Original Article

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Dexmedetomidine and Clonidine as an Adjuvant to Bupivacaine in Ultrasound Guided Supraclavicular Brachial Plexus Block- A Randomised Clinical Trial

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ABSTRACT

Introduction: Alpha-2 agonists are used as adjuvants with Local Anaesthetic (LA) agents to prolong the duration of regional nerve blocks.

Aim: To compare clonidine and dexmedetomidine as an adjuvant to bupivacaine in supraclavicular brachial plexus block with respect to onset and duration of sensory and motor block and duration of analgesia.

Materials and Methods: In this randomised clinical trial, 70 American Society of Anesthesiologists (ASA) class I and class II patients, scheduled for elective upper limb surgeries under ultrasound guided supraclavicular brachial plexus block, were divided into two equal groups. Group-I received clonidine 1 µg/kg and group-II received dexmedetomidine 1 µg/kg added to bupivacaine 0.5% (20 mL). Onset and recovery time of sensory and motor block, duration of analgesia were studied in both the groups. Data analysis was done using Analysis of variance (ANOVA) and Student t-test for analysis of continuous data and Chi-square test used to know the difference of significance in categorical data.

Results: A total of 70 subjects between age group of 18-60 years were included in the study. The onset of sensory blockade was faster in group-I (3.54±0.74 min) than group-II (3.86±0.88 min) but statistically not significant. The onset of motor blockade was faster in group-I (5.4±1.12 min) than group-II (6.34±1.14 min) and difference was statistically significant. Duration of sensory blockade was longer in group-I (616.23±62.05 min) than group-II (574.71±61.14 min) and motor blockade in group-I (635.86±57.82 min) was longer than group-II (562.80±66.89 min) and the differences were statistically significant. The duration of analgesia was longer in group-I (797.29±108.06 min) than group-II (695.00±91.14 min) and the difference was statistically significant.

Conclusion: Dexmedetomidine shortens the onset, prolongs the duration of sensory and motor block and also provides longer postoperative analgesia as compared with clonidine when used as an adjuvant to bupivacaine in ultrasound guided supraclavicular brachial plexus block.

Keywords: Duration of analgesia, Opioid adjuvant, Postoperative analgesia, Sensory and motor blockade

INTRODUCTION

Regional anaesthesia techniques provide important advantages over general anaesthesia by providing excellent analgesia, minimum duration of stay in postanaesthesia care unit and less side-effects. Supraclavicular approach of brachial plexus block, a useful alternative to general anaesthesia, provides the most effective anaesthesia for upper extremity surgeries and is carried out at the level of trunks of brachial plexus where it is most compact, resulting in homogenous spread of anaesthetic throughout the plexus with a fast onset and complete block. It provides excellent and ideal operating conditions by complete muscle relaxation, stable haemodynamics intraoperatively and extended postoperative analgesia. However, these early advantages can be short lived and limited by the relatively brief duration of action of LA, potentially resulting in block resolution before the period of worst postoperative pain. Increasing the volume (dose) of LA may prolong the duration of analgesia, but may also increase the risk of LA systemic toxicity. Although continuous catheter based nerve blocks can extend postoperative analgesia, their placement requires additional time, cost and skill [1].

Alpha-2 adrenergic receptor agonists have multiple actions and they provide sedation, analgesia, anxiolysis, sympatholysis and cardiovascular stabilising effects. Studies shows that addition of clonidine and dexmedetomidine to LA in peripheral nerve block fastens the onset of sensory and motor block, and prolongs the duration of analgesia [2,3]. Clonidine, an imidazoline, α-2 adrenoreceptor agonist, has been extensively studied as an adjuvant to LA in peripheral nerve blocks. Dexmedetomidine is also α-2 adrenoreceptor agonist and its selectivity to α-2 adrenoreceptor is eight times greater than clonidine and eight times more potent than clonidine [4,5]. The anaesthetic and analgesic requirements get reduced to a large extent by the use of these two adjuvants because of their analgesic properties and augmentation of LA effects [4].

