

## A comparative study to know the effectiveness of clonidine versus midazolam as an adjuvant in ultrasound guided supraclavicular brachial plexus block

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### Article Info

Received: 8<sup>th</sup> July, 2019

Accepted: 1<sup>st</sup> August, 2019

Published Online: 22<sup>nd</sup> August, 2019

**Keywords:** Clonidine, Midazolam, Supraclavicular brachial plexus block, Postoperative analgesia.

### Abstract

**Introduction:** Peripheral nerve blocks are becoming popular day by day because of their relative safety and precision. The present study aimed to compare the effectiveness of clonidine versus midazolam as an adjuvant to local anesthetics in ultrasound guided supraclavicular brachial plexus block.

**Materials and Methods:** A prospective randomised control study where total of 100 adult patients of either sex, aged between 18 -60 years of ASA physical status 1 and 2 undergoing elective upper limb surgeries were divided equally into two groups by computer generated random number method. Group C: where inj. clonidine -150mcg was used as an adjuvant in addition to inj xylocaine plain 2% -10ml and inj bupivacaine plain 0.5%- 20ml in ultrasound guided supraclavicular brachial plexus block. Group M: where inj. Midazolam (preservative free)- 5mg was used as an adjuvant in addition to local anesthetics as mentioned above for group C. In both groups onset of sensory block, onset of motor block, duration of sensory block, duration of motor block, sedation measured by sedation scale(culebras), post operative analgesia using VAS at 0 min, 30min, 1hr, 2hr, 3hr, 6hr and 12hr were recorded.

**Results:** Post operative analgesia was significantly prolonged in Group C (VAS $\leq$ 3) when compared to group M and sedation score for Group C are higher when compared to group M intraoperatively

**Conclusion:** clonidine as an adjuvant in ultrasound guided brachial plexus block for upper limb elective surgeries prolongs post operative analgesia (VAS score $\leq$ 3 for 345 min) when compared to preservative free midazolam (VAS score $\leq$ 3 for 280min) and also has higher sedation scores compared to midazolam. No complications were observed in any patients of either groups.

### Introduction

Peripheral nerve blocks have become an alternative to general anaesthesia which has become a standard practice throughout the world. The brachial plexus provides the complete motor and nearly total sensory innervation to the upper limb.<sup>1</sup> Brachial plexus block is often called "spinal anaesthesia of the upper extremity" because of its rapid onset, predictable and complete anaesthesia and ubiquitous use in all upper limb surgeries. Block is performed at the level of distal trunks and origin of divisions where brachial plexus is confined to its smallest surface area on first rib. The three trunks carry entire sensory, motor and sympathetic innervations of upper extremity, with exception of uppermost part of medial side of arm (T2).<sup>1</sup> Percutaneous supraclavicular brachial plexus blockade was introduced in clinical practice by Kulenkampff in 1911.<sup>2</sup> Brachial plexus block provides complete muscle relaxation stable intraoperative hemodynamics and smooth transition to post operative pain relief. Bupivacaine is longer acting and

lignocaine has quicker onset of action combination of both are used most frequently among all local anaesthetics.<sup>3</sup>

Midazolam, a water soluble benzodiazepine, is known to produce anti-nociception and potentiates local anaesthetics when given in neuraxial block. It produces this action by potentiation of gamma aminobutyric acid-A (GABA-A) receptors and peripheral nerves have these receptors.<sup>4</sup>

Clonidine is also known to potentiate local anaesthetics when given in neuraxial block. It produces this action by acting through  $\alpha_2$  receptors agonism.<sup>5</sup> But in peripheral blocks like brachial plexus block it prolongs duration of analgesia by hyperpolarisation of cyclic nucleotide gated cation channels.<sup>6,7</sup>

In the present study our aim is to compare both these adjuvants to local anesthetics i.e inj clonidine -150 mcg and inj midazolam (preservative free) 5mg with respect to sensory blockade, motor blockade, postoperative analgesia, sedation and possible adverse effects.

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<http://doi.org/10.18231/j.ijca.2019.085>

## Materials and Methods

The present prospective randomised control study was conducted in the Department of Anaesthesiology, B.L.D.E. (deemed to be university) Shri B.M Patil Medical College, Hospital and Research centre, Vijayapur. Study was conducted on ASA grade I or II adult patients, of either sex, aged between 18-60 years undergoing elective upper limb surgeries (distal to midhumerus). Informed consent was taken from all patients. Ethical committee clearance from hospital was taken to conduct the study.

