ORIGINAL RESEARCH PAPER

Volume-7 | Issue-1 | January-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

# "COMPARATIVE STUDY OF INTRATHECAL 0.5% HYPERBARIC BUPIVACAINE ALONE WITH INTRATHECAL LOW DOSE CLONIDINE - 0.5% HYPERBARIC BUPIVACAINE FOR HEMODYNAMIC RESPONSE AND POST OPERATIVE ANALGESIA IN ORTHOPAEDIC LOWER LIMB SURGERIES".

Medical Science

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## ABSTRACT

Use of subarachnoid block (intrathecal) has become an established and reliable method of providing anesthesia for orthopedic lower limb surgery.

**Aim:** To compare intrathecal low dose clonidine – hyperbaric bupivacaine 0.5% combination with hyperbaric bupivacaine 0.5% in respect to hemodynamic response, analgesia duration and side effects in orthopedic lower limb surgeries.

**Material and Methods**: 90 patients enrolled in this study were randomly divided in 3 group of 30 each. Group I - received only 3ml 0.5% hyperbaric bupivacaine (15 mg) intrathecally while Group II & III- received 25µg and 50 µg Clonidine as adjuvant to 3 ml 0.5% hyperbaric bupivacaine respectively.

**Results:** The duration of anaesthesia i.e: regression of sensory level below L1, duration of analgesia and sedation score was maximum (clinically significant) in group III followed by group II then group I. The incidence of side effects like bradycardia , hypotention , sedation & nausea /vomiting were more in Group III followed by group II then group I.

**Conclusion**: clonidine as an adjuvant to bupivacaine significantly increase the duration of anesthesia and post – operative analgesia. In view of sedative effect of 50 µg clonidine it should be used judiciously in ASA class>II patient.

## KEYWORDS

Intrathecal, adjuvant, clonidine, hyperbaric, American society of Anaesthesiologist (ASA)

## INTRODUCTION

Pain is an inevitable component of post –operative period. Hence an effective pain relief after surgery is essential.Spinal anesthesia provide intense analgesia by segmental blockade of central neural axis. Local anesthetics are the commonest drugs used for spinal anesthesia, but their relatively short duration of action may lead to early analgesic intervention in the postoperative –period. [1] Various drugs are used intrathecally to prolong the intraoperative as well as postoperative analgesia.[2]

Clonidine a selective $\alpha_2$-adrenergic agonist is being extensively evaluated as an adjuvant to local anesthetics and is free of opioid related side effects. [3] It is known to increase both sensory and motor blockade of local anesthetics.[4] Intrathecal clonidine has been used as an adjuvant to local anesthetics in various surgical procedures without any clinically significant side effects.[5-6]

Previous studies have described the use of clonidine in a wide range (15-150 µg). [5-8] In present observational study, we evaluated and compared intrathecal 0.5% hyperbaric bupivacaine -clonidine combination with 0.5% hyperbaric bupivacaine in respect to hemodynamic changes, analgesic duration and incidence of side effects in orthopedic lower-limb surgeries.

## METHOD AND MATERIALS

This prospective, observational study was conducted after obtaining ethical clearance from the institute. Ninety patients of either sex in the age group of 30–60 years belonging to American Society of Anesthesiologists (ASA) physical status I or II and scheduled for lower limb orthopedics surgery were included while patients having contraindication to spinal anesthesia (raised ICP, bleeding diathesis, progressive neurological disorder, severe cardiac dysfunction), sensitive/ allergic to study drug and pregnant females were excluded from the study.

Pre-anesthetic check-up of all the 90 patients were done and details meticulously recorded with informed written consent. Also linear visual analog scale (VAS 0 = no pain and 10 = worst imaginable pain) was taught to every patient.[9] In the operating room, after the establishment of intravenous (IV) line and attachment of standard monitors [non-invasive blood pressure (NIBP), electrocardiography (ECG), and pulse oximetry (SpO2)], IV preloading with 10 ml/kg of lactated Ringer's solution was done and pulse rate, systolic/ diastolic and mean arterial blood pressure, SpO2 were noted as baseline values. All the participants were randomly allocated to one of the three groups ($n$ = 30 each).