Use of ultrasound in supraclavicular nerve block provides anaesthesia of the entire upper extremity in the most consistent and time efficient manner. Use of ultrasound not only avoids the injury to the nerves associated with blind paraesthesia technique but also decreases the total dose but also provides optimal tourniquet coverage [6,7]. The aim of the present study was to investigate the efficacy of dexmedetomidine as an adjuvant and to compare with that of clonidine added to LAs 0.5% bupivacaine in supraclavicular brachial plexus block. The current study was designated to evaluate the efficacy of dexmedetomidine and clonidine as an adjuvant to 0.5% bupivacaine in ultrasound guided supraclavicular brachial plexus block. The primary outcomes were onset of sensory and motor blockade, duration of sensory and motor blockade and duration of analgesia and secondary outcomes were haemodynamic parameters (Heart Rate {HR}, Mean Arterial Pressure {MAP}), complications associated with the drugs used and procedure. Ultrasound guided supraclavicular route for brachial plexus block was used in this study, as it lends itself as a safe, easy technique to perform and a small volume of solution can be delivered resulting in a rapid onset of reliable block.

MATERIALS AND METHODS

The randomised clinical trial was conducted in the Department of Anaesthesiology, Meenakshi Mission Hospital, Madurai, Tamil Nadu, India between February 2014 to December 2014, after obtaining approval from Institutional Ethical Committee bearing number MMHRC/IEC/14/O14.

Inclusion criteria: Patients belonging to age group between 18-60 years with a weight between 55-75 kg, undergoing elective upper limb surgery, with ASA class I and II were included in the study.

Exclusion criteria: Patient who refused to participate in the study, patients with history of bleeding disorders, who had local infection at the site of block, who were documented with neuromuscular disorders were excluded from the study. Also patients with respiratory compromise/post pneumonectomy cases having one functional lung and who were known allergic to LA drugs were excluded from the study.

Patients were randomised into the following groups using closed envelope method:

Group-I: Patients receiving 0.5% Bupivacaine+Dexmedetomidine (1 µg/kg)-total volume of 20 mL.

Group-II: Patients receiving 0.5% Bupivacaine+Clonidine (1 µg/kg)-total volume of 20 mL.

Sample size calculation: A power analysis of this study, using a software N master version 2.0, indicated that a sample size of 33 was sufficient to detect a significant statistical difference with alpha error of 0.05 (5%) and power (1-β)=0.8 (80%). Hence, 35 patients were recruited in each group.

Preanaesthetic evaluation was done on the evening before surgery. Subjects were put in supine position with pillow under the shoulder and head turned opposite to side of intended supraclavicular block and, arm on the same side adducted and pulled down gently to make the field more prominent.

Technique

On arrival of the patient in the operation theatre all standard ASA monitors like pulse oximetry, Electrocardiography (ECG) and Non Invasive Blood Pressure (NIBP) was connected. Baseline pulse rate, saturation and blood pressure were recorded. An intravenous (i.v.) cannula 18 to 20 gauge (G) was inserted on the non operative upper limb. Injection midazolam 0.05 mg/kg intravenous was given to relieve anxiety. The procedure was done using GE health care venue 40 ultrasound machine with 6-12 MHz linear probe by in plane approach using 22G, 50 mm needle. Ultrasound machine and probe were prepared for the procedure under all aseptic precautions. Block was performed after real time visualisation of the vessels, nerve and bone by 'in plane' approach and 20 mL LA solution was injected and the drug distribution was noted.

During the procedure and thereafter, the patient was observed vigilantly for any complications and for the toxicity of the drugs injected.

The primary objective was to check

- Onset of sensory and motor blockade by pinprick [8] and modified Bromage scale [8], respectively.
- Duration of sensory and motor blockade

Pain was assessed by pinprick by using 27G blunt end needle compared with the contralateral upper limb. Onset of sensory block was considered when there was a dull sensation to pinprick and complete sensory block was considered when there was a complete loss of sensation to pinprick. Sensory block was graded as Grade 0: Sharp pain felt, Grade 1: Analgesia, dull sensation felt, Grade 2: Anaesthesia, no sensation felt after completion of drug injection every minute till no sensation recorded.

Assessment of motor block was carried every minute till complete motor blockade. Motor block was determined according to a modified Bromage scale for upper extremities on a 3-point scale.

Grade 0: Normal motor function with full flexion and extension of elbow, wrist and fingers.