Patients were randomly divided using computer generated random number method into 2 groups containing 50 patients each. Patients in both groups received 20ml of 0.5% bupivacaine plain and 10ml of 2% of lignocaine plain and in Group C injection clonidine 150mcg and Group M preservative free injection midazolam 5mg along with above mentioned local anaesthetics were administered. Pregnant patients, Patients with ASA physical status III and IV, patients with bleeding disorders, coagulopathies and on anticoagulants, with psychiatric disorders, having allergy to local anaesthetics and local site infection, with pre existing neuropathy were all excluded from the study.

All patients were examined the day before surgery and thoroughly investigated according to institute protocol. Patients were counselled with regards to anaesthesia as well as procedure. They were explained about visual analogue scale (VAS) score (0-10) where 0 indicates no pain and 10 indicates worst possible pain. In the operating room multipara monitors were applied to the patients. All cases were then premedicated with I.V. Inj Glycopyrrolate-0.004mg/kg and Inj Ondansetron 4mg. Intravenous fluid was given in the form of lactated Ringer solution 500ml. Senior and experienced anaesthesiologist gave ultrasound guided brachial plexus block using supraclavicular approach. Each patient was placed supine with the head turned 30° towards the contralateral side and ipsilateral arm is adducted. After aseptic preparation of area, a linear, high frequency transducer of sonosite M turbo was placed in the supraclavicular fossa superior to the clavicle and angled slightly toward the thorax. The subclavian artery should be easily identified. The brachial plexus appears a multiple hyperechoic disks just superficial and lateral to the subclavian artery. 23-gauge 1.5" needle was inserted lateral to the transducer in a direction parallel to the ultrasound beam. The needle is advanced medially toward the subclavian artery until the tip is visualized near the brachial plexus just lateral and superficial to the artery. After negative aspiration of blood the study drug was injected depending on group. The following parameters were studied.

### Onset of Sensory Block

After injection patients were assessed for sensory blockade by using pinprick. The time from injection till there will be absence of sensation in the areas supplied by median, radial, ulnar and musculocutaneous nerves were measured.

### Onset of Motor Block

The onset of motor block by assessing the following motor functions i.e. flexion at elbow (musculocutaneous nerve), wrist and elbow extension, opposition of thumb and index finger (median nerve) and opposition of thumb and little finger (ulnar nerve).

### Duration of Sensory Block

Time elapsed between injection of the drug and appearance of pain requiring analgesia.

### Duration of Motor Block

Time elapsed between injection of the drug to complete return of motor power.

Sedation was assessed by using the sedation scale described by Culebras et al<sup>8</sup>.

1. Awake and alert,
2. Sedated, responding to verbal stimulus,
3. Sedated, responding to mild physical stimulus.
4. Sedated, responds to moderate or severe physical stimulus.

Sedation scores were recorded at 0minute, 30minutes, 1st hour, 2nd hour, 3rd hour, 6th hour and 12th hour.

Pain score using visual analogue scale where 0 is no pain and 10 is worst possible pain score (VAS) were recorded at 0minute, 30 minutes, 1<sup>st</sup> hour, 2<sup>nd</sup> hour, 3<sup>rd</sup> hour, 6<sup>th</sup> hour and 12<sup>th</sup> hour.

All vitals were also monitored throughout the procedure

Only patients with complete sensory and motor block were included in the study. Patients who had to be supplemented general anaesthesia at any time during the intraoperative period were excluded from the study.

Number of patients demanding analgesia in the postoperative period: Analgesia in the form of Injection Diclofenac 75mg intramuscular was given on demand by the patient or when the VAS score will be  $\geq 4$ .

### Statistical Analysis

Data was presented by means of descriptive statistics viz, means, standard deviations, percentages and diagrams.

Paired t test was used to compare pain and sedation scores at different time periods.

Unpaired t test was used to compare variables of 2 groups

Chi-square test was used for qualitative data.

### Results

During the study period total of 100 patients, 50 each in clonidine and midazolam group showed there is no stastically significant difference with respect to age, sex and weight between the two groups as shown in Table 1.

