ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 8, Issue, 09, pp.38847-38850, September, 2016

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

TO STUDY EFFICACY AND SAFETY OF ADDITION OF INTRATHECAL CLONIDINE AND MIDAZOLAM TO HYPERBARIC BUPIVACAINE ADDED AS AN ADJUVANT FOR POST OPERATIVE ANALGESIA

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ARTICLE INFO

Article History:
Received 22nd June, 2016
Received in revised form
25th July, 2016
Accepted 17th August, 2016
Published online 30th September, 2016

Key words:

Clonidine,
Midazolam,
Bupivacaine,
Spinal anaesthesia.

ABSTRACT

Introduction: We compared the effects of addition of intrathecal clonidine and midazolam to 0.5% hyperbaric bupivacaine in terms of efficacy of sensory and motor block achieved and observed the side effects if any.

Method: Forty patients of ASA Grade I and II between 18 – 60 years age of either sex undergoing lower limb surgeries were randomly allocated to any of the groups of 20 each by lottery method. Group M: Patients received Midazolam 2.5 mg preservative free (0.5 ml). Group C: Patients received Clonidine 75 micrograms (0.5 ml). These drugs were given with bupivacaine 15 mg (3 ml of 0.5 % hyperbaric solution) intrathecally. The time of onset, peak sensory and motor, 2 segment regression, time of rescue analgesia, haemodyanmic changes and any other side effect were recorded.

Result: The motor blockade was significantly prolonged in group C (809.56 ± 290.38) than group M (533.80 ± 164.91). Two segment sensory regression, motor regression and time of rescue analgesia in group C (110.44 ± 28.77, 411.11 ± 82.07, 8.69 ± 0.92) was significantly more as compared to group M (66.10 ± 10.15, 159.80 ± 35.28, 4.28 ± 0.7) suggesting prolonged analgesia in intra-op & post-op periods.

Conclusion: 75 micrograms clonidine when added to 0.5% hyperbaric bupivacaine prolongs the sensory and motor block and reduces requirement of rescue analgesia as compared to 2.5mg midazolam.

Citation: Piyush Kumar Sengar, Smita Priyadarshini and Piyush Setu, 2016. "To study efficacy and safety of addition of Intrathecal clonidine and midazolam to hyperbaric Bupivacaine added as an adjuvant for post operative analgesia" *International Journal of Current Research*, 8, (09), 38847-38850.

INTRODUCTION

Pain is not just sensory modality but is an experience (Wylie and Churchill 7th edition). The international association for the study of pain defines pain as "an unpleasant sensory or emotional experience associated with actual or potential tissue damage in terms of such damage (Edward morgan *et al*., 2009)". Many drugs opioids and nonopioids have been tried as an adjuvants to local anaesthetic agents used intrathecally (Robert. K. Stoelting 4th edition), not only to potentiate and increase the duration of block but also to provide good long lasting analgesia thus providing any untoward complications that may appear due to pain. Clonidine produces effective analgesia in postoperative patients (Uma srivastav *et al*., 2008). The agonist action of clonidine on alpha 2 adrenergic receptors of spinal cord are responsible for its analgesic effect (PanditRao *et al*., 2005; HO and Ismail, 2008). Clonidine does not have respiratory depressant effect (Sylvie Roasting and Francis Bonnet, 1991) and also incidence of pruritus and vomiting are less frequent. Clonidine as an adjuvant also reduce the incidence of postanaesthetic shivering (Piper *et al*., 2002). Midazolam, an imidobenzodiazepine has been used as an adjuvant to bupivacaine for prolongation of analgesic effect in lower limb surgeries (Panditrao *et al*., 2005). It also reduces the incidence of nausea and vomiting (Ho and Ismail, 2008). The goal of postoperative pain management is to reduce an individual patient's pain to a tolerable level with minimal or no associated suffering or distress (Wylie and Churchill 7th edition). Successful outcome is the most desirable end point of any surgical procedure (Robert 4th edition). Therefore anaesthetic and analgesic technique should aim not only to provide optimal conditions surgery but also to reduce postoperative morbidity and mortality (Srivastav Uma *et al*., 2008).

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MATERIALS AND METHODS

The study was conducted at patliputra medical college and hospital dhanbad. After getting IEC clearance and taken written informed consent 40 patients of ASA grade I and II undergoing lower limb surgeries in the age group 18- 60 years were randomly allocated in 2 groups by lottery method. All the

patients not willing to get enrolled in the study, not willing for spinal anaesthesia, age below 18 years and above 60 years, patients having previous history of allergies especially to benzodiazepines and adrenergic alpha 2 agonists, patients with local skin infections overlying lumbar vertebral region, patients with bleeding and /or coagulation disorders, patients with abnormal physiological profile were excluded from the study.

