Section: Anaesthesiology

Original Research Article

EFFECTS OF ADDITION OF MIDAZOLAM TO EPIDURAL BUPIVACAINE HYDROCHLORIDE ON INTRAOPERATIVE SEDATION, BLOCK CHARACTERISTICS AND POST-OPERATIVE ANALGESIA IN PATIENTS UNDERGOING INGUINAL HERNIA REPAIR

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Abstract

Background: Pain management aims to reduce pain to tolerable with minimal or no associated suffering or distress. Recent advances in neurophysiology and neurochemistry have developed selective benzodiazepine receptors to ensure effective, safe and prolonged post-operative analgesia. The aim was to study the effects of 0.5% bupivacaine with midazolam 2mg through lumbar epidural in patients undergoing inguinal hernia repair. **Materials and Methods:** This prospective interventional study was conducted at Rajah Muthiah Medical College and Hospital from January 2011 to September 2012 on sixty patients for inguinal hernia repair surgery. Sixty patients were divided into Group I patients (30) received 15ml of 0.5% bupivacaine with 0.4 ml of 0.9% NS, and the remaining 30 patients received 15ml of 0.5% bupivacaine with 0.4ml of 2 mg of midazolam (Group II) through lumbar epidural route. **Result:** Sixty patients were divided into Group I (30 patients) and II (30 patients). The mean age was 38 years for group I patients and 43 years for group II patients, which was statistically significant, but no significant difference in weight and height. The quicker onset of the sensory blockade and delay in the two-segment regression with a longer duration of action was observed in group II patients than in group I patients, which was significant. A significant difference in the two-segment regression time and the duration of post-operative analgesia between groups. No significant difference in pulse rate, mean arterial blood pressure, respiratory rates, and SpO2 between groups. **Conclusion:** Midazolam combined with bupivacaine administered epidurally increases post-operative analgesia without respiratory depression.

INTRODUCTION

Pain is a common human experience, a symptom frequently encountered in clinical practice, usually associated with actual or impending tissue damage. Pain is a consistent and predominant complaint of all individuals following most surgical interventions. Pain is a neuropsychological phenomenon with an unpleasant intrusive nature, is associated with the threat of actual tissue damage and disrupts normal physiological and psychological homeostasis, manifesting clinically as organ dysfunction and altered human behaviour.[1-4]

A visit to most post-operative wards shows that the patients experiencing ineffective post-operative pain relief are unable to breathe adequately, cough effectively, move enough even to tend to their own daily needs or participate in their own rehabilitation and experience feelings of helplessness, fear, anxiety, low mood and loss of control.[5,6] Successful pain management from disease or surgery has long been a great challenge to the medical community. Fast and effective pain relief always gratifies the patient and the physician managing him. Pain management aims to reduce a patient's pain to tolerable with minimal or no associated suffering or distress.

Recent advances in neurophysiology and neurochemistry of pain have developed novelly developed selective benzodiazepine receptors acting at the spinal cord level, administered via an epidural or intrathecal route, which ensure effective, safe and prolonged post-operative analgesia.[7,8] In the present study, the effect of 0.5% bupivacaine with midazolam 2mg versus 0.5% bupivacaine administered through lumbar epidural space in patients undergoing inguinal hernia repair was

compared. The intensity of blockade, hemodynamics, respiratory parameters, and efficacy for post-operative analgesia was analysed in all the cases in both groups.

MATERIALS AND METHODS

This prospective interventional study was conducted at Rajah Muthiah Medical College and Hospital from January 2011 to September 2012 on sixty patients for inguinal hernia repair surgery. Informed consent was obtained from all the patients, and approval was obtained before the study started.

The study was conducted on 60 patients, divided into two groups. Each group contained 30 patients. 30 patients received 15ml of 0.5% bupivacaine with 0.4 ml of 0.9% NS (Group I), and the remaining 30 patients received 15ml of 0.5% bupivacaine with 0.4ml of 2 mg of midazolam (Group II) through lumbar epidural route. The time of requirement for the first analgesic dose was recorded in all the cases.

