

# ORIGINAL ARTICLE

## COMPARISON BETWEEN 0.5% BUPIVACAINE-DEXAMETHASONE COMBINATION & 0.5% BUPIVACAINE - CLONIDINE COMBINATION IN BRACHIAL PLEXUS BLOCKS BY SUPRACLAVICULAR APPROACH

Hari Kishore<sup>1</sup>, Rajagopal P.<sup>2</sup>, Binu Puthur Simon<sup>3</sup>, Karthika Asokan<sup>4</sup>

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**ABSTRACT: BACKGROUND:** Brachial plexus blocks, alone or in combination with general anesthesia, has become one of the most important anesthesia techniques for surgeries in the upper limb. Prolongation of analgesia using perineural catheters are not yet popular, and we are in need for an adjuvant that can prolong the action of local anesthetics after single injection peripheral nerve blocks. Dexamethasone and clonidine are two commonly used adjuvants. This study was undertaken to compare the analgesic efficacy of dexamethasone and clonidine. **MATERIALS AND METHODS:** Ninety adult patients fitting under the inclusion criteria were assigned to three groups of thirty each and received ultrasound guided supraclavicular brachial plexus block. They received either dexamethasone 8 mg (Group D) or clonidine 1mcg/kg (Group C) or saline 2 ml (Group S) with 15 ml of 0.5% bupivacaine. The onset of sensory and motor blocks, duration of analgesia and the duration of motor block were assessed. **RESULTS:** The onset of sensory and motor block were comparable in all the three groups (17.50±2.86 minutes and 30.33±4.14 minutes; 17.17±3.13 minutes and 31.0±4.8 minutes; 18.33±3.55 minutes and 31.0±5.48 minutes for groups D, C and S respectively. The duration of analgesia and motor blockade was markedly prolonged in dexamethasone group (19.41±2.60 hours and 17.19±2.13 hours) and moderately prolonged clonidine group (11.49±1.66 hours and 10.41±1.18 hours) when compared to saline group (7.56±1.65 hours and 6.22±1.43 hours). **CONCLUSION:** Dexamethasone proves to be a better adjuvant compared to clonidine, as it considerably prolongs analgesia and is devoid of significant side effects. But the prolonged motor block is still a matter of concern and the search for an adjuvant that selectively prolongs analgesia without impairing motor function continues.

**KEYWORDS:** Dexamethasone; Clonidine; Bupivacaine; Ultrasound; Supraclavicular block.

**INTRODUCTION:** Brachial plexus blocks, alone or in combination with general anesthesia, has become one of the most important anesthesia techniques for surgeries in the upper limb or shoulder. It provides excellent analgesia and muscle relaxation and considerably decrease the peri and postoperative opioid requirements.<sup>1, 2</sup> If we limit the block to a single injection, the effect begins to wane after few hours.<sup>3</sup> Methods to prolong analgesia beyond the actual duration of the local anesthetic used include either placement of perineural catheters to allow continuous infusion or co-administration of adjuvant like epinephrine, clonidine, dexamethasone, dexmedetomidine or midazolam.<sup>4, 6</sup>

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It is well established that dexamethasone provides superior analgesia when mixed with local anesthetics for peripheral nerve blocks. Similar results have also been obtained with clonidine when combined with local anesthetics like bupivacaine.

There has been many studies comparing the efficacy of these two adjuvants along with bupivacaine, but not many studies have been done comparing the efficacies of these two drugs in a single study. Hence, a study was undertaken to compare the efficacy of dexamethasone and clonidine as adjuvant to 0.5% bupivacaine in supraclavicular block. Objectives of the study were to compare the time of onset of sensorimotor block, compare total duration of analgesia and motor blockade and to report any complications when these two drugs were used as adjuvant to bupivacaine in brachial plexus block.

