ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Comparison between Dexamethasone and Clonidine as an adjuvant to 0.5% Levobupivacaine in Supraclavicular brachial plexus block

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Submission: 11-01-2023 Revision: 03-04-2023 Publication: 01-05-2023

ABSTRACT

Background: Regional anesthesia avoids airway instrumentation, preserves conscious level and provide rapid recovery with significant postoperative analgesia. There has always been a search for adjuvants to the regional nerve block with drugs that prolong the duration of analgesia but with lesser adverse effects. The search for the ideal additive still continues, and therefore in this study, we investigated the effects of addition of dexamethasone versus clonidine to levobupivacaine for supraclavicular brachial plexus block. The primary outcome of this study was the onset and duration of sensory block, motor block, and the secondary outcome was postoperative analgesia. **Aims and Objectives:** The aim of the study was to compare the effect of dexamethasone and clonidine on onset and duration of anesthesia, when used as an adjuvant to levobupivacaine in supraclavicular brachial plexus block. **Materials and Methods:** In this prospective, double-blind, randomized controlled trial, 60 patients with American Society of Anaesthesiologists physical status I/II scheduled to undergo upper limb surgeries below shoulder were enrolled. The patients were randomly divided into two groups: Group I (n = 30): 20 mL of 0.5% isobaric levobupivacaine with 2 mL of dexamethasone. Group II (n = 30): 20 mL of 0.5% isobaric levobupivacaine and 30 mcg clonidine (diluted in normal saline, making volume of 2 mL). **Results:** Clonidine when added to levobupivacaine provide early onset of sensory and motor block but less duration of analgesia and motor blockade as compared to dexamethasone. **Conclusion:** Dexamethasone should be preferred as compared to clonidine as an adjuvant whenever longer duration of post-operative analgesia is required.

Key words: Clonidine; Dexamethasone; Supraclavicular brachial plexus block; Upper limb surgery

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v14i5.51342

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Regional anesthesia avoids airway instrumentation, preserves conscious level, and provides rapid recovery with significant postoperative analgesia.[1] Supraclavicular brachial plexus block is the commonly practiced and most consistent method for anesthesia and perioperative pain management in surgery below the shoulder joint. Pneumothorax (1–6%), hemothorax, Horner's syndrome, and phrenic nerve block are the potential complications.[2-4]

Levobupivacaine is the S (-)-enantiomer of racemic bupivacaine; it has less cardio- toxicity compared with bupivacaine, and its pharmacology and duration of anesthesia are similar to those of bupivacaine.[5] Levobupivacaine is more lipid soluble and highly protein bound resulting in more potency and longer duration of action. Dexamethasone has been selected as an adjuvant to local anesthetic in brachial plexus block as they prolong the duration of action of local anesthetics without causing respiratory depression.[6]

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Alpha-2 adrenergic receptor agonists have been the focus of interest for their sedative, analgesic, perioperative sympatholytic, and cardiovascular stabilizing effects with reduced anesthetic requirements. Furthermore, various methods of administration, such as epidural, intrathecal and peripheral injections, have been tried either alone or in combination with another drug to prolong and intensify the anaesthesia.[7-9] Since the 1980s clonidine has been used as an adjuvant to local anesthetics in various regional techniques to extend the duration of block.[10,11] One study of three different anesthetics in combination with clonidine reported mixed results.[12]

There has always been a search for adjuvants to the regional nerve block with drugs that prolong the duration of analgesia but with lesser adverse effects. The search for the ideal additive still continues, and therefore in this study, we investigated the effects of addition of dexamethasone versus clonidine to levobupivacaine for supraclavicular brachial plexus block. The primary outcome of this study was the onset and duration of sensory block, motor block, and the secondary outcome was post-operative analgesia.

Aims and objectives

The aim of the study was to compare the effect of dexamethasone and clonidine on onset and duration of anesthesia, when used as an adjuvant to levobupivacaine in supraclavicular brachial plexus block.