Inclusion Criteria

Age group 20-50 years, ASA -I physical status, and elective cases for inguinal hernia repair were included.

Exclusion Criteria

Patient refusal, local Infection, coagulopathy, severe hypovolemia, severe spine deformity, hypersensitivity to local anaesthetics, and patients with a previous history of cardiac, respiratory, renal, neurological and hepatic disorders were excluded.

Haemoglobin, blood sugar, urea, serum creatinine, serum electrolytes, bleeding time, clotting time, urine - albumin, sugar, electrocardiogram, and X-ray - chest (PA view) were assessed. All the patients taken up for the study were given premedication with an injection of glycopyrrolate 0.2mg IM 45 minutes before the anaesthetic procedure started. Pre-anaesthetic preparation includes an overnight fasting period for a minimum of 6 hours. All the patients were cannulated with an 18G intravenous cannula, and preloading was done with ringer lactate solution 15-20ml/kg body weight over 20 minutes before block induction. The procedure was re-explained to the patients on arrival at the operation theatre. The monitors connected were non-invasive blood pressure, pulse oximeter and electrocardiogram. The anaesthesia machine and resuscitation equipment were checked and kept ready. Baseline vital signs were recorded. The patient was positioned in the right or left lateral position with a table in a horizontal position. Under strict aseptic precaution, the skin over the back was thoroughly cleaned with betadine and draped. Drugs were loaded and kept ready, and L3-L4 intervertebral space was identified using the highest point of the iliac crest as the reference. Skin and subcutaneous tissues overlying the midline of the identified space were infiltrated with 2ml of 2% lignocaine using a 25-gauge hypodermic needle. An 18-gauge Tuohy needle with the stylet was inserted up to the interspinous ligament, and the stylet alone was removed. Air filled up to 3-4ml in a 5ml glass syringe was attached to the hub of the Tuohy needle, and epidural space was identified using a loss of resistance technique. With the needle tip pointing to cephalad and after negative aspiration of CSF and blood, a precalculated drug dose was injected slowly, and the patient was turned supine immediately. At the end of the surgical procedure, patients were shifted to the recovery room and monitored for 2 hours postoperatively, after which the patients were shifted to the postoperative ward. All the patients were monitored for heart rate, respiratory rate, oxygen saturation and blood pressure in the pre-operative and perioperative period for 3-4 hrs. Dermatomal sensory blockade to pinprick was evaluated – maximum level of impaired sensation noted. Duration of analgesia and motor blockade intensity (using the modified Bromage scale) were studied. The degree of pain post-operatively was evaluated by using Visual Analogue Scale. The most common form consists of a scale with a 10 cm horizontal line with two end-points labelled 'no pain' and 'worst pain ever'. The patient must place a mark on the 10 cm line at a point corresponding to the level of pain intensity the patient felt. The time of requirement of the first analgesic dose was recorded in all the cases. Using the Ramsay sedation scale, sedation was assessed in all the cases. An injection of Diclofenac Sodium 75mg through the intramuscular route was administered when the patient complained of pain in the postoperative period (Demand analgesia). Any neurological deficits and bowel and bladder dysfunction were noted for 72 hours in the postoperative period.

All parameters were subjected to appropriate statistical analysis before inference was drawn. The statistical analyses were performed by using SPSS version 21. Data were presented as mean with Standard deviation for normal distribution. The unpaired t-test and Chi-square test were used to compare the means between the groups, and a p-value <0.05 was considered statistically significant.

RESULTS

Sixty patients were divided into Group I (30 patients) and II (30 patients). The mean age was 38 years for group I patients and 43 years for group II patients, which was statistically significant ($p<0.0001$).

The mean weight was 61.5 kgs for group-I patients and 58.76 kgs for group II patients, which was statistically insignificant. The mean height was 162.8 cm for group I patients and 160.8 cm for group II patients, which was statistically insignificant.

The quicker onset of the sensory blockade and delay in the two-segment regression with a longer duration of action was observed in group II patients than in

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group I patients, which was significant (p<0.001). No significant deviation in the level of block in the groups.