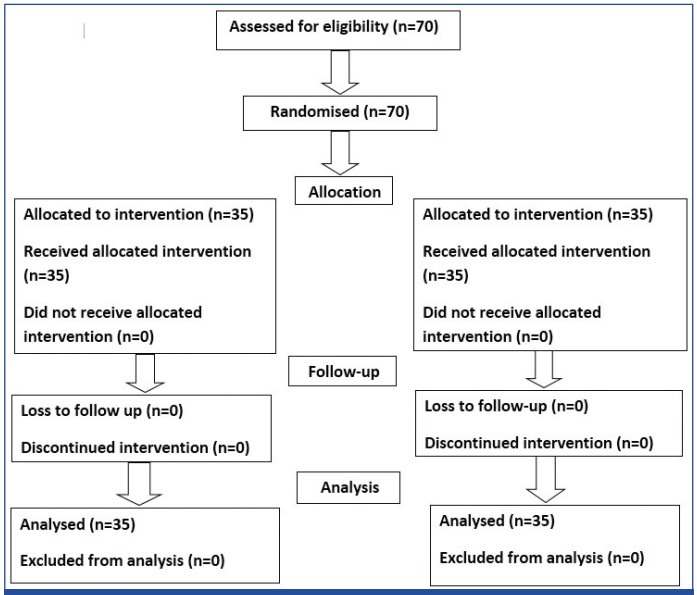
Grade 1: Decreased motor strength with ability to move the fingers only.

Grade 2: Complete motor block with inability to move the fingers.

Patient with complete block failure or sparing of any one of four nerve distributions or discomfort during surgery were managed by titrated doses of intravenous fentanyl (maximum of 2 mcg/kg). If patients continued to have pain and discomfort, general anaesthesia was administered as a backup plan. The block was considered failed if complete sensory and motor block was not achieved after 30 minutes and the failed block was converted to general anaesthesia.

Duration of sensory block (till appearance of pain requiring analgesia) and duration of motor block (till complete return of the muscle power) was recorded. Duration of analgesia was assessed by considering the time taken from the onset of sensory blockade till the request for first rescue analgesia (Visual Analog Scale (VAS) score >3). Injection paracetamol one gm was given intravenously as rescue analgesia.

The secondary objectives were heart rate, mean arterial pressure. Incidence of nausea, vomiting, Horner's syndrome, phenic nerve palsy, pneumothorax, haematoma, respiratory depression/dyspnoea, desaturation and signs and symptoms of LA toxicity, if any were looked for and noted intra and postoperatively. Patient distribution is shown in [Table/Fig-1].



[Table/Fig-1]: CONSORT flowchart.

STATISTICAL ANALYSIS

Data analysis was done using Statistical Package for the Social Sciences (SPSS) version 16.0 and SigmaStat 3.5 version. Continuous data was analysed and p-values were calculated by one-way ANOVA and student t-test. Chi-square test was used to test the significance of difference in categorical data. A p-value of <0.05 was considered significant.

RESULTS

A total of 70 subjects between age group of 18-60 years were included in the study and the mean age was 39.34±12.93 years in group-I and 37.34±13.24 years in group-II. In group-I number of males and females were 26 (74.29%) and 9 (25.71%), respectively and in group-II number of males and females were 27 (77.14%) and 8 (22.86%), respectively. Onset of sensory and motor blockade was faster and duration of sensory and motor blockade was prolonged with prolonged duration of analgesia in group-I patients [Table/Fig-2].

The baseline heart rate was comparable in both groups. Although there was significant fall in heart rate in group-I as compared to group-II at 360, 420, 480, 540 and 600 minutes, but the fall in heart rate requires no treatment [Table/Fig-3].

Variables (in minutes)	Group-I Mean±SD	Group-II Mean±SD	t-value	p-value
Onset of sensory blockade	3.54±0.74	3.86±0.88	-1.62	0.111
Onset of motor blockade	5.40±1.12	6.34±1.14	-3.50	<0.001
Duration of sensory blockade	616.23±63.05	574.71±61.14	2.82	0.006
Duration of motor blockade	635.86±57.82	562.80±66.72	-3.50	<0.001
Duration of analgesia	729.29±108.06	695±91.14	4.28	<0.001

[Table/Fig-2]: Block characteristics in minutes.
p<0.05 was considered statistically significant

Heart rate	Group-I Mean±SD	Group-II Mean±SD	t-value	p-value
Baseline	83.54±6.04	82.40±6.77	0.74	0.459
5 min	83.29±6.55	83.26±6.93	0.02	0.986
10 min	79.77±5.71	80.26±7.06	-0.32	0.753
20min	77.20±5.86	77.49±6.51	-0.19	0.847
30 min	74.20±5.72	73.34±6.36	0.59	0.555
45 min	70.89±5.22	70.89±6.26	0.00	1.000
60 min	68.06±5.73	69.46±5.29	-1.06	0.292
75 min	66.71±5.21	68.09±5.22	-1.10	0.275
90 min	66.03±3.87	67.37±4.99	-1.26	0.213
120 min	66.69±3.60	67.68±4.17	-1.07	0.287
150 min	67.34±3.55	68.00±4.39	-0.69	0.493
180 min	67.74±3.62	69.40±4.14	-1.78	0.079
210 min	68.83±3.74	70.69±4.57	-1.86	0.067
240 min	69.97±4.38	70.60±4.02	-0.63	0.534
300 min	70.34±4.04	71.80±3.89	-1.54	0.129
360 min	71.00±4.12	73.63±4.07	-2.68	0.009
420 min	72.17±4.70	74.57±4.09	-2.28	0.026
480 min	72.06±4.32	76.00±4.89	-3.57	<0.001
540 min	73.63±4.80	76.48±5.02	-2.43	0.018
600 min	73.77±4.61	77.40±4.94	-3.18	0.018

