

Comparison of effects of Buprenorphine and clonidine as adjuvants to Bupivacaine (0.35%) for supraclavicular brachial plexus block

Omer Bashir Itoo^{1*}, Vasudha Jadhav², Jyotsna Paranjpe³

¹1st Year PG, ²Professor, ³Professor and HOD, Department of Anesthesiology, BVDU Medical College and Hospital, Sangli, Maharashtra.

Email: omeritoo@gmail.com

Abstract

Background: Adjuvant to local anesthetics have been tried to enhance analgesic profile. Opioids prolong analgesia but have unfavorable side effect profile. So, search for non-opioid with comparable analgesic duration and minimal side effect continues. Hence our study aims to compare Buprenorphine; an opioid similar in structure to morphine but approx. 33 times more potent, to a novel drug Clonidine; an imidazoline derivative with α_2 -adrenergic agonistic activity. **Settings and Design:** A total of 60 patients belonging to ASA status I & II posted for orthopedic upper limb surgery were enrolled and randomly divided into three Groups of 20 each. All patients received 20ml Bupivacaine (0.5%) in supraclavicular brachial plexus block. Group corresponding adjuvant and normal saline were added to make total solution to 40ml. VAS score and other block characteristics were observed at fixed intervals for 24 hours post operatively. "Graph Pad Prism version 5.03" used for descriptive, analytic and comparative statistics. **Results:** Onset of sensory block was significantly delayed in clonidine group (Group BC). Analgesia lasted significantly longer in buprenorphine group (Group BB). VAS scores were found to be better in Group BB and BC and these scores were lower than Group B (bupivacaine alone) except at 24 hr. Time to first rescue analgesia and total number of doses were significantly lower in Group BB and Group BC. Incidence of nausea, vomiting and sedation were more in Group BB. **Conclusions:** Buprenorphine and clonidine are acceptable adjuvants.

Key Word: Bupivacaine, Buprenorphine, Clonidine, Supraclavicular brachial plexus block,

*Address for Correspondence:

Dr. Omer Bashir Itoo, 1st Year PG Student MBBS, Department of Anesthesiology, BVDU Medical College and Hospital, Sangli, Maharashtra, INDIA.

Email: omeritoo@gmail.com

Received Date: 18/03/2017 Revised Date: 12/04/2017 Accepted Date: 10/05/2017

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	DOI: 14 May 2017

INTRODUCTION

The Supraclavicular brachial plexus block with local anesthetic is one of the most commonly employed regional nerve block technique for upper limb surgery. However, large volume of local anesthetic required to produce desirable effects may result into systemic side effects. A variety of adjuvant has been added to increase

analgesia and reduce total dose of local anaesthetic used. Buprenorphine's prolonged analgesic benefit has been reported with brachial plexus block. Clonidine appears to have significant analgesic benefit when used in doses up to 150 μ g at the same time not having the serious side effect profile associated with the use of narcotics.

Subjects and methods:

This prospective randomized double blind study was conducted after obtaining Institutional Ethics Committee approval and written informed consent. A total of 60 patients of both sexes in the age group 20-60 years belonging to ASA physical status I & II posted for upper limb orthopedic surgeries were enrolled and randomly divided into three Groups— Group B (n=20), Group BC (n=20) and Group BB (n=20). Patients received solution in the following manner: Group B - 0.5% bupivacaine (isobaric) 100mg(20ml) + 20ml NS. Group BB - 0.5% bupivacaine (20ml) + 0.3mg Buprenorphine(1ml) + 19ml NS. Group BC - 0.5% bupivacaine (20ml) + 150mcg

Clonidine (1ml) + 19ml NS. Patients not willing to be a part of the study, having known allergy or addiction to study drugs, in which regional block was contraindicated in general (local infection, coagulation b normality and personality disorders or mental illness etc.) or with specific contraindications (pnemothorax or phrenic nerve block) were excluded from the study. Also barred from the study were pregnant or lactating women, those with significant systemic diseases, taking medications with psychotropic or adrenergic activities and chronic analgesic therapy other than simple analgesics (e.g. non-steroidal anti-inflammatory drugs). In operating theatre standard monitoring including NIBP (non invasive blood pressure), pulse-oximeter and ECG (Electrocardiogram) leads were attached to the patient. Baseline systolic BP (blood pressure), diastolic BP and heart rate along with SPO2 on air and respiratory rate were recorded. An 18G i.v. cannula secured. Supraclavicular block (Kulenkampff /Classic approach) was given utilizing parasthesia technique without administering any analgesic or sedative drugs to the subjects as premedication. The drug to be used for block was supplied by a concerned person and injected by the researcher totally blinded to the medication being used. After injection of drug and having being assured of complete analgesia surgical procedure was allowed to start. Sensory and motor block of the musculocutaneous, radial, ulnar, and median nerve were determined at frequent intervals after completion of the injection.