Group I: Patients were administered Midazolam 2.5 mg preservative free (0.5 ml) + bupivacaine 15 mg (3 ml of 0.5 % hyperbaric solution).

Group II: Patients were administered Clonidine 75 micrograms (0.5 ml) intrathecally + bupivacaine 15 mg (3 ml of 0.5 % hyperbaric solution) intrathecally.

Vital parameters like P.R, B.P, E.C.G, R.R, was recorded at interval of 3 minutes. The level of sensory blockade was tested by pin prick test until it reaches T5-T6 level, the motor blockade by Bromage scale and then surgical incision was allowed. The following readings was noted for assessment of onset of block T_0: Time of spinal anaesthesia T_1: time of onset of sensory block T_2: Time of onset of motor block. During surgery – complication of spinal anaesthesia was treated as following: - Hypotension: - Head low position upto 15 – 30 degrees, Rapid Infusion of fluids upto 100 ml- Vasopressors, ephedrine 2-6 mg, Mephenteramine 6 mg upto 30 mg max, Dopamine, Bradycardia -inj atropine 0.6 mg given. Respiratory discomfort- oxygenation and IPPV required Nausea and vomiting - correct hypotension inj.ondansetron 4 mg. Apprehension and anxiety – calm the patient. At the end of procedure patient were shifted to the recovery room and monitored for vital signs and VAS every 15 minutes for 1st hour and then every 30 minutes for vital signs and thereafter. Postoperative pain will be assessed by: 1. Visual analogue scale (VAS), Verbal numeral rating scale [The analysis was done by SPSS software version 11 by using percentage unpaired‘t’ test]. ‘P’ value less than 0.05 is considered as significant.

RESULTS

There was no significant difference in the demographic data (age) as shown in Table 1.

Table 1. Comparison of age is study groups

Parameters	Midazolam Mean ± SD (n=10)	Clonidine Mean ± SD (n=10)	t Value	P Value
Age (Yrs)	48.50 ± 8.51	34 ± 14.89	2.67	<0.01

There was significant bradycardia in midazolam group in 20 min (60.80 ± 8.44) and the F value of 15.79, 30 min (62.70 ± 6.98) and the F value of 13 and at end of procedure (64.70 ± 4.19) and the F value of 10 was as shown in Figure 1, which was stastically significant with P value < 0.001, P value <0.05, P value <0.05 respectively. There was slight fall in systolic blood pressure at 1min (119.11 ± 20.13) with F value of 4 and 5 min (114.22 ± 15.67) with F value of 8 in the clonidine group which was statistically significant with P value< 0.001 and P value <0.001 respectively as shown in Figure 2. It was clinically significant and required intervention but was manageable.

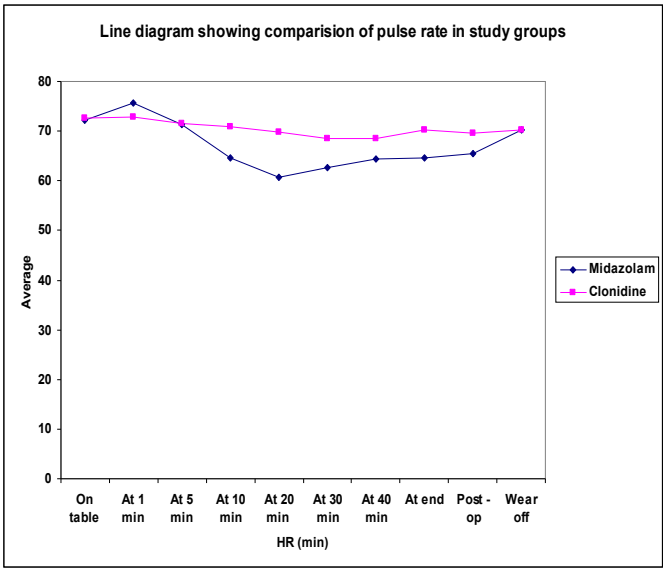

Figure 1.