[Table/Fig-3]: Comparison of heart rate.
p<0.05 was considered statistically significant

The mean arterial pressure was comparable in both groups. Although there was significant fall in blood pressure in group-I as compared to group-II at 60, 75, 90, 120, 150, 180, 210, 240, 300, 360, 420, 480, 540 minutes [Table/Fig-4].

MAP	Group-I Mean±SD	Group-II Mean±SD	t-value	p-value
Baseline	92.14±9.97	91.54±8.85	0.26	0.791
5 min	91.57±9.96	90.54±8.36	0.47	0.641
10 min	89.31±11.20	89.09±8.06	0.10	0.922
20 min	87.91±11.49	87.89±8.06	0.01	0.990
30 min	85.03±11.68	86.97±8.24	-0.80	0.424
45 min	82.51±11.14	85.74±8.04	-1.39	0.169
60 min	79.60±11.29	84.37±7.91	-2.05	0.044
75 min	76.03±11.02	83.20±7.94	-3.12	0.003
90 min	75.17±10.49	82.40±8.21	-3.21	0.002
120 min	74.71±9.27	81.48±8.54	-3.18	0.002
150 min	74.77±11.25	81.26±8.70	-2.70	0.009
180 min	74.74±9.81	81.23±8.44	-2.97	0.004
210 min	76.31±9.45	81.48±8.43	-2.41	0.018
240 min	76.74±9.72	82.86±8.43	-2.81	0.006
300 min	77.80±9.93	84.14±8.75	-2.83	0.006
360 min	77.63±9.22	85.11±8.92	-3.45	<0.001
420 min	79.68±8.51	85.77±8.43	-3.01	0.004
480 min	81.09±10.31	87.31±8.02	-2.82	0.006
540 min	83.57±9.48	88.34±8.11	-2.26	0.027
600 min	92.31±9.89	89.94±7.97	1.11	0.273

[Table/Fig-4]: Comparison of mean arterial pressure.
MAP: Mean arterial pressure; p<0.05 was considered statistically significant

In group-I, two patients had fall in systolic Blood Pressure (BP) (>30% from baseline or MAP <60 mm Hg) and four patients had bradycardia (HR <60 Beats Per Minute {bpm}) which required no treatment apart from i.v. fluids. There were no complications noted in group-II. No procedure related complications were noted and none of the patients had failed block in either group. The VAS scores were comparable in both the groups and rescue analgesia was not required intraoperatively. Rescue analgesia used in both the groups after eight hours of beginning of the surgery.

DISCUSSION

The brachial plexus block consists of injecting LA drugs in the fascial spaces surrounding the brachial nerve plexus. It is a simple, safe and effective technique of anaesthesia having distinct advantages over general and i.v. regional anaesthesia. This study compared the efficacy and complications of recently introduced adjuvants, alpha-2 agonists i.e., Dexmedetomidine one µgm/kg (Group-I) and Clonidine 1 µgm/kg (Group-II), added to 0.5% bupivacaine with a total volume of 20 mL in ultrasound guided supraclavicular approach of brachial plexus block for upper limb surgeries. Dexmedetomidine showed faster onset of sensory and motor blockade, prolonged duration of action with longer duration of analgesia.

Onset of blockade: In this study, the onset of sensory and motor blockade was faster in dexmedetomidine group than clonidine group but the difference was statistically significant only for onset of motor blockade. A randomised study done by Swami S et al., reported that the onset of sensory and motor block was shorter with dexmedetomidine (1 µg/kg) group than clonidine (1 µg/kg) group [9]. The earlier onset of sensory and motor blockade (by about 1-2.5 min) in the index study may be attributed to the higher volume (35 mL) of LA drug used. Onset of sensory block was faster with dexmedetomidine and the difference was not statistically significant, similar to the index study. The onset of motor block was significantly faster with clonidine, contrary to the index study. These differences may be related to variations in rate and extent of penetration of injected anaesthetic solutions through neurons and the method used to administer the anaesthetic agents (nerve stimulator versus ultrasound).