**MATERIALS AND METHODS:** After obtaining approval from the ethical committee of Institute, A prospective cohort study was undertaken at Amala Institute of medical sciences over a period of 2 years (Oct 1, 2012 to Oct 1, 2014) on patients posted for orthopedic surgeries on the upper limb. Sample size was fixed at 90 with 30 patients in three groups based on previous study by Islam S M et al.<sup>7</sup> Patients aged between 18 and 65, posted for orthopedic surgeries of upper limbs and willing to participate in the study were included if they belong to American Society of Anesthesiologists grade I or II. The exclusion criteria included hypersensitivity to local anesthetics, infection at the site of injection, Coagulopathy, failed or partial block and who had contraindication either to steroids or clonidine. Pregnant and lactating women were also not included in the study.

After detailed pre anesthesia checkup, patients were informed about the procedure and consent obtained. An intravenous (iv) line was secured in the non-operating hand and electrocardiogram (ECG), noninvasive blood pressure (NIBP) and oxygen saturation by pulse oximetry (SpO<sub>2</sub>) were monitored. All patients received Inj. Midazolam 0.03mg/kg iv as sedation and were given oxygen 5 liters/ minute by Hudson mask. Under aseptic precautions, the patients were given supraclavicular brachial plexus block using high frequency linear probe 6-16 MHz of Venue 40 GE healthcare® ultrasound machine.

Patients were grouped as follows:

Group C (CLONIDINE): Received 15 ml 0.5% bupivacaine +1 mcg/kg clonidine (made up to 2ml with normal saline).

GROUP D (DEXAMETHASONE): Received 15 ml 0.5% bupivacaine + 8 mg dexamethasone (2ml)

GROUP S (SALINE) Received 15 ml 0.5% bupivacaine + 2 ml normal saline.

## THE FOLLOWING PARAMETERS WERE STUDIED:

1. Onset of sensory block: Defined as the time from end of injection to onset of complete analgesia in each of the major peripheral nerve distributions (ulnar, radial, medial and musculocutaneous). Sensory block was assessed by cold stimulation method at 0, 2, 5, 10, 15, 20 and 30 minutes. Sensory block was graded according to the following scale: 0 = no block (normal sensation), 1 = partial block (decreased sensation), and 2 = complete block (no sensation).

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2. Onset of motor block: Defined as the time from end of injection to the inability of the patient to move his/her fingers and raise the hand. Motor block was measured at 0, 10, 20, 30 and 40 minutes. Motor block was graded according to the 3-point modified Bromage score.
3. Duration of analgesia: Defined as the time interval from onset of block to the time when the patients began to experience nagging, uncomfortable pain (Visual Analogue Score  $\geq 4$ ). The duration of analgesia was noted according to 0-10 visual analogue score (VAS) for pain every half an hour for the first 10 hours and then hourly till 24 hours. Rescue analgesic (Inj. Tramadol 2mg/kg intramuscularly) was given upon termination of analgesia.
4. Duration of motor block: Defined as time interval from onset of motor blockade to the time when the patients were able to lift their hand and move their fingers with normal muscle power. Motor block was assessed hourly for 24 hours in the postoperative room.
5. The patients were monitored for any drug related side effects and immediate block related complications.

All data was collected using a preformed performa and in Microsoft Excel sheet and analysed using statistical software SPSS version 16.0. Parametric tests were used for statistical analysis since study variables were normally distributed ( $p > 0.05$ ) and normality of variables were checked using Sapiro Wilks test.

Demographic data was described in terms of frequency and percentages for categorical data, and in means for continuous data. Comparison of demographic characteristics were done using the Chi – square test for categorical data and independent t- test for continuous data. The results were described as mean $\pm$  standard deviation. A p value of  $\leq 0.05$  was considered significant.

