lactated Ringer's solution was preloaded. Patient was then put in lateral position with head, neck, and knees flexed and back arched. Hip and shoulders were maintained in vertical plane and patient was brought to the edge of the table (positioned horizontally).

Under aseptic precautions, lumbar puncture was performed at L3-4 interspace with 23G Quincke needle, after preparing local infiltration with 2cc of 0.2% lignocaine. After free flow of CSF was obtained, 2ml of hyperbaric 0.5% bupivacaine with 0.4ml of normal saline was injected in group I. 2ml of hyperbaric bupivacaine 0.5% with 0.4 ml (2mg) of midazolam was injected slowly over a period of 10 seconds in patients of group II. After the drug was injected, the patient was turned to supine position. Pulse rate and blood pressure were recorded immediately after spinal anaesthesia.

Effectiveness of pain relief in the postoperative period was assessed by Visual Analogue Score. The patient makes a mark on a 10cm scale horizontal or vertical one end of which is 0.61marked as 'No pain' and the other as 'The worst pain one can imagine'. The position of the mark on the line measures how much pain the patient experiences.

Systolic and diastolic blood pressure, pulse rate and respiratory rate were recorded at every 5 minutes till 20 minutes and then every 10 minutes till regression of block.

After surgery, patients were monitored in the recovery room till spinal anaesthesia wore off and were then shifted to the ward. The patients were monitored for post-operative complications viz., nausea, vomiting, respiratory depression, drowsiness etc.

RESULTS

A clinical study of 50 patients belonging to different age groups was done. These patients belonged to ASA I or II and underwent elective caesarean delivery under spinal anaesthesia. The mean onset time for sensory blockade was 4.7±0.56 min. & 4.52±0.61 min. in group I & II respectively which was no statistical significance between the two groups with regard to mean onset time for sensory blockade. The duration of sensory blockade is increased from 90.5 minutes in group I to 116.4 minutes in group II and P value is < 0.001 which is highly significant. In group I, the duration of maximum motor blockade is 151.7±3.9 min and in group II, was 150.6±3.6minutes. As the p value is 0.51 it is not statistically significant.

Here, the duration of analgesia has been increased considerably from 120.7 minutes in group I to 220.9 minutes in group II which is statistically highly significant with the p value being < 0.001.

The visual analogue score for effectiveness of pain relief is shown. In group I, the mean score is 3.7±0.5 and in group II, it is 3.6±0.4. The p >0.05 and based on them, there is no statistical significance between the two groups [Table 1].

In group I, 2 patients had bradycardia, 3 had hypotension, 5 patients had nausea and vomiting.

In group II, 1 patient had drowsiness and hypotension was seen in 2 patients [Table 2].

Table 1: Comparison of mean value of different variables in between groups.

Variables	Group I	Group II	P-value
Time for onset of sensory blockade (Min.)	4.7±0.56	4.52±0.61	>0.05
Duration of sensory blockade (Min.)	90.5±4.23	116.4±7.9	<0.001*
Duration of maximum motor blockade (Min.)	151.7±3.9	150.6±3.6	>0.05
Duration of analgesia (Min.)	120.7±5.6	220.9±12.8	<0.001*
Vas effectiveness of pain relief	3.7±0.5	3.6±0.4	>0.05

Table 2: Complications

Complications	Group I	Group II
Bradycardia	2	0
Drowsiness	-	1
Hypotension	3	2
Nausea and vomiting	5	0
Total	10 (40%)	3 (12%)

DISCUSSION

Effective control of postoperative pain remains one of the most important and pressing issues in the field of surgery and anaesthesia with significant impact on our health care system. Inadequate or improper application of available information and therapies is certainly the most important reason for inadequate postoperative pain relief.

During the past two decades, epidural and intrathecal narcotic therapies have been used increasingly for the relief of postoperative pain.

Various drugs added with local anaesthetics have been studied with regard to intrathecal administration for the treatment of postoperative pain viz –opioids – morphine, pethidine, Fentanyl, Pentazocine, centrally acting alpha agonist – clonidine, anticholinesterase – neostigmine, benzodiazepine – midazolam, non-steroidal anti-inflammatory drugs – tramadol etc.