A significant difference in the two-segment regression time and the duration of post-operative analgesia between groups (p<0.0001) [Table 1].

Table 1: Patient characteristics between the groups

	Group I	Group II	P-value
Age (Years)	38.93 ± 3.11	43.96 ± 3.63	<0.0001
Weight (Kgs)	61.53 ± 7.23	58.76 ± 5.69	0.105
Height (Cms)	162.8 ± 4.4	160.8 ± 5.03	0.107
The onset of sensory block (min)	10.63 ± 2.55	7.46 ± 1.13	<0.001
Level of sensory block (Dermatome level)	8.93 ± 1.01	8.93 ± 1.01	1.000
Two-segment regression time (min)	112.5 ± 10.64	147 ± 10.38	<0.0001
Duration of post-operative analgesia	167.16 ± 8.57	212.83 ± 19.98	<0.0001

Table 2: Motor block and sedation between groups

		Group I	Group II	P-value
Motor block	B2	7 (23.3%)	5 (16.7%)	0.519
	B3	23 (76.7%)	25 (83.3%)	
Sedation	Conscious and oriented (Score 2)	30 (100%)	0	<0.0001
	Response to verbal commands (Score 3)	0	30 (100%)	

In group I, seven patients had incomplete motor blockades. In comparison, 23 patients had complete motor blockade compared to 5 patients who had incomplete motor blockade, and 25 patients had a complete motor blockade in group II which was insignificant.

In group I, all 30 patients were oriented in comparison to all the 30 patients in group II, who were drowsy but responded to verbal commands, which was significant (P<0.0001) [Table 2].

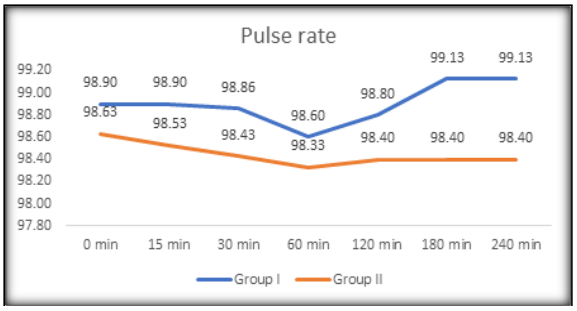

Figure 1: Pulse rate between groups

The mean pulse rate differed significantly at different periods in both groups of patients [Figure 1].

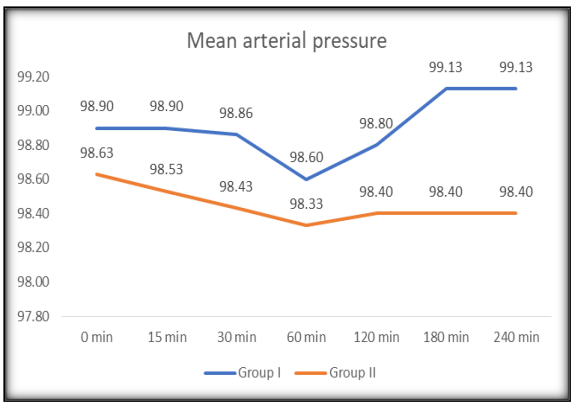

Figure 2: Cell Block Of Ascitic Fluid Showing "Signet Ring Cells'' In A Case Of Carcinoma Stomach (H&E,40X)

No significant deviation in mean arterial blood pressure between groups [Figure 2].

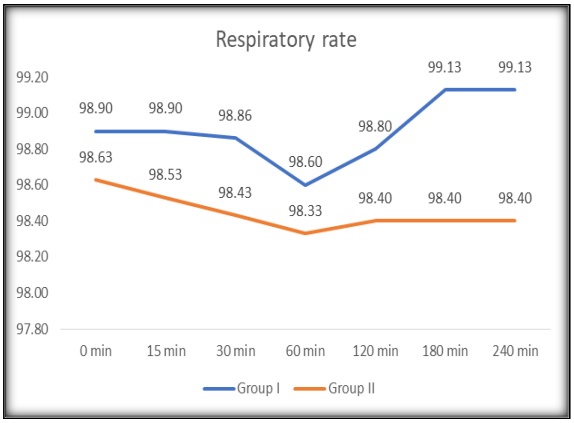

Figure 3: Respiratory rate between groups

Both groups' mean respiratory rates at various intervals were similar and insignificant [Figure 3].

