Original Research Article

Indian Journal of Anesthesia and Analgesia
2018; 5(3): 372-376
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.5318.3

An Observational Study to Compare Intrathecal Midazolam and Clonidine for Post Operative Analgesia in Patients Undergoing Elective Hernia Surgeries

Gandhi Gunjan P.[1], Malini Mehta[2]

[1]3rd year Resident [2]Professor, Department of Anesthesiology, SBKS MI & RC, Sumandeep Vidyapeeth, Piparia, Waghodia, Vadodara, Gujarat 391760, India.

Abstract

Background and Objectives: This observational study is designed to compare the intrathecal preservative free midazolam and clonidine, used as an adjuvant with hyperbaric bupivacaine for post operative analgesia in patients undergoing elective hernia surgeries. *Material & Methodology:* The observational study was conducted on 60 patients (using formula for Estimation of mean difference) of ASA grade I/II aged between 20 and 55 years posted for elective hernia surgeries under spinal anaesthesia. Group BM (midazolam group)– 15mg 0.5% hyperbaric bupivacaine+2mg preservative free midazolam made 3.5 ml with normal saline and Group BC (clonidine group) –15mg 0.5% hyperbaric bupivacaine +30µg preservative free clonidine made 3.5ml with normal saline. Onset and duration of sensory and motor blockade, Duration of Analgesia, Hemodynamic changes, Postoperative analgesic consumption in 24 hrs, Side effects/Complications (if any) were recorded. *Results:* There was a statistically significant difference in onset of sensory & motor block (pvalue< 0.01), and Duration of sensory & motor block (p value< 0.01) in BM group than BC group. Duration of analgesia was significantly prolonged in BM group (351.6±39.1min) as compared to BC group (252.5±21.1 min) (p value<0.01). *Conclusion:* Addition of 2mg midazolam (preservative free) to 0.5% hyperbaric Bupivacaine as an adjuvant intrathecally leads to early onset of sensory and motor block, prolongation of duration of sensory and motor blockade and prolongation of duration of analgesia as compared to 30 µg clonidine (preservative free) without any side effects in both the groups.

Keywords: Bupivacaine; Intathecal; Clonidine; Midazolam.

Introduction

Spinal anaesthesia with local anaesthetic is a favourable technique during both emergency and elective surgeries [1] but only local anaesthetics provide shorter duration of action. Hence many adjuvant are used to hasten the onset and to prolong duration of post operative analgesia.

Clonidine is used as an adjuvant in spinal anaesthesia to improve the quality and duration of post-operative analgesia [2].

Midazolam has been used in both animal [3,4] and humans [5,6], as an adjuvant intrathecally without any adverse effect.

This study is designed to compare the intrathecal midazolam (preservative free) and clonidine (preservative free) when used as adjuvant with hyperbaric bupivacaine for post operative analgesia in patients undergoing elective hernia surgeries.

Material & Methods

This study was conducted in Dhiraj general hospital in Department of Anaesthesiology, after institutional ethical committee approval on 60 patients aged between 20 and 55 years of both gender scheduled for undergoing elective hernia surgeries under spinal anaesthesia.

Corresponding Author: Malini Mehta, Professor, Department of Anesthesiology, SBKS MI & RC, Sumandeep Vidyapeeth, Piparia, Waghodia, Vadodara, Gujarat 391760, India.
E-mail: m_malini17@yahoo.in

Received on 23.12.2017, **Accepted on** 24.01.2018

Patients were divided into 2 groups with 30 patients in each group. Group BM (Midazolam group)– received 15mg 0.5% hyperbaric bupivacaine +2mg preservative free midazolam made 3.5 ml with normal saline and Group BC (clonidine group) –received 15mg 0.5% hyperbaric bupivacaine + 30µg preservative free clonidine made 3.5ml with normal saline.

Sample size is calculated using formula below:

$$n = \frac{f(a,b)\times 2\times(SD1 - SD2)^2}{(d1 - d2)^2}$$

Where

n= sample size required in each group

SD1 = 2.21 hours is standard deviation of reference study for duration of analgesia of 2mg midazolam

SD2 = 0.87 hours is standard deviation of reference study for duration of analgesia of 30 µg clonidine

d1= 6.52 hours is mean of reference study for duration of analgesia of 2mg midazolam

d2= 4.94 hours is mean of reference study for duration of analgesia of 30 µg clonidine

ASA I & ASA II patients undergoing spinal anaesthesia and patients in the age range 20-55 years were included in the study.

