Original Research Article

Indian Journal of Anesthesia and Analgesia
2019; 6(1) (Part - II): 207-210
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.6119.29

Intrathecal Midazolam for Post Operative Pain Relief in Lower Segment Caesarean Section

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Abstract

Background: Postoperative pain relief is one of the important component which needs to be managed in patients undergoing lower segment cesarean section. Midazolam is a drug which can be used for postoperative pain relief as an adjunct to anaesthetic medication. *Methods:* The study was conducted at tertiary care health institute. Total of 90 patients, 30 patients in each group were included in the study. Each group was evaluated for onset, intensity and duration of sensory and motor block, central side effects, time to first pain medication. Visual analog scale was used to assess the postoperative pain. *Result:* Time to first pain medication was significantly prolonged in group XM_1 (n=30 with 2 mg midazolam) as compared to group X (n=30, 5% xylocaine hydrochloride). Nevertheless VAS at first pain medication was comparable in all the three groups. The side effects were no different in three groups. *Conclusion:* Addition of intrathecal midazolam at these dosages appears safe and has clinically proven analgesic properties with no major side effects.

Keywords: Intrathecal Midazolam; Post-Operative; Pain Relief; Xylocaine.

How to cite this article:

Suman Gupta, Preeti Goyal. Intrathecal Midazolam for Post Operative Pain Relief in Lower Segment Caesarean Section. Indian J Anesth Analg. 2019;6(1):207-10.

Introduction

Pain is an unpleasant sensory and emotional experience associated with actual and potential tissue damage or described in term of such damage. The distress and pain which a patient often experiences in immediate post-operative period is beyond description. Post-operative pain relief can improve functionality, reduce physiological and emotional morbidity and improve quality of life of the patients. As an anaesthetist it is our duty as well as priviledge to use all legitimate means to bring down the physical sufferings of patient in terms of pain not only during operation itself but also during post-operative period. Various modalities available for pain relief include intra muscular injection of strong analgesics, nerve block using local anaesthetic, intrathecal injection of certain drugs like opiods, ketamine, benzodiazepine either via subarachnoid or epidural route. They have advantages, as they reduce the dose of local anaesthetic medications; provide long lasting post-operative analgesia with reduced incidence of central nervous system depression, motor effects or hypotension [1]. Midazolam, synthesized by Walsar and colleagues in 1976, was the first clinically used

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Received on 13.11.2018, **Accepted on** 03.12.2018

water-soluble benzodiazepine [2]. It is also the first benzodiazepine that was produced primarily for use in anaesthesia.

Midazolam has marked analgesic properties with minimal adverse effect. It can be used either epidurally or intrathecally [3]. Hence, it was planned to do a comparative evaluation of inrathecal preservative free midazolam and 5% lignocaine in patients undergoing lower segment caesarean section for its analgesic properties.

Material and Methods

The study was conducted at tertiary care health institute of northern India. Patients between age groups of 20-35 years who underwent lower section cesarean section were divided into three groups of 30 each to receive either 1.2 ml of 5% heavy Xylocaine Hcl for group X, one mg of midazolam in 0.2 ml along with 1.2 ml of 5% heavy Xylocaine Hcl for group XM_1 and 2 mg of midazolam in 0.4 ml along with 1.2 ml of 5% heavy XylocaineHcl for group XM_2. All patients received an uniform premedication of injection Glycopyrrolate bromide 0.2 mg I.M. Injection Ondeansetron 4 mg I/V, injection Metoclopromide 10 mg I/V were given 30 minutes prior to operative procedure upon arrival into the operation theater. Ringer Lactate solution 500 ml was infused as a preload, followed by dextrose 5%. Under all aseptic conditions lumber puncture was performed at l2-L3 space and following drugs were injected.

Group X: 1.2 ml of 5% heavy Xylocaine Hcl

Group XM_1: 1 mg of midazolam in 0.2 ml along with 1.2 ml of 5% heavy Xylocaine Hcl

Group XM_2: 2 mg of midazolam in 0.4 ml along with 1.2 ml of 5% heavy Xylocaine Hcl.

The onset, intensity and duration of analgesia and motor loss, sedationscore, time of first pain medication, duration of surgery were recorded. Changes in pulse rate, systolic blood pressure, diastolic blood pressure, respiratory rate were recorded every minute till 5 minutes, then every 5 minutes till 15 minutes, then every 10 minutes until completion of surgery.