Table 2 shows information regarding sensory blockade, motor blockade. Here also the two groups are comparable and there is no statistically significant difference with respect to onset of sensory blockade, onset of motor blockade, duration of sensory blockade and duration of motor blockade.

**Table 1:** Demographic data

|              | Group C (n=50) | Group M (n=50) | 'p' value |
|--------------|----------------|----------------|-----------|
| Age in years | 30.2± 10.40    | 31.80± 11.20   | 0.9538    |
| Sex M:F      | 36:14          | 32:18          |           |
| Weight in Kg | 58± 7.5        | 60±8.4         | 0.0997    |

**Table 2:** Onset and duration of sensory and motor blockade

|                                     | Group C(n=50) | Group M(n=50) | P value |
|-------------------------------------|---------------|---------------|---------|
| Time of onset of sensory block(min) | 5.92±1.20     | 5.81±1.01     | 0.601   |
| Time of onset of motor block(min)   | 8.80±1.60     | 9.61± 1.11    | 0.1773  |
| Duration of sensory block(hrs.)     | 4.62±0.62     | 4.30±0.43     | 1.22    |
| Duration of motor block(hrs.)       | 4.21±0.28     | 3.80±0.31     | 1.123   |

**Table 3:** Sedation score

| Sedation score | Group C(n=50) | Group M(n=50) |
|----------------|---------------|---------------|
| 1              | 15(30%)       | 32(64%)       |
| 2              | 31(62%)       | 16(32%)       |
| 3              | 4(8%)         | 2(4%)         |
| 4              | 0             | 0             |

**Table 4:** VAS scores of both groups

| Time  | Group C(n=50) | Group M(n=50) | P value |
|-------|---------------|---------------|---------|
| 0 min | 0             | 0             | -       |
| 30min | 0             | 0             | -       |
| 1hr   | 0             | 0             | -       |
| 2hr   | 0             | 1±0.3         | -       |
| 3hr   | 0             | 1±0.2         | -       |
| 6hr   | 2±0.4         | 3±0.6         | 1.22    |
| 12hr  | 4±0.6         | 5±1.2         | 1.124   |

Table 3 shows sedation score of two groups. Group C shows more sedation (score-2) than group M (score-1). Hence clonidine causes more sedation.

Table 4 shows VAS scores of two groups. Group C has lower VAS scores compared to group M which is more significant at 6hr and 12hr. VAS score  $\leq 3$  for group C is 345min and for group M is 280 min.

In group C total of 24 patients required rescue analgesics in 24 hrs while 29 patients required rescue analgesics in group M in the same time period

## Discussion

Supraclavicular approach of brachial plexus block is most commonly performed for the surgeries of upper limbs mainly those distal to midhumerus, where this approach of block is more appropriate. With the advent of ultrasound, success rates of these nerve blocks now nearing 100 percent

The objective of the present study was to determine efficacy of clonidine and preservative free midazolam in ultrasound guided supraclavicular brachial plexus block. Our study revealed post operative analgesia was more prolonged and sedation scores were also higher for the group C where clonidine was used as adjuvant to local anesthetics when compared to group M in which midazolam was used as an adjuvant to local anesthetics

Reinhart DJ, Wang W, et al (1996) in their study noted that postoperative analgesia was prolonged by adding

clonidine with local anaesthetics in brachial plexus block.<sup>8</sup> The study conducted by Singelyn FJ, Robert A et al. (1996) showed that clonidine 5 mcg/kg in axillary brachial plexus block along with local anaesthetics prolongs significantly the duration of both anaesthesia and analgesia without reported any side effects.<sup>9</sup> Gulec et al. (1998) also noticed bupivacaine-midazolam to provide prolonged postoperative analgesia compared to bupivacaine-morphine combination when given caudally.<sup>10</sup>

In our present study clonidine group showed more prolonged postoperative analgesia without any adverse effects at dose of 150mcg with local anesthetics which is statistically not significant.

Culebras X et al (2001) in their study found that clonidine combined with local anaesthetics in brachial plexus block does not prolong the duration of postoperative analgesia and induces hemodynamic changes.<sup>11</sup> In their study total of 60 adult patients underwent elective rotator cuff repair using interscalene approach of brachial plexus block. Those 60 patients were randomly divided into three groups.