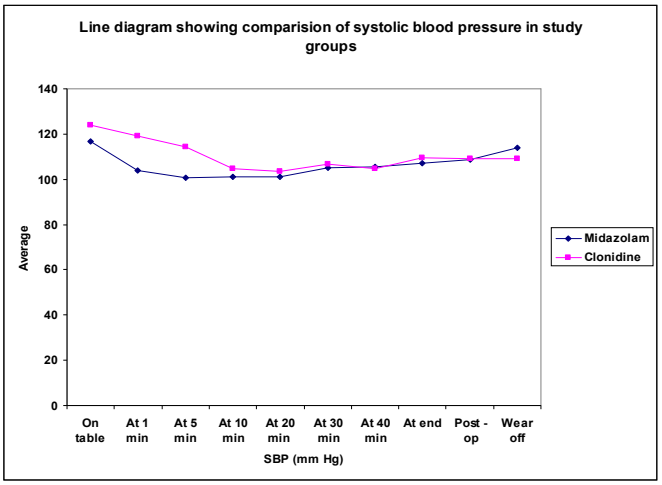

Figure 2.

No significant difference was found in diastolic blood pressure, SPO2, respiratory rate, onset of motor and sensory blockade. The peak action, weaning off and total duration of sensory and motor blockade was more in clonidine group.

Table 2. Comparison of total duration of motor blockade in study groups

Motor blockade	Midazolam Mean ± SD (n=10)	Clonidine Mean ± SD (n=10)	t Value	P Value
Total (Hrs)	2.65± 0.59	6.85± 1.37	8.90	<0.0001

Table 3. Comparison of total duration of analgesia in study groups

Analgesia	Midazolam Mean ± SD (n=10)	Clonidine Mean ± SD (n=10)	t Value	P Value
Total (Hrs)	4.28 ± 0.7	8.69 ± 0.92	13.13	<0.0001

The total duration of motor blockade was significantly longer in the clonidine group ($p<0.05$) as compared to midazolam group. The total duration of analgesia compared using VAS score was more in clonidine group shown in Table 3. Clonidine significently prolonges postoperative analgesia as compared to midazolam although it causes mild transient hypotension and bradycardia. So, we conclude clonidine is a better adjuvant for spinal anaesthesia as compared to midazolam.

DISCUSSION

Our data indicates that in spinal anaesthesia the addition of Clonidine 75 mcg or Midazolam 2.5 mg to hyperbaric bupivacaine (0.5 %) 3 ml prolongs the duration of analgesia (Table 3). The addition of either of the drugs prolongs the duration of analgesia and reduces the strain of postoperative care. Previously studies have been done by Karchana, P deepanjali, S jayshree using Intrathecal clonidine as an adjuvant to caudal analgesia in children (Uphadyay *et al*., 2005) has been done with clonidine 0.75 ml /kg of bupivacaine with clonidine 2 mcg/kg and got the prolonged analgesia. P. Lena, N. Balarac, J. J. Arnulf in coronary artery bypass grafting surgery clonidine 1 mcg/kg along with intrathecal morphine (Lena *et al*., 2003) 4 mcg / kg given intrathecally before general anaesthesia and they found early extubation and good pain relief. Jellish WS, Abodeely A, Fluder EM, Shea J used Clonidine 150 mcg epidurally in patients undergoing laminectomy (Scott Jellish *et al*., 2003) at the incision site and found prolonged analgesia. Our experience with clonidine was same and consistent with the results obtained from other studies where clonidine was used in orthopaedic surgeries (Stephan Strebel *et al*., 2004) clonidine was used < 150 mcg have prolonged sensory blockade along with bupivacaine 18 mg. Some studies in our group have the hypotension which was early manageable by routine and standard methods. We does not observed any clinically significant bradycardia or retention of urine in our clonidine group and any sedation which was finded in our midazolam group. The study have done previously using clonidine in oral preparation and intrathecally but no prolongation of analgesia was in oral and subarachnoid with 150 mcg found profound analgesia (Bonnet *et al*., 1990) by Bonnet F, Buisson VB, Francois Y. Clonidine used in our cases does not have reported any retention of urine. The studies have been done by TalwarVandana, RaiAnutam, Gandhi Radhika and Agarwal Nidhi, Usmani A., Sehgal R using midazolam used intrathecally and they found good results at reduced doses of 1 mg (Talwar Vandana *et al*., 2008; Agarwal Nidhi *et al*., 2005) but did not found bradycardia which was found in our study. In our groups clonidine takes more time to regress and have prolonged analgesia which is shown in our study. The patients administered clonidine has a much prolonged duration of analgesia. This combination of clonidine along with bupivacaine is best alternative to have pain free intraoperative and postoperative period with low cost proves it as a best adjuvant in present times.