The following characteristics of the block were observed:

1. Onset time of Sensory block: Pinprick test (time of injection of test drug to reduction of pain at the site of surgery).
2. Motor block : Time of onset (times of injection of test drug to development of motor weakness): Quality of block (Bromage scale)
3. Duration of analgesia: interval between onset of analgesia to the time patient first complains of pain.
4. Pain : VAS score(0-10scale)

5. Rescue analgesic (inj. diclo fenac 75mg im) : whenever VAS score ≥ 4
6. Sedation score
7. Side effects: nausea, vomiting, itching, urinary retention etc
8. Haemodynamic changes: Bradycardia (pulse < 60 beats/minute), hypotension (reduction of MAP $\geq 30\%$ of baseline), respiratory depression (respiratory rate ≤ 8 breaths/minute or arterial oxygen saturation $< 90\%$). SEDATION SCORE 0 – Alert, 1 – Awake but sedated, 2 – Asleep but easily aroused 3 – Asleep and not arousable by verbal contact

Statistical analysis

The statistical analysis was performed with “Graph Pad Prism version 5.03”. Arithmetic mean, median(range), Standard Deviation(SD), Standard error of mean(SEM), carried out as descriptive statistics. ANOVA(with Tukey’s, Dunn’s, or Bonferroni’s test comparison post test) and Chi -square test for qualitative values adopted for analytic and comparative statistics. Post ANOVA multiple comparison test was also performed to compare the groups. A $p < 0.05$ was considered to be statically significant.

RESULTS

There was no statistically significant difference between the demographic profile (age, sex ratio and body weight), ASA physical status, baseline heart rate and mean arterial pressure of the three groups. The groups were also similar with regard to duration and type of surgery ($p > 0.05$). Sensory block onset was delayed in clonidine group compared to plain bupivacaine group and the difference is significant Table- 1. This is in contrast to earlier study which shows no effect² or faster onset¹³. This needs further evaluation. No difference in onset of sensory block was noted in buprenorphine group as earlier studies^{1,14}. However significant difference exists when BC compared to BB.

Table 1: Block characteristics

		Group B 5-10	Group BC 4-22	Group BB 5-20
Sensory Block Onset (Mins)	Range			
	Mean \pm SD	8.45 \pm 2.25	12.05 \pm 6.3	8.25 \pm 3.93
Motor block onset (Mins)	Range	10-25	8-26	10-25
	Mean \pm SD	16.75 \pm 4.865	17.05 \pm 6.219	16.25 \pm 4.327
Quality of motor block	Grade 3(no. ofpatients)	7(35%)	4(20%)	6(30%)
	Grade 2(no. ofpatients)	13(65%)	16(80%)	14(70%)
Duration of analgesia in min	Range	180-630	250-990	390-1830
	Mean \pm SD	369.3 \pm 111.5	578.5 \pm 201.3	822.8 \pm 417.5

Motor block onset was slightly prolonged in Group BC but quality of motor block showed no significant difference among the three groups.

Table 2: Distribution of Patients according to Time for First Rescue Analgesic (InjDiclofenac75 mg i.m)

Time(hours)	No Of Patients		
	Group B	Group BC	Group BB
<6	1	0	0
6-12	19	6	4
13-18	0	7	8
19-24	0	7	4
>24	0	0	2

Table 3: Distribution of Patients according to Total Doses of Analgesic (Diclofenac) required in24 hr

Doses of analgesic	Group B(no. of patients)	Group BC (no. of patients)	Group BB(no. of patients)
1	2(10%)	14(70%)	11(55%)
2	9(45%)	3(15%)	6(30%)
3	8(40%)	2(10%)	1(5%)
4	1(5%)	1(5%)	0(0%)
Total	20	20	20
Range	1-4	1-4	0-3
Median	2	1	1
Mean±SD	2.4 ±0.7539	1.5 ±0.8885	1.3 ± 0.7327
SEM	0.1686	0.1987	0.1638
P value	BvsBC– 0.001-0.01 (**),BvsBB– <0.001(***) ,BCvsBB – >0.05(ns)		

Table 4: Incidence of side effects

Side Effects	No Of Patients		
	Group B	Group BC	Group BB
Sedation	0	5	8
Nausea	1	1	6
Vomiting	1	2	5
Pruritis	0	0	2
Hypotension	0	0	0
Bradycardia	0	0	0
Respiratory Depression	0	0	0

Sedation as side effect was encountered in 40% in group BB compared to 5% showed in BC group. Also higher sedation score was achieved in buprenorphine group compared to clonidine group.