Other study by Yatindra Kumar Batra, Nidhi panda et al (2001) revealed that midazolam (50 mcg/kg) in combination with 30 ml of (0.5%) bupivacain hastened onset of sensory and motor block and improves postoperative analgesia when used in brachial plexus block without producing any adverse effects.<sup>12</sup> This was a

prospective randomised double blind study conducted on 40 ASA I or II adult patients divided randomly into two groups one group receiving midazolam 50mcg/kg undergoing upper limb surgeries.

Chakraborty S, Chakrabarti J et al (2010) concluded that addition of a small dose of clonidine to 0.5% bupivacaine significantly prolonged the duration of analgesia without producing any clinically important adverse reactions other than sedation in supraclavicular brachial plexus block.<sup>13</sup> In this study 70 ASA I or II patients undergoing upper limb orthopaedic surgeries were equally divided into two groups one group received 30 mcg of clonidine along with bupivacaine 0.5% 25 ml, control group received only bupivacaine 0.5% 25ml.

Trivedi.V, Patel.N et al, (2010) conducted a randomised clinical study was conducted on 60 ASA I-II patients undergoing elective upper limb orthopaedic surgeries (duration of surgery < or =120 minutes) and concluded that injection clonidine provides better postoperative analgesia and more sedation than midazolam.<sup>4</sup> This study is comparable to our study in that here also clonidine (150mcg) and midazolam (5mg) are used. Local anesthetic combination used were also same i.e xylocaine 2% 10ml and bupivacaine 0.5% 20ml. But in this trial 60 patients were studied and supraclavicular approach of brachial plexus block was given by paraesthesia technique. Results of the study are comparable to our study.

Swami SS, Keniya VM et al(2012) compared clonidine and dexmedetomidine as adjuvants to local anesthetics in supraclavicular brachial plexus block which was a randomised double blind prospective study.<sup>14</sup> They came to a conclusion that dexmedetomidine as an adjuvant to local anesthetic enhances the duration of sensory and motor block and also the duration of analgesia compared to clonidine.

Kohli S, Kaur M et al (2013) in their study compared two doses of clonidine as an adjuvant to local anesthetic in supraclavicular brachial plexus block in 60 adult patients equally divided into two groups.<sup>15</sup> Their conclusion was that clonidine in higher dose hastens the onset, prolongs the duration of sensorimotor blockade and postoperative analgesia without significant haemodynamic changes and it also causes more sedation.

In our study clonidine in fixed dose of 150mcg produced more sedation than midazolam 5mg as adjuvants added to local anesthetics in USG guided supraclavicular brachial plexus block.

Jaiswal R, Bansal T et al (2013) studied effect of adding clonidine to ropivacaine in axillary approach of brachial plexus block.<sup>16</sup> They concluded that the group which received clonidine 150 mcg(1ml) as an adjuvant to ropivacaine 0.5% 35ml has no benefit over other group which received only ropivacaine.

Agarwal S, Aggarwal R et al (2014) compared dexmedetomidine (100mcg) which is more potent alpha 2 agonist than clonidine added to bupivacaine 0.325% 30ml in supraclavicular brachial plexus block.<sup>17</sup> This prospective randomized double blind placebo – controlled trial was conducted on 50 patients which were divided into two

groups control and the study group. The study group was the one where dexmedetomidine was added. Finally they concluded that dexmedetomidine significantly shortens the onset time and prolongs the duration of sensory and motor blocks and duration of analgesia.

### Conclusion

We conclude that the doses of clonidine 150mcg and midazolam 5mg as adjuvants to local anesthetic combination of xylocaine 2%(10ml) and bupivacaine 0.5%(20ml) in USG guided brachial plexus block for upper limb surgeries are comparable with respect to sensory motor block. Post operative analgesia was clinically more prolonged by clonidine. Sedation was also clinically more for clonidine. But statistically not significant. Both drugs are safe at these doses without any adverse effects

**Conflict of Interest:** None.

**Source of Funding:** None.

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**How to cite this article:** Patil B, Shivanand LK, Sharadhi R. A comparative study to know the effectiveness of clonidine versus midazolam as an adjuvant in ultrasound guided supraclavicular brachial plexus block, *Indian J Clin Anaesth* 2019;6(3):441-5.