## RESULTS:

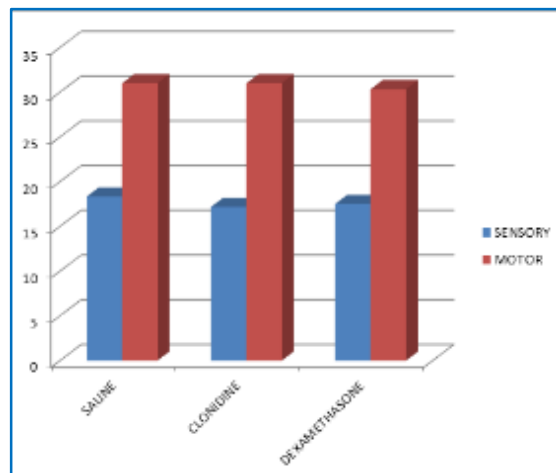
**Demographic Data:** Patients were well matched with regard to age, weight and height ( $p > 0.05$ ). The gender distribution and ASA physical status of patient population were also well matched. There was no significant change in the trend of heart rate, systolic blood pressure, diastolic blood pressure or oxygen saturation by pulse oximetry (SpO<sub>2</sub>) among both groups.

Parameters	Saline group	Clonidine group	Dexamethasone group
Age (in years)	39.32 $\pm$ 14.96	40.57 $\pm$ 15.91	39.74 $\pm$ 15.05
Sex (male/female)	18/12	18/12	19/11
Height (in cms)	165.86 $\pm$ 7.84	166.22 $\pm$ 7.02	166.87 $\pm$ 7.43
Weight (in kgs)	68.13 $\pm$ 8.82	69.74 $\pm$ 9.11	68.87 $\pm$ 7.18
Asa status (grade I/ grade II)	14/16	16/14	18/12

Table 1: Showing Demographic Variables and ASA Grading among the three Groups

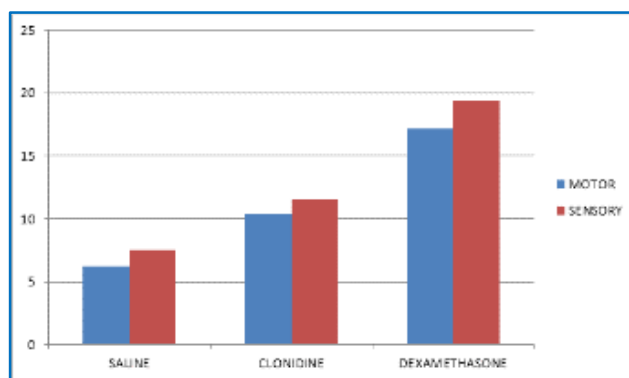
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**Onset of Sensory and Motor Blockade:** The mean onset of sensory block was  $17.50 \pm 2.86$  minutes,  $17.17 \pm 3.13$  minutes and  $18.33 \pm 3.55$  minutes in Group D, Group C and Group S respectively. Whereas, the mean onset of motor block was  $30.33 \pm 4.14$  minutes,  $31.0 \pm 4.8$  minutes and  $31.0 \pm 5.48$  minutes in Group D, Group C and Group S respectively.



**Diagram 1: Mean Onset of Sensory and Motor Blockade in all three Groups (in minutes)**

**Duration of Analgesia and Duration of Motor Blockade:** The mean duration of analgesia was  $11.49 \pm 1.66$  hours,  $19.41 \pm 2.60$  hours and  $7.56 \pm 1.65$  hours in Groups C, D and S respectively. The mean duration of motor block was  $10.41 \pm 1.18$  hours,  $17.19 \pm 2.13$  hours and  $6.22 \pm 1.43$  hours in Groups C, D and S respectively.



**Diagram 2: Mean Total Duration of Sensory And Motor Blockade In All Three Groups (In Hours)**

**COMPLICATIONS:** In two patients who received clonidine, the heart rate dropped below 50 beats per minute and they were given inj. Atropine 0.6 mg intravenously. There were no such episodes later in these patients. No complications were noted in the dexamethasone and saline groups in the perioperative period. There was also no block – related complications.