Patients with systemic diseases, anaemia, severe hypovolemia, shock, septicemia, hypertension, coagulation disorders or on anticoagulant therapy, local infection at the site of proposed puncture for spinal anaesthesia, spinal deformities, known allergy to the trial drug and those who are not willing for spinal anaesthesia were excluded from the study.

Pre–anaesthetic check up was done one day prior to the surgery. Patient was evaluated for any systemic diseases and laboratory investigations were recorded. The procedure of spinal anaesthesia was explained to the patients and written and informed consent obtained. All patients were kept NBM for atleast 8 hours.

On the day of surgery, the patient was shifted to the operating room. On arrival in the operating room standard monitoring was applied; ECG, non invasive arterial blood pressure, pulse rate and arterial oxygen saturation were monitored. Baseline vitals were recorded – Pulse, B.P, SpO_2. IV line was secured and preloading was done with 10ml/kg of ringer lactate. Patient was premedicated with Inj. Glycopyrrolate 0.2mg IV and Inj. Ondansetron 4 mg IV. Patient was positioned in the sitting position. Painting & draping of patients back was done with povidine iodine solution, study drug was injected in L3-L4 intervertebral space with 23 G spinal needle after free flow of cerebrospinal fluid. The patient was placed supine immediately after injection.

All Patients of Both Groups were Monitored for

Sensory block: Onset, level using pinprick test, Motor block: Onset and duration of block using modified Bromage scale, pulse rate, systolic blood pressure, diastolic blood pressure, SpO_2, were monitored at: 0, 5, 10, 15, 20, 30, 45, 60, 75, 90, 120 minutes.

When the sensory block reached at T_8 level surgeon was allowed to start the surgery. Data was collected regarding the onset of sensory block (Time taken from intrathecal injection to loss of pinprick sensation at T_8) and duration of sensory block (Time from intrathecal injection to 2 segment regression) Motor block was tested by Bromage scale, time of onset (Time from intrathecal injection to grade 3 motor block) and duration of motor block (Time from intrathecal injection to grade 0 motor block) was recorded.Side effects/complications were noted and treated. Bradycardia was defined as pulse rate < 60/min and treated with IV atropine sulfate 0.6mg. Hypotension was defined as systolic BP less than 20% of the basal value and treated with IV mephentermine 6mg.

After completion of surgery patient was shifted to recovery room and watched for pulse,blood pressure, sensory level and duration of motor blockade. Pain score was assessed by prince henry's visual rating scale in postoperative period. Duration of analgesia was calculated from the time of intrathecal injection to the time when visual rating scale was 2. Total number of analgesics required in the first 24 hours were recorded.

Observation & Results

The distribution of patients with respect to age, height, weight, gender, ASA was statistically not significant in both the groups (p value > 0.05).

The mean time from intrathecal injection to onset of sensory analgesia at T8 level was 5.13±0.62 minutes in group BC and 4.28±1.28 minutes in group BM. The onset of sensory analgesia was significantly earlier in group BM as compared to group BC, which was highly significant (p value < 0.01).

The mean duration of sensory block was 154.46± 20.41 minutes in group BC & 199.66±15.80 minutes in group BM. It was significantly prolonged in Group BM as compared to Group BC (P<0.01)

The mean time from intrathecal injection to onset of motor block was 4.90 ± 0.75 minutes in group BC & 3.06±0.63 minutes in group BM . It was significantly faster in Group BM as compared to Group BC which was highly significant (p<0.01)

The mean duration of motor block was 164.86± 25.89 minutes in Group BC and 217.90±19.60 minutes in Group BM. It was significantly prolonged in Group BM as compared to Group BC which was highly significant (p<0.01).

There was statistically no significant difference in pulse rate between the two groups (p value > 0.05), at any interval of time during intraoperative and post-operative period.

There was statistically no significant difference in systolic and diastolic blood pressure and SpO_2, between the two groups (p >0.05) at any time interval intra as well as post operative period.