MATERIALS AND METHODS

In this prospective, double-blind, randomized controlled trial, 60 patients with American Society of Anesthesiologists physical status I/II scheduled to undergo upper limb surgeries below shoulder were enrolled. The patients were randomly divided into two groups using a computer-generated program. Assigned random group was enclosed in a sealed envelope to ensure concealment of allocation sequence. The anesthesiologist was not involved in the study, opened the envelope in operation theatre and prepared the drug accordingly. Group I (n=30): 20 mL of 0.5% isobaric levobupivacaine with 2 mL of dexamethasone. Group II (n=30): 20 mL of 0.5% isobaric levobupivacaine and 30 mcg clonidine (diluted in normal saline, making volume of 2 mL).

A written informed consent was obtained from each patient after explaining the technique prior to inclusion in this study in their own vernacular language. Exclusion criteria were patient's refusal, infection at the site of block, history of cardiac, respiratory, renal or hepatic failure, coagulation disorders, allergy to amide local anesthetics, neurological disorders, and pregnant women.

Technique of supraclavicular brachial plexus block

We used the classical approach to supraclavicular block using a single-injection, nerve-stimulator technique. We started the stimulation with an intensity of 2.0 mA and a pulse width of 100 μs. Once the desired response was obtained – that is a muscle twitch of the fingers that is clearly visible – we started to decrease the current gradually up to 0.6 mA. If still, we got the desired response the drug solution was injected. If the response was obtained at 0.4 mA also, then the needle was repositioned again to get response at 0.6 mA but not at 0.4 mA. If we did not get adequate response or if reposition of the needle was necessary, the needle was withdrawn and the penetration angle was adjusted in the anteroposterior plane. As a goal we aimed to elicit an isolated muscle twitch in all fingers either in flexion or extension.

Sensory and motor blocks of the median, radial, ulnar, and musculocutaneous nerves and HR, BP, and SpO_2 values were recorded 5, 10, 15, 20, 25, 30, 45, 60, 75, 90, and 120 min after the block and 30 min and 3, 6, and 12 h after the end of the surgery.

Sensory block of each nerve was assessed by a pinprick test using a 3-point scale

- 0=normal sensation
- 1=loss of sensation of pinprick (analgesia)
- 2=loss of sensation of touch (anesthesia).

Motor block was evaluated by thumb adduction (ulnar nerve), thumb abduction (radial nerve), flexion of the elbow and pronation of forearm (musculocutaneous), and thumb opposition (median nerve). Motor block evaluation was performed using a modification of the Lovett rating scale from 6 (normal muscular force) to 0 (complete paralysis).

Lovett rating scale

- 6 - Normal muscular force
- 5 - Slightly reduced muscular force
- 4 - Pronounced reduction of muscular force
- 3 - Slightly impaired mobility
- 2 - Pronounced mobility impairment
- 1 - Almost complete paralysis
- 0 - Complete paralysis.

The onset time of the sensory and motor block was defined as the time between the end of the local anesthetic injection and complete loss of sensation and complete paralysis respectively. The duration of the sensory block was considered as the time interval between complete sensory block and the return of normal sensation, and the duration of motor block was defined as the time interval between the complete paralysis and complete recovery of motor function.

The time to first analgesic use and total need for analgesics were recorded during the first postoperative 12 h. Postoperative pain levels were evaluated by a 10-cm visual analog scale from 0 (no pain) to 10 (severe pain).

Hypotension, bradycardia, hypoxemia, and nausea and vomiting occurrences were also recorded. Data were analyzed using Microsoft Excel sheet and SPSS 22 version software. Frequencies and proportions were used to represent categorical data. Chi-square was used as test of significance. Mean and standard deviation were used to represent continuous data. Independent t-test was used as test of significance. Paired t-test is the test of significance for paired data such as before and after drug. $P<0.05$ was considered statistically significant.

RESULTS

In this study, Table 1 shows distribution of patients according to their age. 32.56±10.10 years was mean age in Group 1 and in Group 2 it was 32.79±10.12 with P=0.9. Hence, both the groups were comparable in terms of age. There were more male patients than female in both the groups. There was no significant difference regarding the sex distribution between two groups.

There was no statistically significant difference in heart rate, blood pressure and SpO_2 on addition of dexamethasone and clonidine to 0.5% levobupivacaine noted (Figures 1-3).

In this study, sedation score described by University of Michigan Sedation Scale was applied for assessment of sedation (Figure 4). There was statistically significant difference between sedation scores between two groups but Group 2 patients were also arousable and maintaining O_2 saturation.