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**DISCUSSION:** Brachial plexus blocks are effective options to provide adequate intraoperative as well as postoperative analgesia. In addition, ultrasound – guided upper limb blocks has established its effectiveness and safety when compared to older techniques.<sup>8</sup> Plain bupivacaine can hardly provide analgesia beyond few hours following a peripheral nerve block,<sup>3</sup> and hence prolongation of its action may be attempted through placement of indwelling catheters to provide continuous infusion of local anaesthetic or by addition of analgesic adjuvant. Limitations of the former technique include difficulties in placement, inherent secondary failure rate, difficulties with catheter removal, or sometimes infection.<sup>9, and 10</sup>

Clonidine is used as an analgesic adjuvant for general and regional anaesthesia, and the proposed mechanism in regional anaesthesia include local vasoconstriction and C – fibre blockade. Among steroids, dexamethasone produces maximum prolongation of the effects of bupivacaine.<sup>11</sup> The proposed mechanisms of analgesic action include attenuating release of inflammatory mediators, reducing ectopic neuronal discharge and inhibiting potassium channel – mediated discharge of nociceptive C – fibres.

Since both clonidine and dexamethasone used to be combined with bupivacaine regularly in brachial plexus blocks to prolong the analgesic properties, a study was made to compare the duration of extended block with either drugs and to find out which among the two is a better agent. In the present study, we assessed 90 patients belonging to ASA physical status I and II, posted for upper limb surgery under supraclavicular block. Patients fulfilling the inclusion criteria received either dexamethasone 8 mg (2 ml) with 15 ml 0.5% bupivacaine or clonidine 1 mcg/kg (made up to 2 ml with normal saline) with 15 ml 0.5% bupivacaine or 15 ml 0.5% bupivacaine with 2 ml normal saline under ultrasound guidance (with 30 patients in each group).

Singelyn,<sup>12</sup> et al in 1996 concluded that a minimum dose of 0.5 mcg/kg of clonidine has to be added to local anesthetics to prolong its analgesic effects. Further Murphy,<sup>13</sup> et al reviewed 24 studies and concluded that doses of clonidine up to 150 mcg did not produce significant adverse effects. Hence we decided to use a dose of 1 mcg/kg of clonidine for our study.

Although Tandoc et al,<sup>14</sup> in 2011 observed equal efficacy in prolongation of analgesia and motor blockade when dexamethasone 4 mg or dexamethasone 8 mg is added to bupivacaine in brachial plexus blocks, we chose to administer 8 mg in our study as majority of the studies were done using this dosage. The dose of 8mg of dexamethasone was a routine one for intravenous injections and single dose is devoid of significant side effects. We were also aware of the fact that dexamethasone has been found to protect from bupivacaine induced neurotoxicity in vitro studies.<sup>15, 16</sup>

In our study, all three groups were comparable with respect to demographic data, gender distribution and ASA class distribution.

As clonidine is a lipophilic drug, much of it gets absorbed systemically after perineural administration, resulting in sedation. Bernard et al,<sup>17</sup> and Gaumann et al,<sup>18</sup> reported significant sedation with the use of clonidine than with plain local anaesthetic. Sedation was not specifically studied in our study as all patients were premedicated with midazolam and hence could interfere with the results.

Two patients who received clonidine as part of the study developed bradycardia (heart rate below 50 beats/minute) and were given Inj. Atropine 0.6 mg intravenously. There were no

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statistically significant hemodynamic alterations in all the three groups in our study. Several other studies had also observed stable hemodynamics while using clonidine in brachial plexus blocks.<sup>12, 19, 20, 21</sup> this was in contrast to the observations made by Bernard et al,<sup>17</sup> who observed a 30% fall in SBP with 300 mcg, 20% fall with 90 mcg and 15% fall with 30 mcg clonidine. In addition, 4 out of 14 patients in their study had episodes of hypoxemia (SpO<sub>2</sub> <90% lasting 20 seconds or more) with the highest dose of clonidine (300 mcg). Hypoxia was not seen in any of our patients since all were given supplemental oxygen.