Group I received only 3ml 0.5% hyperbaric bupivacaine (15 mg) while **Group II and Group III** received 25 µg and 50 µg Clonidine as adjuvant to 3 ml 0.5% hyperbaric bupivacaine respectively.

Under all aseptic and universal precautions, spinal anesthesia was administered in sitting posture at the L3–L4 intervertebral space and the study drug injected according to group allocated to them. Patient was turned supine immediately and onset of sensory and motor block was assessed by pin-prick test using 22-G short beveled needle and Bromage scale respectively[10]

**Bromage scale[10]:**

| Grade | Criteria | Degree of block |
|---|---|---|
| I | Free movement of legs and feet | Nil (0%) |
| II | Just able to flex knees with free movement of feet | Partial (33%) |
| III | Unable to flex knees, but with free movement of feet | Almost complete (66%) |
| IV | Unable to move legs or feet | Complete (100%) |

After intrathecal (spinal) drug injection hemodynamic parameter were recorded during 1st hour at 15$^{th}$, 30$^{th}$, 45$^{th}$, 60$^{th}$ minute then hourly up to 6$^{th}$ hour followed by 4$^{th}$ hourly up to 24 hour ( i.e 2$^{nd}$ ,3$^{rd}$ ,4$^{th}$,5$^{th}$ ,6$^{th}$,10$^{th}$, 14$^{th}$, 18$^{th}$ &24$^{th}$ hour). Greater than 20% decrease in mean arterial pressure or a systolic pressure less than 90mmHg systolic was treated with boluses of phenylepherine (0.5-1µg/kg) and i.v. fluids where appropriate.

Duration of anesthesia was measured as time interval from intrathecal injection to regression of sensory block below L1.

Intensity of pain was assessed by 10 point visual analogue scale:

Grade 0 (0-1) No pain
Grade 1 (1-4) Mild pain
Grade 2 (4-7) Moderate pain
Grade 3 (7-10) severe pain

Rescue analgesic Inj.Diclofenac 75mg i.m, was given when VAS > 4.

Duration of analgesia was measured as time from intrathecal injection to rescue analgesic.

**Sedation was judged by Ramsay Sedation Score -**

1. Anxious & agitated or restless, or both.

2. Co-operative, oriented & tranquil.
3. Responding to commands only.
4. Brisk response to light glabellar tap.
5. Sluggish response to light glabellar tap.
6. No response to light glabellar tap.

The data was analyzed statistically using ANOVA, Post Hoc Tukey-test, Kruskal-wallis test, Mann Whitney test depending upon the nature of data.

## RESULTS

All the patients were comparable in age, weight, height, sex distribution in the three groups. Also pre-operative pulse, SBP, DBP, duration of surgery,onset of sensory and motor action was comparable. [Table 1]

The duration of action/ anesthesia, duration of analgesia, sedation score, incidence of bradycardia, hypotension, nausea ,vomiting were recorded and compared.

Mean duration of anesthesia and analgesia was significantly prolonged in group III and II as compared to group1 ($p<0.005$).(Table 2)

Mean sedation score was more in group III (2.66) > group II (2.06) > group 1(1.90) and the difference was significant between Group I & III and Group II & III but insignificant between Group I & II (Table 2). The incidence of bradycardia, hypotension, nausea and vomiting was more in Group III followed by Group II then Group I (Table 2) but the same was insignificant (Fisher exact test p value >0.005).

## DISCUSSION

Clonidine is a selective agonist for α-2 adrenoreceptors. It is known to increase both sensory and motor block of local anesthetics.[4] The analgesic effect following its intrathecal administration is mediated spinally through activation of post synaptic α -2 receptors in substantia gelatinosa of spinal cord [11-12]. The rationale behind intrathecal administration of clonidine is to achieve a high drug concentration in the vicinity of α -2 adrenoreceptors in the spinal cord.