The mean time of onset of sensory blockade was 13.21 (±0.97) min in Group 1 and 8.57 (±0.43) min (mean)in Group-2 while the onset time of motor blockade was 15.55 (±0.80) in Group 1 and 12.29 (±0.45) min in Group 2 (Table 2). The mean duration of sensory blockade was 1031.96 min in Group 1 and 423.27 min in Group 2 while the duration of motor blockade was 406.06 min in Group 1 and 316.73 min in Group 2 (Table 2).

There were statistically highly significant differences ($P<0.001$) between two groups in all block characteristics.

DISCUSSION

The supraclavicular approach to brachial plexus blockade provides satisfactory anesthesia for upper limb surgery.

Table 1: Demographic characteristics

	Group 1 (Mean±SD)	Group 2 (Mean±SD)
Age (years)	32.56±10.10	32.79±10.12
Sex (Male/Female)	18/12	17/13

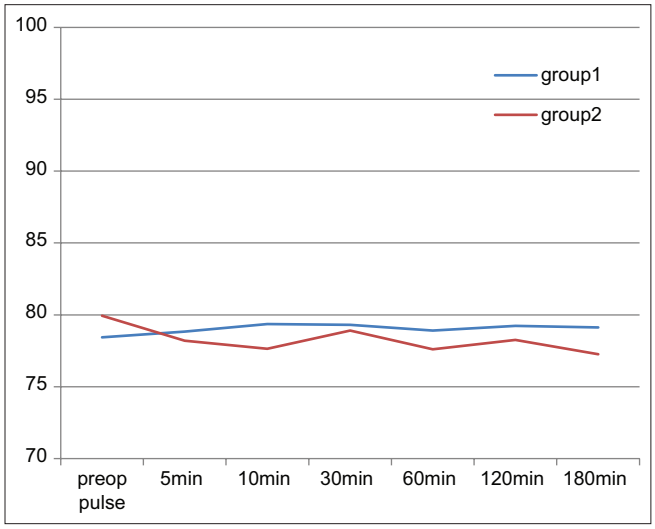

Figure 1: Comparison of change of pulse between two groups

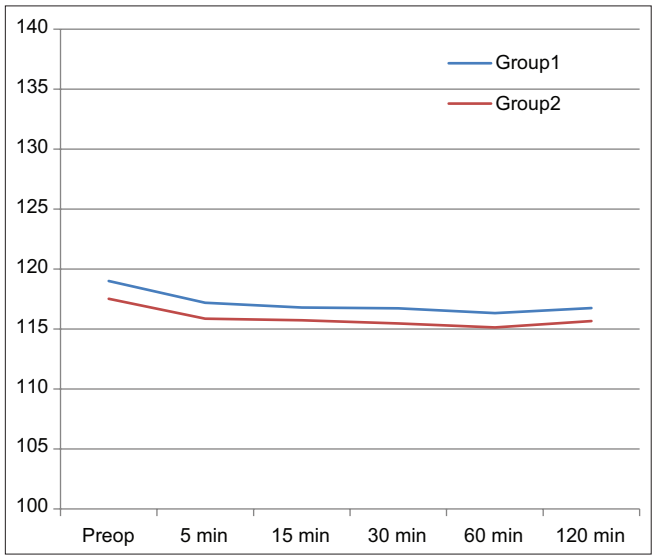

Figure 2: Comparison of systolic blood pressure (SBP) between the groups at different times

Local anesthetics are the most common agents used for this purpose but they are associated with short duration of action and thus requiring analgesic intervention in the early post-operative period. To enhance and prolong the effect of local anesthetics and reduce their side effects various drugs have been used in combination with local anesthetics. These drugs are called adjuvants. Most commonly used adjuvants are opioids. However, side effects such as pruritus, nausea and vomiting, urinary retention, and delayed respiratory depression limit their use as an adjuvant.