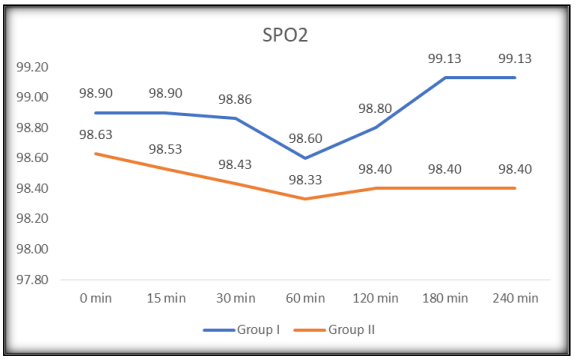

Figure 4: SPO2 between groups

The mean of SpO2 at various intervals in both groups was similar and insignificant [Figure 4].

DISCUSSION

Pain management has become one of the principal missions of the anaesthesiologist. Establishing and

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organising acute pain management services are essential for high-quality pain management, but it isn't very easy. From the early 1980s, the practice of epidural analgesia for post-operative pain relief had set in. Earlier, it was routinely used for orthopaedic surgeries, later it was used routinely for surgical and obstetric procedures, and at present, it is practised for thoracotomies too.[9,10]

Using benzodiazepines epidurally and intrathecally has opened up a new avenue in post-operative analgesia. Benzodiazepine receptors, including the spinal cord, are in the central nervous system.[11,12] Several experimental investigations were carried out to study the effects of epidural midazolam. It produced amnesia, sedation, and analgesia without any adverse effects. In children, adding midazolam with local anaesthetics to the caudal epidural space for post-operative pain relief has proved effective without side effects.[13-16]

Our clinical study aimed to compare the effects of 0.5% bupivacaine with midazolam 2mg through lumbar epidural for cases of inguinal hernia repair. The mean time of onset of sensory block was 10.5 minutes in group I compared to 7.5 minutes in group II patients, which was significant (P<0.001). The mean dermatomal level of sensory blockade was T9 in both groups. The mean of the two-segment regression time was 113 minutes in group I compared to 146 minutes in group II which was significant (P <0.0001). There was no significant difference in the dermatomal level of sensory block and motor block in both groups.

Using Ramsay's sedation score, both groups of patients were evaluated. In group I, all the patients was cooperative and oriented (score- 2) for up to 150 minutes. In group II, all the patients scored three up to 180 minutes, and only three patients were sedated for 4 hrs in a group. All these results are similar to the studies done by Nishiyama et al.[17] and Sharma et al.[18] They concluded that a combination of bupivacaine and midazolam induced significantly better analgesia, with significant amnesia, slight sedation and more stable haemodynamic and respiratory condition. In our study, the mean duration of post-operative analgesia was 169 minutes in group I compared to 212 minutes in group II patients, which was significant (P<0.0001). This result is similar to the studies done by Naguib et al.[16]

In our study, both groups' duration of surgery varied from 60-90 minutes. Post-operatively pain was evaluated by a visual analogue scale, which was 5-6 up to 150 minutes in group I and up to 180 minutes in group II. The first dose of systemic analgesia was given when the visual analogue score reached 3-4. Here we evaluated the post-operative pain status with a visual analogue scale at various time intervals and time of first demand analgesia in all the cases. The study showed no significant change in both groups during the first 150 minutes as per the visual analogue scale.

From the 150 minutes onwards, there was a significant change in the visual analogue scale reading. In group II, 5 demanded analgesia after 180 minutes, 2 demanded analgesia after 190 minutes, 2 demanded analgesia after 195 minutes, three required analgesia after 200 minutes, one demanded analgesia after 205 minutes, four demanded analgesia after 210 minutes, and 2 demanded analgesia after 215 minutes. Six patients didn't require any analgesia, and post-operative analgesia lasted 230-240 minutes.