Patients in the three groups were comparable with respect to age, weight, height and gender(Table 1). Similar observation was seen in study done by Ramila H *et al*.[13] and Jeshnu prakash topple *et al.* [14]

Preoperative baseline hemodynamic parameters (Pulse rate, SBP, DBP) were comparable among patients in the three groups (Table1). Kriton S.Filos *et al in their study have similar findings.*[15]

Duration of surgery in the 3 group was comparable (Table 1). Similar observation was seen in studies done by B.S. Sethi *et al* [6] Kriton S.Filos *et al* .[15] onset of sensory and motor action was comparable in the 3 groups (Table 1) In contrast the study conducted by Hema Saxena *et al* [16] reported significant lowering of mean time of onset of sensory and motor block in clonidine group.

Mean duration of action was longest in Group III followed by Group II then Group I and the difference was significant (ANOVA F value 32.098) (Table 2). Hema saxena [17] *et al* reported prolongation of two segment regression by 200% in Clonidine Group which was similar to our finding.

Mean duration of analgesia was longest in Group III followed by Group II then Group I and the difference was statistically highly significant (Table 2). In study conducted by Ramila H jamliya [13] *et al* total duration of sensory block for Bupivacaine alone was 227.6±9.8 min while Clonidine group( 30µg) had 351.9±17.5 min. Similar observations noted in studies by Agreta Gecag Gashi [18] *et al,* Zahoor ahmad shah *et al* [19]

Mean sedation score was more in Clonidine groups (Group II and III) than Bupivacaine alone (Group I) and the difference was significant between group I & III and group II & III but insignificant between group I & II which is similar with the study done by B.S.Sethi *et al*.[6] and Hema saxena[17] *et al* though they have used less dose of Clonidine ( 15, 30 & 37.5 µg) . Bradycardia was more in Group III ( 4/ 30) followed by Group II (3/30) than Group I(2/30) but was insignificant (Table 2) In contrast, study done by Ramila H jamliya [13] *et al* found significant bradycardia in Clonidine group than bupivacaine alone group. Incidence of hypotension was Group III (4/30) > Group II (2/30) > Group I (1/30) (Table 2) and was insignificant while study done by B.S. Sethi *et al* [6] shows significant decrease in mean arterial pressure (MAP) in the Clonidine Group than control group ($p <0.001$). Incidence of Nausea and vomiting was group III (2/30), ) > Group II (1/30) > Group I (0/30) (Table 2) and was insignificant similar results were seen in study of B.S.Sethi *et al*[6] and Ramila H jamliya[13] *et al.*

## CONCLUSION

To conclude use of Clonidine with bupivacaine intrathecally does significantly increase the duration of anesthesia, post-operative analgesia and provides sedation. Clonidine in a dose of 25µg has a better efficacy/side-effect profile as compared to 50µg dose.