Duration of blockade: In this study, duration of sensory and motor blockade was longer with dexmedetomidine and the differences were statistically significant. These results were similar to the study done by Swami S et al., Kirubahar R et al., conducted a study in 60 ASA I/II patients aged between 20-50 years undergoing upper limb orthopaedic procedures were selected and divided into two groups of 30 each [9,10]. Both the groups received 35 mL of 0.375%. Bupivacaine with addition of adjuvants, clonidine two µg/kg and dexmedetomidine two µg/kg in different groups. The addition of dexmedetomidine to bupivacaine during supraclavicular brachial plexus block produces a shorter onset of time to sensory and motor block with prolonged duration of analgesia when compared to clonidine added to bupivacaine.

Pathak DG and Phatowali M, conducted a study in 80 patients undergoing elective upper limb surgeries with ropivacine 0.5% (31 mL) and ropivacaine and dexmedetomidine one mcg/kg (31 mL) and concluded that dexmedetomidine significantly shortens the onset time and prolongs the duration of sensory and motor blocks, with longer duration of postoperative analgesia, with associated significant sedation and a few manageable side-effects like bradycardia and hypotension [11].

Duration of analgesia: In this study, the duration of analgesia was longer with dexmedetomidine and the difference was statistically

significant. Similarly, in the study done by Swami S et al., there was significant increase in duration of analgesia in dexmedetomidine group [9]. Lalwani J et al., conducted a study on 64 patients who underwent upper limb surgery under brachial plexus block [12]. Patients received either bupivacaine or bupivacaine with dexmedetomidine and were randomly divided into two groups. Addition of dexmedetomidine to bupivacaine was associated with prolonged analgesia, prolonged sensory and motor blockades with mild sedation. Chakraborty S et al., found that addition of 30 µg clonidine to 25 mL of 0.5% bupivacaine compared with 25 mL of 0.5% bupivacaine alone significantly prolonged the duration of analgesia without producing any clinically important adverse reactions other than sedation in clonidine group [3]. Similarly in this study, there was longer duration of analgesia with one µg/kg of clonidine added to bupivacaine compared with bupivacaine alone. Longer duration of analgesia was because of higher dose of clonidine and usage of ultrasound. Mahmoud K and Ammar A, conducted a prospective randomised controlled trial and concluded that addition of dexmedetomidine to bupivacaine hastens the onset of sensory and motor blockade, prolongs duration of analgesia, increases duration of sensory and motor blockade [13].

Side-effects: Two patients in group-I had hypotension (MAP <60 mm Hg) and none in group-II. But this hypotension required closed monitoring apart from i.v. fluids and the effect was transient. Four patients in group-II and two patients in group-II had bradycardia (HR <60 bpm/min), however, bradycardia was transient, not less than 55 bpm/ min & responded well to awakening the patient and required no treatment apart from closed monitoring. All patients were stable and there were no other side effects like nausea, vomiting or respiratory depression.

Chakraborty S et al., also did not report any clinically important adverse reactions other than sedation [3]. Agarwal S et al., conducted a prospective, randomised trial in 50 patients and noted bradycardia in one patient in dexmedetomidine group, which responded to injection atropine [14]. Lalwani J et al., conducted a study in 64 patients and noted slightly higher Ramsay sedation score in dexmedetomidine group as compared to group without adjuvant [12]. The side-effects were found to be insignificant and incidental. Only two cases of bradycardia (6.25%) and one case (3.12%) of hypotension were noticed in dexmedetomidine group and concluded that addition of dexmedetomidine to bupivacaine was associated with prolonged analgesia, prolonged sensory and motor blockades with mild sedation. Esmaoglu A et al., conducted a study in 60 patients and found bradycardia in seven patients of dexmedetomidine group [15].

Limitation(s)

The limitation of the study is equipotent doses of dexmedetomidine and clonidine were not used as there were no enough studies to determine them. There is also need for larger studies, using different concentrations of both drugs to find equipotent doses of dexmedetomidine and clonidine in supraclavicular block.

CONCLUSION(S)

The use of dexmedetomidine shortens the onset, prolongs the duration of sensory and motor block and also provides longer postoperative analgesia as compared with clonidine, when used as an adjuvant to bupivacaine in ultrasound guided supraclavicular brachial plexus block. Though dexmedetomidine was superior to clonidine, its use as adjuvant resulted in decrease in heart rate and mean arterial pressure more than that caused by clonidine, though without significant clinical impact.

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