Table 1: Mean Duration of analgesia

Duration of analgesia	Group BC (mean ±SD)	Group BM (mean ±SD)	P value
Time interval (min)	252.50 ±21.16	351.66 ±39.11	< 0.01

Table 2: Postoperative analgesic consumption in 24 hours

Analgesic consumption (24 hours)	Group BC (mean±SD)	Group BM (mean±SD)	P value
Number	2.35 ±0.48	1.23 ±0.43	< 0.01

The mean duration of analgesia was 252.50 ± 21.16 minutes in Group BC and 351.66±39.11 minutes in Group BM. It was significantly prolonged in Group BM as compared to Group BC which was statistically highly significant (p<0.01).

Analgesic consumption for 24 hours postoperatively was less in Group BM as compared to Group BC which was statistically highly significant (p< 0.01).

No side effects were observed in either of the group.

Discussion

One of the mainstay of balanced anaesthesia is relief of pain during operation and in postoperative period. "Postoperative pain relief" is a growing concern for an anaesthesiologist, as an uneventful postoperative period makes all surgery comfortable proposition for surgical patients.

Spinal anaesthesia using local anaesthetics alone has shorter duration of action with early requirement of analgesia for postoperative pain relief.

So, many adjuvants have been used along with local anaesthetics "to hasten the onset of sensory & motor block and to improve quality and duration of postoperative analgesia, reducing postoperative analgesic requirements, without significant side effects, facilitating early ambulation & reducing the hospital stay of the patient".

In Our study, we had observed that the difference in demographic data (Age, Height, Weight, Gender distribution, American Society of Anaesthesiologists status) were statistically not significant among both groups. (p>0.05)

Similarly, *Agrawal Nidhiet al (2005)* [7], *Suchita A. Joshi et al (2012)* [8] observed no significant difference between the two groups with respect to age, weight, height, gender of the patient and ASA status.

Racle et al (1987) [9]: used 150 µg of clonidine interathecally with isobaric bupivacaine for hip surgery. He observed more episode of hypotension.

Shah BB et al (2012) [10]: used 60µg, 30µg and 15µg clonidine in spinal anaesthesia for caesarian section & observed that addition of 60µg clonidine to intrathecal bupivacaine provided longer duration of postoperative analgesia than 15µg or 30 µg clonidine but with more sedation than 15µg or 30

µg clonidine, so 15µg or 30 µg clonidine as a preferred option when sedation is not desirable. Duration of analgesia was significantly higher in 30µg clonidine than 15µg clonidine ($p<0.05$).

In our study, we used 30 µg of clonidine intrathecally with hyperbaric bupivacaine as150 µg of clonidine causes more hypotension and duration of analgesia was less with 15 µg as observed in above studies. 30µg was safer dose with minimal side effect. In our study, we had added 2mg of midazolam to hyperbaric bupivacaine.

Kim M.H. (2001) [11] used 1 mg and 2 mg of midazolam with bupivacaine intrathecallyand he found dose dependent effect of intrathecal midazolam. *Bharti N et al (2003)* [12] *and Yegin A et al (2004)* [13] administered 2 mg midazolam with bupivacaine intrathecally.

The dose of 2 mg midazolam was chosen because this was the optimal dose to relieve pain without producing negligible side effects.

In our study, we observed the onset of sensory block was statistically highly significantly early in Group BM as compared to Group BC ($p < 0.01$) and duration of sensory block was statistically highly significantly longer in group BM as compared to group BC. ($P<0.01$)

Vaswani RK et al (2002) [14]: observed same result as in our study regarding onset and duration of sensory block. ($p< 0.01$)where as *Yegin A et al (2004)* [13]: observed no statistically significant difference in the onset and duration of sensory block in both groups. In our study, we observed the onset of motor block was statistically highly significantly early in Group BM as compared to Group BC ($p < 0.01$) and duration of motor block was statistically highly significantly longer in group BM as compared to group BC.($P<0.01$).

Bharti N et al (2003) [12] observed same result as in our study regarding onset and duration of motor block. ($p< 0.01$) whereas *Yegin A et al (2004)* [13]*:* observed no statistically significant difference in the onset and duration of motor block in both groups.

In our study, we observed duration of analgesia was statistically highly significantly prolonged in Group BM as compared to Group BC ($p < 0.01$).

Suchita A. Joshi et al (2012) [8]: observed same result as in our study regarding duration of analgesia ($p< 0.01$).

In our study, there was no statistically significant change in mean pulse rate, systolic blood pressure, diastolic blood pressure and SpO_2, in both groups intraoperatively and post operatively ($p>0.05$).