Conclusion

The addition of clonidine to bupivacaine may be suitable and better alternative. We conclude that addition of 75 mcg clonidine to 0.5% hyperbaric bupivacaine prolongs motor and sensory block.

REFERENCES

Agarwal Nidhi, Usmani A., Sehgal R. 2005. Effect of intrathecal midazolam bupivacaine combination on postoperative patients; *Indian Journal of Anaesthesia*; 49(1); 37 – 39.

Bonnet F, Buisson VB, Francois Y; Effects of oral and subarachnoid clonidine on spinal anesthesia with bupivacaine; *Reg Anesth*., 15(4): 211-4 ; 1990 Jul-Aug.

Edward morgan Jr G, Maged. S. Mikhail, Michael .J. Murray, 2009. Pain management : 4 th Edition : 361.

HO KM and Ismail, H. 2008. Use of Intrathecal Midazolam to improve perioperative Analgesia – a meta analysis : Anaesthesia intensive care : 365 – 73 : 36 (3).

Ho KM and Ismail, H. Use of intrathecal midazolam to improve perioperative analgesia – a meta analysis; Anaesthesia intensive care ; 365-73 ; 36 (3); 2008 May.

Lena P., N.baralac, J.J.Arnulf; 2003. Intrathecal clonidine and morphine for coronary artery bypass grafting; *Br J.Anaesth*., Vol 90 ; 300-3.

PanditRao M M, Suryawanshi CM, Palhade, PS, PanditRao M M. 2005. Evaluation of Addition of midazolam to bupivacaine forspinal Anaesthesia:Indpain, Vol.no.19: No.1.

Panditrao MM, Suryawanshi CM, Palhade PS, Panditrao MM. 2005.Evaluation of addition of midazolam to bupivacaine for spinal anaesthesia; *Ind Pain*; Vol No 19 ; No. 1.

Piper S.N., S. W. Suttner, C.C . Schimidt, W .H Maleck, B. kumle and J . Boldt: Anaesthesia : Volume 54 Issue 7 : pg 695 – 699 : 6 Apr 2002.

Robert K. Stoelting; Pain; Pharmacology and physiology in anaesthetic practice; Robert. K. Stoelting and Simon.C. Hillier; 4th edition; 707.

Robert. K. uStoelting : pain : pharmacology and physiology in anaesthetic practice: Robert .k . stoelting&simon . hillier : 4 th edition : 707.

Scott Jellish W., Adam Abodeely, John Shea, 2003. Effect of spinal bupivacaine in combination with epidural clonidine and / or 0.5% bupivacaine at incision site on postoperative outcome in patients undergoing lumbar laminectomy., *Anaesthesia Analgesia*, 96(3):874-80; Mar.

Srivastav Uma, Singh S. P, Rana *et al*. 2008. Role of epidural anaesthesia and analgesia in reducing postoperative morbidity and mortality during major abdominal surgeries, *Indian Journal of Anaesthesia*, 52(5) ; 541-545.

Stephan Strebel, Jürg A. Gurzeler, Markus C. Schneider; Small-Dose Intrathecal Clonidine and Isobaric Bupivacaine for Orthopedic Surgery: A Dose-Response Study, Anaesthesia and Analgesia; Vol no 99; 1231 -38; Oct 2004.

Sylvie Roasting and Francis Bonnet, 1991. Effect of epidural clonidine on analgesia and pharmacokinetics of epidural fentanyl in post operative patients : Anaesthesiology : 75 : 420 – 25.

Talwar Vandana, Rai Anutam, Gandhi Radhika *; J.Anaesthesia Clin Pharmacol*, 24 (4) ; 447 – 50 ; 2008.

Uma Srivastav, Shiv Pratapsingh, Rana, 2008. Role of epidural anaesthesia and analgesia in reducing post operative morbidity & and mortality during major abdominal surgery: *Indian Journal of Anaesthesia*, 52 (5) : 541 – 545.

Uphadyay K.K.Col, Prabhakar. T Col, Haridas Been, Study of efficacy and safety of clonidine as an adjuvant to bupivacaine for caudal analgesia in children; *Indian J of Anaesthesia*, 49 (3) ; 199-201 ;2005.

Wylie and Churchill – Davidson's; A practice of anaesthesia; Thomas J. Healy, Paul. R. Knight; 7th edition; 1217.

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