Measurement of analgesia

Analgesia was assessed by pinprick method. Onset time was taken as time from injection of drug into subarachnoid space and complete sensory loss. From this point to the time when sensation recorded to segments as noted as duration of Analgesia.

Measurement of motor loss

Motor loss was assessed by straight leg raising test. Time interval between injection of drug into subarachnoid space to patient's inability to lift the leg was taken as onset time. From this point to the time when patient was able to lift leg was recorded as duration of motor loss.

Time to first medication

This was the time taken from the onset of analgesia to the time at first pain medication. Assessment of Pain was done by patients themselves and for this assessment visual analogue scale (VAS) was used (Pilowsky and Bond 1956). During the pre-operative interview subjects were familiarized with the recording of scale. VAS rating was done as follows; 0 as No pain, 1-25 as mild pain, 26-50 as moderate pain, 51-75 as severe pain and 76-100 as very severe pain.

All the recorded variables were recorded in predesigned proforma. The variables were checked for normal distribution. The continuous variables were presented as mean±SD. The continuous variable related to time of sensory and motor blockade and the post operative pain relief were analysed using Annova test. p value <0.05 was considered as statistically significant.

Results

There were total of 90 patients involved in the present study with 30 patients in each group. All the three groups were demographically comparable with respect to age, sex and type of surgery performed. In all three groups there was statically insignificant alteration in pulse rate, systolic and diastolic blood pressure and respiratory rate.

Sensory and motor block

All the ninety patients had intense grade three analgesia after the intrathecal administration of drugs in Group X, 10 patients each (33%) had analgesia upto T7-T8 and T10. In group XM_1, 17 patients (56.66%) had highest level upto T7, where as in Group XM_2 19 patients (63.33%) had level upto T6.

There was no significant difference in onset time intensity and duration of sensory and motor block, central side effect in intergroup statistical comparison (Table 1). The time of first pain medication was significantly delayed in group XM_1 & XM_2 as compared to X ($p<0.001$) (Table 2)

Table 1: Time of onset of sensory block and time of onset, degree, duration of motor block

Grade	Group X	Group XM_1	Group XM_2
Sensory block			
onset time (min)	2.05 +0.58	2.016 + 0.46	2.0 +0.70
Motor block			
onset time (min)	4.8+0.89	4.266+0.79*	4.233+0.40*
Degree of motor blockade	2.03 + 0.40	2.13+0.33	2.23+0.42
Duration of motor blockade (min)	92.16 + 6.53	94.06 + 10.46	92.36+9.4

*p value <0.05 (statistical significant); Group X = 5% Xylocaine hydrochloride; Group XM_1 = 5% Xylocaine hydrochloride ±1 mg midazolam; Group XM_2 = 5% Xylocaine hydrochloride ±2 mg midazolam

Table 2: Intergroup comparison of post operative pain relief

Parameters	Grade X	Grade XM_1	Grade XM_2
Time of first pain medication in hours	2.9+0.63	3.99+0.62**	4.37+5.09**
VAS at first pain medication	35+4.3	36+5.76	34+5.2

**p value <0.001 (statistically highly significant)

There was no incidence of bradycardia, sedation, dizziness, pruritis, respiratory depression neurological deficit. Thus addition of intrathecal midazolam is devoid of any side effects.

Discussion

The present study entitled "Evaluation of intrathecal midazolam (preservative free) for postoperative pain relief in lower segment caseraean" section was carried out to assess the effects of Intrathecal midazolam and to study the sideeffects and complication related to the use of this drug in different dosage during spinal anaethesia.

The onset of analgesia (mean±SD) recorded in the present study was 2.05±0.58 minutes, 2.016±0.46 and 2.0±0.7 minute in group X, XM_1, and XM_2 respectively and in the intergroup comparison the differences were found to be statistically insignificant (p>0.05). No local anaesthetic effect of midazaolm on afferent nerve going into spinal cord has been reported [4,5]. The onset and duration of motor block (mean±SD) in group X was 4.8±0.79 and 94.06±10.46 minutes and in group XM_2 was 4.23±0.40 and 92.36±9.4 minutes. The differences were found to be statistically significant (p<0.05).