In the present study we found that the mean time of onset of sensory and motor block were shorter when clonidine or dexamethasone was added to bupivacaine. However, statistical analysis of the onset of sensory and motor blocks among the three groups revealed that they are not statistically significant. ( $p > 0.05$ ). Hastening of onset of sensory and motor blocks were noted with clonidine,<sup>6,17,22,23</sup> as well as dexamethasone,<sup>24,26</sup> in various studies. However, Singelyn et al,<sup>12</sup> Murphy et al,<sup>13</sup> El Saied et al,<sup>27</sup> and Erlacher et al,<sup>19</sup> observed no hastening of onset of block with clonidine added to local anaesthetic, irrespective of the dosage of clonidine used.

Duration of analgesia was assessed according to the Visual Analogue Scale. The duration of analgesia was considerably prolonged in dexamethasone group (19.41±2.60 hours) and clonidine group (11.49±1.66 hours) when compared to Saline group (7.56±1.65 hours). Even though both clonidine and dexamethasone were found to prolong analgesia when compared with saline, duration of analgesia with dexamethasone was marked (almost 3 times compared to saline group). This was statistically highly significant ( $p$  value equaling 0.0001). This feature significantly contributed to decreased postoperative use of opioids and patient comfort.

In our study, we found that the motor block was also prolonged from 6.22±1.43 hours in Saline group to 10.41±1.18 hours in Clonidine group and to 17.19±2.13 hours in dexamethasone group. This was also highly significant ( $p = 0.0001$ )

We compared our results of clonidine group with previous studies. Studies done by Singelyn et al,<sup>17</sup> and review of studies done by Murphy et al,<sup>13</sup> (24 studies), McCartney et al,<sup>28</sup> (27 studies) and a meta-analysis by Popping et al,<sup>5</sup> in 2009 had also observed a significant prolongation of analgesia and muscle relaxation when clonidine was added to local anesthetics. This is in contrary to the conclusions by Erlacher et al,<sup>19</sup> Gaumann et al,<sup>18</sup> and Duma et al,<sup>20</sup> who observed no significant prolongation of analgesia with the addition of clonidine to local anesthetics.

We compared our results of dexamethasone group with a recent meta-analysis in 2014 by Choi et al.<sup>29</sup> They analysed nine randomised controlled trials (801 patients), in which 393 patients received dexamethasone (4–10 mg). They observed significantly prolonged duration of analgesia when dexamethasone was administered along with long acting local anesthetics. The extended motor blockade did create panic in some of our patients but they were properly educated and reassured about the same. This may adversely affect the routine use of dexamethasone in brachial plexus blocks in day care surgeries.

There were also no complications due to supraclavicular block as the technique was safer with ultrasound guidance. There were also no cases of sensory or motor deficits persisting beyond 24 hours. An important limitation of the study was that while we calculated the dose of clonidine depending upon the body weight, the dose of dexamethasone had no relation to body

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weight and was fixed at 8 mg. The long term follow up was not done and hence long term complications were also not studied.

In conclusion, dexamethasone proves to be a better adjuvant compared to clonidine with bupivacaine in brachial plexus blocks, in view of greater duration of analgesia and lack of any serious adverse events. However, prolonged motor block is still a matter of concern and the search for an adjuvant that selectively prolongs analgesia without impairing motor function continues.

Till then, perineural dexamethasone administration will continue to be used as a potent analgesic adjuvant, given the considerable safety profile of the drug in previous studies.

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### **AUTHORS:**

1. Hari Kishore
2. Rajagopal P.
3. Binu Puthur Simon
4. Karthika Asokan

### **PARTICULARS OF CONTRIBUTORS:**

1. Professor, Department of Anaesthesiology, Amala Institute of Medical Sciences, Thrissur, Kerala.
2. Associate Professor, Department of Anaesthesiology, Amala Institute of Medical Sciences, Thrissur, Kerala.
3. Assistant Professor, Department of Anaesthesiology, Amala Institute of Medical Sciences, Thrissur, Kerala.

4. Junior Registrar, Department of Anaesthesiology, Amala Institute of Medical Sciences, Thrissur, Kerala.

### **NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:**

Dr. Hari Kishore,  
Professor,  
Department of Anaesthesiology,  
Amala Institute of Medical Sciences,  
Thrissur, Kerala.  
E-mail: dr.hkishore@gmail.com

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