Midazolam is a newer, water soluble imidazole benzodiazepine derivative which has been tried for intrathecal use since early 1980's. It is short acting and present in aqueous solution. Intrathecal administration of midazolam has been reported to have antinociceptive action because of the interaction of benzodiazepine and GABA on nociceptive systems. Intrathecal benzodiazepine induced analgesia is spinally mediated and binding sites are GABA receptors which are present abundant in dorsal root nerve cells and maximum concentration found within lamina II of dorsal nerve cells, a region which plays a prominent role in processing nociceptive and thermoceptive stimulation.[4]

In our study showed that the mean onset time for sensory blockade was 4.7±0.56 min. & 4.52±0.61 min. in group I & II respectively which was no statistical significance between the two groups with regard to mean onset time for sensory blockade. So, the addition of midazolam to bupivacaine has not made any apparent difference with regard to time for onset of sensory blockade.

Our study compatible with Valentine J.M et al,[5] (2003) & Gupta et al,[6] (2007) showed no difference in onset and found better post-operative analgesia and reduced complications with use of intrathecal midazolam bupivacaine mixture.

The duration of sensory blockade is increased from 90.5 minutes in group I to 116.4 minutes in group II and P value is < 0.001 which is highly significant. It can be attributed to the lipophilicity of midazolam and its synergism with the local anaesthetic. The benzodiazepines and local anaesthetics exert their antinociceptive effect at the spinal cord by different mechanisms. Midazolam exerts its action through GABA A receptor complex i.e. GABA A on getting bound opens ligand gated chloride channels. Chloride conductance is increased leading to hyperpolarisation and presynaptic inhibition of afferent terminals in spinal cord and hence reduction in neuronal activity.

Gupta et al,[6] (2007) & Sen A, Rudra P et al,[7] (2001) showed that 2 segment regression and duration of sensory blockade were statistically significant.

In the present study, the duration of maximum motor blockade, when compared between the two groups was not statistically significant. This is because in the both groups, as soon as the action of local anaesthetic bupivacaine wears off, motor block is not prolonged because midazolam does not have any motor action. In 2004, Yaksh T.L, Allen J.W,[8] study suggested that addition of intrathecal midazolam does not cause motor blockade.

The duration of analgesia has been increased considerably from 120.7 minutes in group I to 220.9 minutes in group II which is statistically highly significant with the p value being < 0.001. In Batra YK et al,[9] study duration of analgesia lasted for more than a mean duration of 258 ± 46.8 minutes. In 2001, M.H Kim,[10] and Y.M. Lee's study suggested the presence of a dose dependent effect of intrathecal midazolam with no evidence of neurological complications. They concluded that the analgesic effect of intrathecal midazolam was segmental, with no alteration in sympathetic tone or reflexes. In 2001, Sen A, et al,[7] study suggested that intrathecal midazolam produced highly significant post-operative analgesia together anti emetic effect. In 2002, Saha J.K, Karmkar S,[11] study suggested that duration of analgesia in midazolam bupivacaine group was 160 +/- 10.75 and was found to be highly significant.

In 2007, Gupta A et al6 found that the mean duration of analgesia in midazolam group were 412.1 +/- 57.3 min. In 2005, Jahangiri B, Jahangiri R,[12] double blind prospective study showed mean duration of analgesia of about 7 +/- 1 hrs.

In 2003, Nishiyama T, Hanaoka K,[13] study suggested midazolam could enhance the analgesic effects of bupivacaine synergistically in intrathecal administration.

There was also high statistical difference observed between the two groups with regard to complications like hypotension, bradycardia, drowsiness, nausea and vomiting. It was found that addition of midazolam to intrathecal bupivacaine had an added advantage in controlling post-operative nausea and vomiting. In 2004, Tucker A.P et al,[14] study showed reduced incidence of post-operative nausea and vomiting in midazolam bupivacaine group than sole bupivacaine group. Another study done by Bharti N et al,[15] (2003) showed improved quality and duration of spinal analgesia and provides prolonged post-operative analgesia without significant side effects.