Two patients also encountered pruritis in buprenorphine group . Nausea and vomiting were encountered in all 3 groups but its incidence was higher in buprenorphine group though difference was statistically insignificant. None showed signs of hemodynamic instability, local anesthetic toxicity or respiratory depression.

DISCUSSION

We observed that clonidine 150 µg added to a 0.25% bupivacaine in brachial block as an adjuvant leads to no significant prolongation of duration of analgesia .It however does decrease analgesic consumption, prolonged the time for first rescue analgesic and lower VAS scores indicating that clonidine modified pain mechanics to

some extent. No significant side effects were observed. On the other hand addition of Buprenorphine(0.3mg) to bupivacaine(0.25% buprenorphine,40ml) in brachialplexus block produced effective analgesia which lasted longer than the two other groups (more than twice as long as that produced by local anesthetic alone) with no difference in sensory or motor onset time ,reduced pain scores (VAS) and less supplemental analgesics. Some usual side effects of opioids are observed, but are mild.

CONCLUSION

Both buprenorphine and clonidine have been found to have favourable effect on brachial plexus block characteristics with acceptable side effects though significant prolongation of duration of analgesia is seen with buprenorphine alone.

REFERENCES

- Viel EJ, Eledjam JJ, De La Coussaye J, D'Athis F. Brachial plexus block with opioids for postoperative pain relief: comparison between buprenorphine and morphine. *RegAnesth* 1989; 14: 274–8.
- Candido KD, Franco CD, Khan MA, Winnie AP, Raja DS. Buprenorphine added to the local anesthetic for brachial plexus block to provide postoperative analgesia in outpatients. *RegAnesth Pain Med*.2001 Jul-Aug;26(4):352-6.
- Candido KD, Winnie AP, Ghaleb AH, Fattouh MW, Franco CD. Buprenorphine added to the local anesthetic for axillary brachial plexus block prolongs postoperative analgesia. *Regional Anesthesia and Pain Medicine*, Volume 27, Issue 2, Pages 162 – 167.
- Bazin JE, Massoni C, Bruelle P, et al. The addition of opioids to local anaesthetics in brachial plexus block: the comparative effects of morphine, buprenorphine and sufentanil. *Anaesthesia* 1997;52: 858–62.
- Bernard JM, Macaire P. Dose-range effects of clonidine added to lidocaine for brachial plexus block. *Anesthesiology* 1997; 87: 277–84.
- Singelyn FJ, Dangoisse M, Bartholomee S, Gouverneur JM. Adding clonidine to mepivacaine prolongs the duration of anesthesia and analgesia after axillary brachial plexus block. *RegAnesth* 1992; 17:148 –50
- Singelyn FJ, Gouverneur J, Robert A. A minimum dose of clonidine added to mepivacaine prolongs the duration of anesthesia and analgesia after axillary brachial plexus block. *AnesthAnalg* 1996; 83:1046 –50.
- Buttner J, Ott B, Klose R. Der einfluss von clonidinzusatzzumepivacain. *Anaesthesist* 1992; 41:548 –54. 15. Singelyn FJ, Dangoisse M, Bartholomee S, Gouverneur JM. Adding clonidine to mepivacaine prolongs the duration of anesthesia and analgesia after axillary brachial plexus block. *RegAnesth* 1992s; 17:148 –50.
- Bone HG, Van Aken H, Brooke M, et al. Enhancement of axillary brachial plexus block anaesthesia by coadministration ofneostigmine. *RegAnesth Pain Med* 1999; 24: 405–10.
- Eledjam JJ, Viel E, Charavel P, du Cailar J. Brachial plexus block with bupivacaine: effects of added alpha-adrenergic agonists: comparison between clonidine and epinephrine. *Can J Anaesth* 1991; 38:870 – 5.
- Gaumann D, Forster A, Griessen M, et al. Comparison between clonidine and epinephrine admixture to lidocaine in brachial plexus block. *AnesthAnalg* 1992;75: 69 –74.
- Bazin JE, Massoni C, Groslier D, et al. Bloc du plexus brachial :effet de l'addition de sufentanil au melanged'anesthesiqueslocaux sur la duree de l'analgesiepostoperatoire. *Ann Fr Anesth. Reanim* 1997;16:9 –13.
- Shivinder Singh,Amitabh Aggarwal.Arandomised controlled double-blinded prospective study of the efficacy of clonidine added to bupivacaine as compared with bupivacaine alone used in supraclavicular brachial plexus block for upper limb surgeries.*Indian Journal of Anesthesia*;Vol.54:2010:552-556.
- Boogaerts J, BalatoniE, LafontN, LecronL,Vanderhaegen JJ. Utilisation des morphiniquesdans les blocsnerveuxperipheriques. *Ars Medici Congress Series* 1982; 3:143-151
- Murphy DB, McCartney CJL, Chan VWS. Novel analgesic adjuncts for brachial plexus block: A systematic review. *AnesthAnalg* 2000; 90 :1122–8
- Eisenach JC, De Kock Marc, Klimscha W. 2-Adrenergic agonists for regional anesthesia. A clinical review of clonidine (1984– 1995). *Anesthesiology* 1996;85: 655–74.
- Hutschala D, Mascher H, Schmetterer L, Klimscha W , Fleck T , Eicher HG, Tschernko EM. Clonidine added to bupivacaine enhances and prolongs analgesia after brachial plexus block via a local mechanism in healthy volunteers. *Eur J Anaesthesiol* 2004;21:198– 204.Wolfgang Erlacher,ChristophSchuschnig, Herbert Koinig, Peter Marhofer, Matthias Melischek, Nikolaus Mayer, and Stephan
- Kapral, .Clonidine as adjuvant for mepivacaine, ropivacaine and bupivacaine in axillary, perivascular brachial plexus block. *Can J Anaesth* 2001; 48: 522–5.
- Duma A, Urbanek B, Sitzwohl C, A. Kreiger, M. Zimpfer, and S. Kapral. Clonidine as an adjuvant to local anaesthetic axillary brachial plexus block: a randomized, controlled study. *Br J Anaesth* 2005; 94:112–16.
- Erlacher W, Schuschnig C, Orlicek F, et al. The effects of clonidine on ropivacaine 0.75% in axillary perivascular brachial plexus block. *ActaAnaesthesiolScand* 2000; 44: 53–7.
- Sia S, Lepri A. Clonidine administered as an axillary block does not affect postoperative pain when given as the sole analgesic. *AnesthAnalg* 1999; 88:1109–12.
- Culebras X, Van Gessel E, Hoffmeyer P, Gamulin Z. Clonidine combined with a long acting local anesthetic does not prolong Post operative analgesia after brachial plexus block but does induce hemodynamic changes. *AnesthAnalg* 2001; 92: 199–204.
- Winnie AP. Brachial Plexus Block. In: Winnie AP, ed. *Plexus Anesthesia* Vol 1. Philadelphia: W.B. Saunders, 1993; 117– 88.
- AH El Saied, MP Steyn and JM Ansermino Clonidine prolongs the effect of ropivacaine for axillary brachial plexus blockade. article- 7, *Canadian Journal of Anesthesia*, Vol 47, 962-967.
- Gaumann DM, Brunet PC, Jirounek P. Clonidine enhances the effects of lidocaine on C-fiber action potential. *Anesth Analg* 1992; 74: 719–25.
- Butterworth JF, Strchartz GR. The 2-adrenergic agonists clonidine and guanfacine produce tonic and phasic block of conduction in rat sciatic nerve fibers. *AnesthAnalg* 1993;76: 295–301.
- Gaumann DM, Brunet PC, Jirounek P. Hyperpolarizing afterpotentials in C fibers and local anesthetic effects of clonidine and lidocaine. *Pharmacology* 1994; 48: 21–9.