**Table 1: Comparison of demographic and baseline characteristics of the patients in the three groups**

| | Group I | Group II | Group III |
|---|---|---|---|
| **Age (years) (Mean ± SD)** | 40.36 ± 5.744 ANOVA (F Value-2.022) p=0.139-NS | 42.26 ± 5.625 ANOVA (F Value-2.022) p=0.139-NS | 43.10 ± 4.765 ANOVA(F Value-2.022) p=0.139-NS |
| **Weight (kg) (Mean ± SD)** | 56.76±8.439 ANOVA(F Value-2.285) p=0.108-NS | 58.33±7.945 ANOVA(F Value-2.285) p=0.108-NS | 60.83±5.602 ANOVA(F Value-2.285) p=0.108-NS |
| **Height (cm) (Mean ± SD)** | 157.96± 4.766 ANOVA(F Value-0.208) p=0.813-NS | 157.10± 6.059 ANOVA(F Value-0.208) p=0.813-NS | 157.16±6.422 ANOVA(F Value-0.208) p=0.813-NS |
| **Sex distribution (M:F ratio)** | 15:15 $X^2$ –Df=2-0.267 (p=0.875-NS) | 16:14 $X^2$ –Df=2-0.267 (p=0.875-NS) | 14:16 $X^2$ –Df=2-0.267 (p=0.875-NS) |
| **Pre-operative pulse (Mean ± SD)** | 79.73± 11.14 ANOVA(F Value-0.935) (p=0.397-NS) | 83.16±11.44 ANOVA(F Value-0.935) (p=0.397-NS) | 80.30±8.37 ANOVA(F Value-0.935) (p=0.397-NS) |
| **Pre-operative SBP (Mean ± SD)** | 124±6.236 ANOVA(F Value-1.064) (p=0.350-NS) | 126.33±5.560 ANOVA(F Value-1.064) (p=0.350-NS) | 124.60±7.734 ANOVA(F Value-1.064) (p=0.350-NS) |
| **Pre-operative DBP (Mean ± SD)** | 78.66±3.209 ANOVA(F Value-0.173) (p=0.841-NS) | 79.13±2.812 ANOVA(F Value-0.173) (p=0.841-NS) | 78.86±3.266 ANOVA(F Value-0.173) (p=0.841-NS) |
| **Duration of surgery (Mean in min ± SD)** | 114.00±16.103 ANOVA(F Value-0.723) (p=0.488-NS) | 119.83±21.714 ANOVA(F Value-0.723) (p=0.488-NS) | 116.3±18.473 ANOVA(F Value-0.723) (p=0.488-NS) |
| **Onset of sensory action (Mean in sec ± SD)** | 107.16±25.075 ANOVA(F Value-1.884) (p=0.158-NS) | 96.66±18.666 ANOVA(F Value-1.884) (p=0.158-NS) | 97.00±26.929 ANOVA(F Value-1.884) (p=0.158-NS) |
| **Onset of motor action (Mean in sec ± SD)** | 142.33±29.90 ANOVA(F Value-0.675) (p=0.512-NS) | 139.50±29.981 ANOVA(F Value-0.675) (p=0.512-NS) | 133.67± 28.460 ANOVA(F Value-0.675) (p=0.512-NS) |

**SD=standard deviation, SBP=systolic blood pressure, DBP=Diastolic blood pressure,**
**ANOVA** = Analysis of variance, **p value**< 0.005 is significant

| Table 2: characteristics of various parameters recorded in the three groups | | | |
|---|---|---|---|
| | **Group I** | **Group II** | **Group III** |
| **Duration of anesthesia/action (Mean ± SD)** | 168.3±18.999<br>ANOVA(F Value-32.098)<br>(p<0.001-HS) | 194.00±22.909<br>ANOVA(F Value-32.098)<br>(p<0.001-HS) | 222.66±34.434<br>ANOVA(F Value-32.098)<br>(p<0.001-HS) |
| **Duration of analgesia (Mean ± SD)** | 192.83±12.295<br>ANOVA(F Value-126.34)<br>(p<0.001-HS) | 350.66±56.56<br>ANOVA(F Value-126.34)<br>(p<0.001-HS) | 406.50±73.477<br>ANOVA(F Value-126.34)<br>(p<0.001-HS) |
| **Sedation score (Mean ± SD)** | 1.90±0.305<br>Kruskal-wallis test($X^2$-37.474)<br>(p<0.001-HS) | 2.06±0.365<br>Kruskal-wallis test ($X^2$-37.474)<br>(p<0.001-HS) | 2.66±0.546<br>Kruskal-wallis test ($X^2$-37.474)<br>(p<0.001-HS) |
| **Incidence of bradycardia** | 2/30 (p=0.905-NS) | 3/30 (p=0.905-NS) | 4/30 (p=0.905-NS) |
| **Incidence of hypotension** | 1/30 (p=0.493-NS) | 2/30 (p=0.493-NS) | 4/30 (p=0.493-NS) |
| **Incidence of Nausea &Vomitting** | 0/30 (p=0.770-NS) | 1/30 (p=0.770-NS) | 2/30 (p=0.770-NS) |
| **p value<** 0.005 is significant, **HS=**highly significant, **NS**= not significant | | | |