Table 2: Comparison of block characteristics between two groups

	Group-1 (Mean±SD)	Group-2 (Mean±SD)	P-value
Onset of sensory blockade (min)	13.21 ±0.97	8.57±0.43	<0.0001
Onset of motor blockade (min)	15.55±0.80	12.29±0.45	<0.001
Duration of sensory blockade (min)	1031.96±31.88	423.27±11.76	<0.0001
Duration of motor blockade (min)	406.06±13.99	316.73±10.03	<0.0001

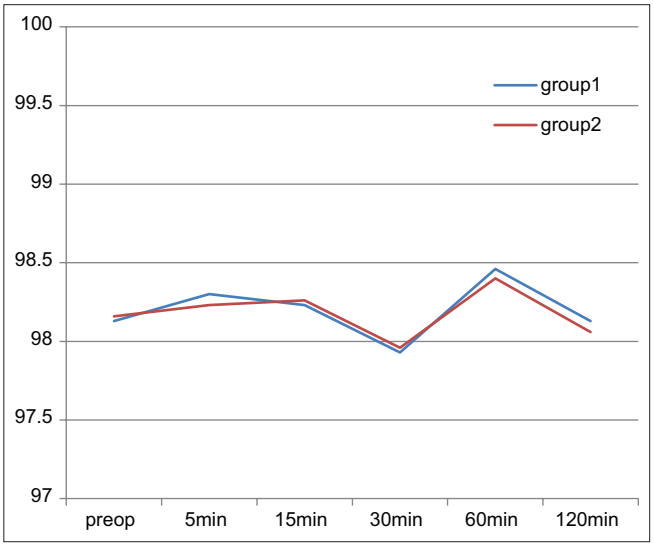

Figure 3: Comparison of SpO_2 between two groups

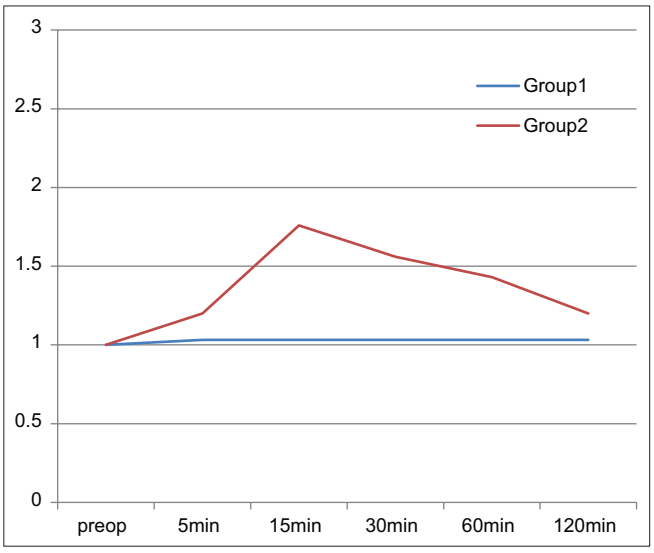

Figure 4: Comparison of sedation score between two groups

This has prompted further research toward non-opioid analgesics with lesser side effects.

In the present randomized, double-blind study, we compared the effect of adding dexamethasone or clonidine as an adjuvant to 0.5% isobaric levobupivacaine in patients undergoing upper limb surgeries under supraclavicular brachial plexus block. There was no significant difference regarding the demographic distribution between the two groups. On comparison of heart rates, systolic and diastolic blood pressure in both groups at different time intervals, there was no statistically significant difference.

In this study, we found that both dexamethasone and clonidine shortens the onset of sensory block and motor block when added to levobupivacaine for supraclavicular brachial plexus block, but clonidine is more effective in shortening the time period for onset of sensory and motor block than that of dexamethasone. This is generally consistent with the previous studies but direct comparisons are difficult because of the variety of local anesthetic mixtures used, different blocks studied and different methods of evaluating block duration.

Why dexamethasone would prolong regional anesthesia is a subject of debate. Steroids produce vasoconstriction, so they reduce local anesthetic absorption. A more attractive theory holds that dexamethasone increases the activity of inhibitory potassium channels on nociceptive C fibers, decreasing their activity.[13]

Shrestha et al.,[14] and Islam et al.,[15] observed that onset of action was 10–30 min in local anesthetic group (mean 18.15±4.25) and 10–20 min (mean 14.5±2.10) in the local anesthetic plus steroid group. They found statistically significant difference between two groups and concluded that addition of dexamethasone to local anesthetics in brachial plexus block leads to significantly faster onset and prolong duration of analgesia without any unwanted side effects. Shivinder Singh and Aggarwal[16] observed that addition of clonidine to bupivacaine resulted in faster onset of sensory block, longer duration of analgesia and motor block without any hemodynamic changes, sedation or any other adverse effects. Similar effects were demonstrated by Chakraborty et al.[17] This study signifies that both dexamethasone and clonidine prolongs the duration of analgesia and motor block when added to levobupivacaine in supraclavicular brachial plexus block, but dexamethasone is more effective in prolonging duration of analgesia and motor block than clonidine.