28. Bernard J-M, Kick O, Bonnet F. Comparison of intravenous and epidural clonidine for postoperative patient controlled-analgesia. *AnesthAnalg* 1995;81: 706–12.
29. Eisenach JC, Detweiler M, Hood D. Hemodynamic and analgesic actions of epidurally administered clonidine. *Anesthesiology* 1993; 78: 525–31.
30. Brooks JHJ, Gupta B. Further evidence for narcotic receptors in human peripheral nerves. *Regional Anesthesia* 1990;15:215
31. Stein C. Control of pain in peripheral tissue by opioids. *New England journal of Medicine* 1995;332:1685-90
32. Gobeaux D, Landais A, Bexon G, et al. Addition of fentanyl to adrenaesed lidocaine for the brachial plexus block. *CahAnesthesiol* 1987;35 :195–9.
33. Gormley WP, Murray JM, Fee JPH, Bower S. Effect of the addition of alfentanil to lignocaine during axillary brachial plexus anaesthesia. *Br J Anaesth* 1996;76 :802–5.
34. Wajima Z, Nakajima Y, Kim N, et al. IV compared with brachial plexus infusion of butorphanol for postoperative analgesia. *Br J Anaesth* 1995; 74:392–5.
35. Kardash K, Schools A, Conception M. Effects of brachial plexus fentanyl on supraclavicular block. *RegAnesth* 1995;20:311–5.
36. Bourke DL, Furman WR. Improved postoperative analgesia with morphine added to axillary block solution. *J ClinAnesth* 1993; 5:114 –7.
37. Gobeaux D, Landais A. Use of two opioids in blocks of the brachial plexus. *Cah Anesthesiol* 1988; 36:437– 40.

Source of Support: None Declared
Conflict of Interest: None Declared