Thus it is reasonable to assume that the midazolam acting at the spinal cord level caused synergistic effect in muscle relaxation produced by local anaesthetic action [6-8].

In this study the time to first pain medication in hours (mean±SD) was 2.9±0.63 minutes, 3.99±0.62 minutes and 4.37±5.09 minutes in group X, group XM_1 and group XM_2 respectively. The differences were statistically highly significant (p<0.001). Our results were similar to various authors who have found midazolam as an effective analgesic by intrathecal route [3,4,9]. The mean±SD of VAS at first pain medication in three groups are 35±4.3, 36±5.76 and 34±5.2 in the control group X, Group XM_1 and Group XM_2 respectively. The intergroup comparison is insignificant (p>0.05).

Interaction of intrathecal midazolam with non opiod GABA receptor complex in dorsal horn have been attributed to anti-nociceptive effect [10-12]. There were no significant changes in hemodynamic parameters in any of the 3 groups. Hypotension is a normalsequelae of centro-neuraxial blockade and it is quite clear that addition of midazolam has not increased the severity of hypotension. Majority of workers who evaluated the hemodynamic effects of epidural/intrathecal midazolam have found it safe [4,13].

Conclusion

From this study it can be concluded that both of intrathecal midazolam 1 mg and 2 mg are effective in increasing the analgesic effects of spinal blockade with xylocaine. Both the doses were able to significantly prolong the time to first pain medication and it was found to be better with increasing dose. Addition of midazolam with xylocaine intrathecally did not have any deleterious effects on the hemodynamic stability. No side effects attributed to midazolam were identified. Thus intrathecal midazolam at these dosages appears safe and has clinically detectable analgesic properties.

References

1. Reves JG. Midazolam: Pharmacology and uses. Anaesthesiology. 1985;62:310-324.
2. Greenblatt DJ. Drug therapy: Current status of benzodiazepines. The New Eng J Med. 1983;309:354-8.
3. Kim MH, Lee YM. Intrathecal midazolam increases the analgesic effects of spinal blockade with bupivacaine in patients undergoing haemorrhoidectomy. Br JrAnaesth. 2001;86:77-9.
4. Batra YK, Jain K, Char P, Dhillon MS, Shabeen B,

Reddy GM. Addition of Intrthecal midazolam to bupivacaine produces better post operative analgesia without prolonging recovery. Int Journal ClinPharmacolTher. 1999;37:519-23.

5. Good Child CS, Nobel J. The effects of Intrathecal midazolam on sympathetic nervous system reflexes in Man: A pilot study. British Journal Clin Pharmacol 1987;23:279-85.
6. Behar M, Cohen ML, Grinshpoon Y, Kopolovic U, Hervert M, Nass D, Chanimov M. An investigation of the possible neurotoxic effects of intrathecal midazolam combined with fentanyl in the rat. Eurp Jr Anaesthesiology. 1998;14:690-701.
7. Dahn LS, Beric A, Dimitrijevic MR, Wall PD. Direct spinal effect of a Benzodiazepine (Midazolam) on spasticity in Man. Stereotoit Funet Neurosurg. 1989;52:85-94.
8. SiCafried J, Rea GI. Intrathecal application of drugs for muscle hypertonia. Scand J Rehabil Med 1998;17:145-8.
9. Nishiyama T Matsukawa T, Hanaoaka K, Continuous epidural administration of Midazolam and bupivacaine for post operative analgesia. Acta Anasethesiol Scand. 1999;43;568-72.
10. Edward M, Serrao JM, Gent JP, Goodchild CS. On the mechanism by which midazolam causes spinally mediated analgesia. Anesthesiology. 1990;73:273-7.
11. Niv D, Whitwam JG, Loh L. Depressionof nociceptive reflexes by intrathecal administration of midazolam. Br JrAnaesth. 1995;55:541-47.
12. Serrao JM, Gent JP, Goodchild CS. Naloxone reverses the spinal analgesic effects of midazolam. Br J Anaesth. 1989;62:233–4.
13. Goodchhild CS, Serrao JM. Intrathecal midazolam in the rats. Evidence for spinally mediated analgesia. Br J Anaesth. 1987;59:1563-70.