Suchita A. Joshi et al (2012) [8]: observed same result as in our study regarding mean pulse rate, systolic blood pressure, diastolic blood pressure and SpO_2, in both groups intraoperatively and post operatively. ($p>0.05$).

In our study, complications like nausea, vomiting, rigors, hypotension, bradycardia were not detected with either agent in any patient.

Nidhi Agrawal et al (2005) [7] observed no episodes of bradycardia, hypotension, sedation and dizziness, vomiting and neurological deficit in both groups.

In our study, the mean postoperative analgesic consumption in 24 hours was statistically highly significantly less in group BM than in group BC ($p<0.01$).

Vaswani RK et al in (2002) [14]: observed same result as our study regarding mean postoperative analgesic consumption in 24 hours in both groups ($p<0.01$).

Conclusion

Addition of 2mg midazolam (preservative free) to 0.5% hyperbaric Bupivacaine as an adjuvant intrathecally leads to early onset of sensory and motor block, prolongation of duration of sensory and motor blockade and prolongation of duration of analgesia as compared to 30 µg clonidine (preservative free) without any side effects in both the groups.

References

1. Dureja GP, Jayalaxmi TS. Colloid preloading before spinal and epidural anaesthesia; Hospital Today 2000;5(11):601-603.
2. Eisenach JC, DeKock M, Klimscha W. Alpha {2}-adrenergic agonist for regional anaesthesia A clinical review of clonidine;Anesthesiology 1996;85:655-74.
3. Goodchild CS and Serrao JM .Intrathecal midazolam in the rat: Evidence for spinally mediated analgesia; British journal of anaesthesia: 1987;(59):1563-1570.
4. Valentine JM, Lyons G, Bellamy MC. The effect of intrathecal midazolam on post-operative pain relief; Eur J Anaesthsiol. 1996;13:589-93.
5. Serrao Juliet M, Marks Ray L, Morley Stephen J and Goodchild Coline S. Intrathecal midazolam for the treatment of chronic mechanical low back pain ; A controlled comparison with epidural steroid in a pilot study: Pain: 1992;(48):5-12.

6. Serrao JM, Mackenzie JM, Goodchild CS, Gent JP. Intrathecal midazolam in rat: An investigation of possible neurotoxic effects; Eur. J. Anaes: 1990; 7:115-122.
7. Agrawal Nidhi, Usmani A, Sehgal R, Rakesh Kumar, BhadoriaPoonam. Effect of intrathecal midazolam bupivacaine combination on postoperative analgesia; Indian Journal of Anaesthesia 2005;49(l):37-39.
8. Suchita A. Joshi et al. comparative evaluation of intrathecal midazolam and low dose clonidine: efficacy, safety and duration of analgesia. A randomized, double blind, prospective clinical trial; Indian J Pharmacol. 2012 May-June;44(3):357-361.
9. Racle, Jean P, Benkhadra, Abdellatif, Poy, JeanY, Gleizal, Bernard. Prolongation of Isobaric Bupivacaine spinal anesthesia with Epinephrine and Clonidine for Hip surgery in the elderly. Anaesthesia and Analgesia, 1987 may;66(5):442-446.
10. Shah BB, Joshi SS, Shidhaye RV, Lakhe JN. Comparison of different doses of clonidine as an adjuvant to intrathecal bupivacaine for spinal anaesthesia and postoperative analgesia in patients undergoing caesarian section. Anaesth pain & intensive care 2012;16(3):266-272.
11. Kim MH and Lee Y.M. Intrathecal midazolam increases the analgesic effects of spinal blockade with bupivacaine in patients undergoing haemorrhoidectomy; British Journal of Anaesthesia: 2001;86(1):77-79.
12. Bharti N, Madan R, Mohanty P.R., Kaul H.L. intrathecal midazolam added to bupivacaine improves the duration and quality of spinal anaesthesia; Acta Anaesthesiologica Scandinavica. 2003Oct;47(9): 1101-1105.
13. Yegin A, Sanli S, Dosemeci L, Kayacan N, Akbar M, Karsii B. The analgesic and sedative effects of intrathecal midazolam in perianal surgery; European Journal of Anaesthsiology: 2004 Aug;21(8):658-652.
14. Vaswani RK, Raiger Lalit Kumar, Purohit Richa, Bajaj Pramila. The effect of intrathecal midazolam on postoperative pain relief in Orthopaedic Surgery; Hospital Today: 2002 April;VII(4):150-153.