## REFERENCES


1. David LB. Spinal, epidural and caudal anesthesia. In: Miller RD, editor.Miller's Anesthesia. 7th ed, Vol.1& 2. Philadelphia: Churchill Livingstone; 2005. p. 1653-83,913-939.
2. Shetty PS, Picard J. Adjuvant agents in regional anaesthesia.Anaesth Intensive Care Med 2006;7:407-10.
3. Eisenach JC. Overview: First international symposium on α 2 adrenergic mechanisms of spinal anesthesia. Reg Anaesth1993;18(4S):i-vi.
4. Chiari A, Eisenach JC. Spinal anesthesia: Mechanisms, agents, methods and safety. Reg Anesth Pain Med 1998;23:357-62.
5. Van Tuijl I, van Klei WA, van der Werff DB, Kalkman CJ. The effect of addition of intrathecal clonidine to hyperbaric bupivacaine on postoperative pain and morphine requirements after caesarean section: A randomized controlled trial. Br J Anaesth 2006;97:365-70.
6. Sethi BS, Samuel M, Sreevastava D. Efficacy of analgesic effects of low dose intrathecal clonidine as adjuvant to bupivacaine. Indian J Anaesth 2007;51:415-9.
7. Grandhe RP, Wig J, Yaddanapudi LN. Evaluation of bupivacaineclonidine combination for unilateral spinal anesthesia in lower limb orthopaedic surgery. J Anaesth Clin Pharmacol 2008;24:155-8.
8. Niemi L. Effects of intrathecal clonidine on duration of bupivacaine spinal anaesthesia, hemodynamic and postoperative analgesia in patients undergoing knee arthroscopy. Acta Anesthesiol Scand 1994;38:724-8.
9. Downie WW, Leatham PA, Rhind VM, Wright V, Branco JA Anderson JA. Studies with pain rating scales. Ann Rheum Dis. 1978;37:378-81.
10. Gammon GD, Starr I. Studies on the relief of pain by counter irritation. J Clin Invest 1941;13:20
11. Reddy SVR, Yaksh TL, Spinal noradrenergic terminal system mediates antinociception. Brain Res 1980; 189 : 391-401.
12. Brandt SA, Livingston A. Receptor changes in spinal cord of sheep associated with exposure to chronic pain. Pain 1990; 42: 323-9.
13. Ramila H. Jamliya, Reema Vansola, B. J. Shah,Dharmesh L Chauhan, Effect of Clonidine Addition To Hyperbaric 0.5% Bupivacaine For Spinal Anaesthesia In Lower Limb Surgery [A Comparative Study]. Low Dose Bupivacaine- Clonidine In Spinal Anaesthesia: January-March2012; NJIRM; Vol. 3(1).p- 101-105
14. Jeshnu Prakash Tople,Amol singam,Satish Gosavi,Aruna vijay chandak.comparison of intrathecal bupivacaine(17.5mg)with preservative free Midazolam (1mg) versus intrathecal bupivacaine (17.5 mg) for postoperative pain relief in lower limb surgeries.IJBAR (2013) 04(02) p 83-88.
15. Filos KS, Goudas LC, Patroni O, Polyzou V. Intrathecal clonidine as a sole analgesic for pain relief after caesarean section.Anesthesiology 1992; 77: 267- 74.
16. M. Gentili and F. Bonnet .Spinal Clonidine produces less urinary retention than spinal morphine British Journal of Anaesthesia, Vol 76, Issue 6 872-873
17. Hema Saxena ,Sudhir Kumar Singh ,SK Ghildiyal . Low Dose Intrathecal Clonidine With Bupivicain Improves Onset And Duration Of Block With Haemodynamic Stability. The Internet Journal of Anesthesiology 2010 vol(23)ISSN: 1092-406.p 1-11.
18. Agreta Gecag Gashi, Hasime Terziqi,Tune Pervorfi, Arben Kryeziu. Intrathecal clonidine added to small-dose bupivacaine prolongs postoperative analgesia in patients undergoing transurethral surgery. Can Urol Assoc J 2012;6(1):25-9.
19. Zahoor ahmad shah,Raksha kundal,Arun kumar gupta, Mohd. Sadiq Malla,Faisal Zahoor,Vijay kundal et al. Efficacy of analgesic effect of low dose Intrathecal Clonidine as adjuvant to bupivicain in urogenital surgeries:study in a Kashmiri population. 2012; SLJA : Vol (20) p 49-52.