Various studies have shown that addition of dexamethasone and clonidine to local anesthetics effectively and significantly prolongs the duration of analgesia and duration of motor block. Holte et al.,[18] found that addition of small amounts of dexamethasone to bupivacaine incorporated

in microcapsules prolonged local analgesia compared with microcapsules with plain bupivacaine after subcutaneous administration in humans. In another study by Droger et al.,[19] it was found that incorporation of dexamethasone into bupivacaine microspheres significantly prolonged intercostal nerve block in sheep. Estebe et al.,[20] studied the effect of dexamethasone on motor brachial plexus block with bupivacaine and with bupivacaine-loaded microspheres in a sheep model and found that the incorporation of dexamethasone in bupivacaine-loaded microspheres dramatically increases the duration of action. Cummings et al.,[13] studied the effect of dexamethasone on the duration of interscalene nerve blocks with ropivacaine and bupivacaine. They found that dexamethasone prolongs analgesia from interscalene blocks using ropivacaine or bupivacaine, with the effect being stronger with ropivacaine. However, block duration was longer with plain bupivacaine (22.4 h) than ropivacaine. Thus, although dexamethasone prolonged the action of ropivacaine more than that of bupivacaine, the combined effect of dexamethasone and either drug produced nearly the same 22 h of analgesia. Tandoc et al.,[21] also found that duration of analgesia and motor block was significantly prolonged in dexamethasone group as compared to plain local anesthetic group.

Numerous studies in which clonidine was used in peripheral nerve block found that Clonidine with local anesthetics improves analgesic characteristics compared to local anesthetic alone. McCartney et al.,[22] found that a Bupivacaine and Clonidine combination prolonged postoperative analgesia compared to a Bupivacaine alone when administered for various peripheral nerve blocks. Eledjam et al.,[23] showed Clonidine is an attractive alternative to epinephrine to prolong duration of analgesia in supraclavicular brachial plexus block. Hutschala et al.,[24] found lower plasma concentration of clonidine after brachial plexus block which strongly suggested its local effect on peripheral nerves. Clonidine produces this additive effect on local anesthetics by its action on the presynaptic alpha-2 receptor complexes present on peripheral nerves. Lee and Rubin[25] found improved efficacy of caudal analgesia in children when clonidine was added to bupivacaine. Dobrydnjovetal.[26] shown the use of clonidine added to small dose of bupivacaine intrathecally increased the spread and duration of analgesia and produced an effective spinal anesthesia. A prospective, randomized, double blind, placebo controlled study was conducted by Chakraborty et al.,[17] to assess the efficacy of clonidine as an adjuvant to bupivacaine in brachial plexus block. The duration of analgesia (clonidine group 415.4±38.18 min and bupivacaine group 194.2±28.74 min) and duration of motor block (clonidine group 330.4±31.68 min and bupivacaine group 144.8±17.31 min) was longer in clonidine group. These results are comparable with this study.

Limitations of the study

Sample Size used in our study is smaller to access neurotoxicity. Follow up was not done up to longer duration to evaluate for dexamethasone induced delayed neurotoxicity if any.

CONCLUSION

This study signifies that both dexamethasone and clonidine prolongs the duration of analgesia and motor block when added to levobupivacaine in supraclavicular brachial plexus block. However, dexamethasone is more effective in prolonging duration of analgesia and motor block than clonidine.

ACKNOWLEDGMENT

We would like to thank the department of Anaesthesia, Government Medical College,Patiala for allowing us to conduct this study.

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Authors' Contributions:
RIB - Definition of intellectual content, Literature survey, Prepared first draft of manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation, and submission of article; **KR -** Concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision; **RUB -** Design of study, statistical Analysis, and interpretation.

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Source of Support: Nil, **Conflicts of Interest:** None declared.