In group I, one patient demanded analgesia after 155 minutes, 6 demanded analgesia after 160 minutes, 5 demanded analgesia after 165 minutes, 5 demanded analgesia after 170 minutes, 3 demanded analgesia after 175 minutes, and five required analgesia after 180 minutes. The pulse rate, mean arterial blood pressure, respiratory rate and oxygen saturation were maintained within the normal range in both groups. No significant side effects were observed in this study in both groups.

CONCLUSION

Midazolam, combined with bupivacaine administered epidurally, has better advantages over bupivacaine alone in increasing the duration of post-operative analgesia without producing any respiratory depression or haemodynamic changes. In clinical practice, epidurally can be used as a safe adjuvant and bupivacaine to increase post-operative analgesia with sedation for cases undergoing inguinal hernia repair.

REFERENCES

1. Tollison CD. Handbook of Pain Management. 2nd ed. Philadelphia, PA: Lippincott Williams and Wilkins; 1994.
2. Linton SJ. Understanding pain for better clinical practice: a psychological perspective.
3. Eccleston C, Crombez G. Pain demands attention: a cognitive-affective model of the interruptive function of pain. Psychol Bull 1999;125:356–66.
4. Branca B, Lake AE. Psychological and neuropsychological integration in multidisciplinary pain management after TBI. J Head Trauma Rehabil 2004;19:40–57.
5. Mackintosh C. Assessment and management of patients with post-operative pain. Nurs Stand 2007;22:49–55; quiz 58.
6. Dahl JL, Gordon D, Ward S, Skemp M, Wochos S, Schurr M. Institutionalizing pain management: the Post-Operative Pain Management Quality Improvement Project. J Pain 2003;4:361–71.
7. Valentine JM, Lyons G, Bellamy MC. The effect of intrathecal midazolam on post-operative pain. Eur J Anaesthesiol 1996;13:589–93.
8. Williams M, Kowaluk EA, Arneric SP. Emerging molecular approaches to pain therapy. J Med Chem 1999;42:1481–500.
9. Momeni M, Crucitti M, De Kock M. Patient-controlled analgesia in the management of post-operative pain. Drugs 2006;66:2321–37.
10. Matthews E, Malcolm C. Nurses' knowledge and attitudes in pain management practice. Br J Nurs 2007;16:174–9.
11. Sanger DJ, Benavides J. Discriminative stimulus effects of omega (BZ) receptor ligands: correlation with in vivo inhibition of [3H]-flumazenil binding in different regions of the rat central nervous system. Psychopharmacology (Berl) 1993;111:315–22.

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12. Young A, Barnard J. Adjuvant intrathecal drugs used with spinal anaesthesia for lower segment caesarean section in New Zealand. Australasian Anaesthesia 2009:169–83.
13. Nishiyama T, Matsukawa T, Hanaoka K. Effects of adding midazolam on the post-operative epidural analgesia with two different doses of bupivacaine. J Clin Anesth 2002;14:92–7.
14. Yegin A, Sanli S, Dosemeci L, Kayacan N, Akbas M, Karsli B. The analgesic and sedative effects of intrathecal midazolam in perianal surgery. Eur J Anaesthesiol 2004;21:658–62.
15. Höhener D, Blumenthal S, Borgeat A. Sedation and regional anaesthesia in the adult patient. Br J Anaesth 2008;100:8–16.
16. Naguib M, Gammal M, Elhattab YS, Seraj M. Midazolam for caudal analgesia in children: comparison with caudal bupivacaine. Can J Anaesth 1995;42:758–64.
17. Nishiyama T, Matsukawa T, Hanaoka K. Continuous epidural administration of midazolam and bupivacaine for post-operative analgesia. Acta Anaesthesiol Scand 1999;43:568–72.
18. Sharma V (kaushal), Kamdar BM, Shroff PP. Comparative study between post-operative continuous thoracic epidural administration of bupivacaine alone V/S bupivacaine with midazolam. J Anaesthesiol Clin Pharmacol 2005;21:25.

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