CONCLUSION

Postoperative pain relief is a growing concern to an anaesthesiologist since no single analgesic is free from side effects. Moreover, it becomes a challenge after caesarean section delivery to provide postoperative pain relief without much sedation, respiratory depression or problems like nausea, vomiting, so that early baby acceptance and care by the mother is promoted. Moreover, intrathecally administered midazolam improves quality of anaesthesia during the spinal procedure.

REFERENCES

1. Agarwal N, Usmani A, Sehgal R, Kumar R, Bhadoria P. Effect of intrathecal midazolam bupivacaine combination on post-operative analgesia. India J Anaesth 2005;49(1):37-9.
2. Bogra J, Arora N, Srivastava P. Synergistic effect of intrathecal fentanyl and bupivacaine in spinal anesthesia for caesarean section. BMC Anesthesiol 2005;5:5.
3. Prakash S, Joshi N, Gogia AR, Prakash S, Singh R. Analgesic efficacy of two doses of intrathecal midazolam with bupivacaine in patient undergoing caesarean delivery. www.sciencedirect .com Regional Anaesthesia and Pain Medicines, 2005.
4. Kohno T, Kumamot E, Baba H, Atka T, Okamoto M, Shimoji K, et al. Actions of midazolam on GABAergic transmission in substantia gelatinosa neurons of adult rat spinal cord slices. Anaesthesiol 2000;92(2):507-15.
5. Valentine J.M.J, Lyons G, Bellamy M.C. The effect of intrathecal midazolam on post-operative pain. European Journal of Anaesthesiology 1996; 13(6): 589 – 593
6. Guptha. A, Prakash.S, Deshpande.S, Kale.K.S. The effect of intrathecal midazolam 2.5mg with hyperbaric bupivacaine on postoperative pain relief in patients undergoing orthopaedic surgery. The Internet journal of anaesthesiology. 2007;14(2).
7. Sen A, Rudra A, Sarkar SK, Biswas B. Intrathecal midazolam for postoperative pain relief in caesarean section delivery. J Indian Med Assoc 2001 Dec; 99(12):683-86.
8. Yaksh. T.L, Allen. J.W. The use of intrathecal midazolam in humans: A case study process. Anaesth Analg 2004; 98:1536 – 45.
9. Batra. Y.K, Jain. K, Chari.P, Dhillon. M.S, Shaheen. B, Reddy. G.M. Addition of intrathecal midazolam to bupivacaine produces better postoperative analgesia without prolonging recovery. Int. J. Clin. Pharmacol. Ther. 37(10): 519 - 523.
10. Kim MH, Lee YM. Intrathecal midazolam increases the analgesic effects of spinal blockade with bupivacaine in patients undergoing haemorrhoidectomy. Br J Anaesth 2001; 86:77-9.
11. Shah. F.R, Halbe. A.R, Panchal. I.D, Goodchild. C.S. Improvement in postoperative pain relief by the addition of midazolam to an intrathecal injection of buprenorphine and bupivacaine. Journal of Anaesthesiology 2003; 20; 11: 904 – 910.
12. Jahangiri. B, Jahangiri. R, Intrathecal midazolam prolongs the analgesic effect of spinal blockade with lidocaine for perineal operations. Acta Medica Iranica 2006; Vol 44(5).
13. Nishiyama.T, Sugai.N, Hanaoka.K. Invitro changes in the transparency and pH of CSF caused by adding Midazolam. European Journal of Anaesthesiology. 1998; 15(1): 27 – 31.
14. Tucker AP, Lai C, Nadeson R, Goodchild CS. Intrathecal midazolam I: A cohort study investigating safety. Anaesth Analg 2004; 98:1512-20.
15. Bharathi. N, Madan. R, Mohanthy. P.R. Intrathecal midazolam added to bupivacaine improves the duration and quality of spinal anaesthesia. Acta. Anaesthesiologica Scandinovica. Oct 2003; 47(9): 1101.