

Study of Dexmedetomidine as an Adjuvant to Bupivacaine-Lignocaine with Adrenaline in Supraclavicular Brachial Plexusblock

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Abstract

Supraclavicular brachial plexus block is a very popular mode of anesthesia for various upper limb surgeries, as it is easiest and most effective and has good post-operative analgesia. It is carried out at the level of trunks *i.e.* at the middle of brachial plexus, resulting in homogenous spread of anesthetic agent throughout the plexus with a fast onset and complete block action.⁹ Dexmedetomidine, is potent, highly selective α_2 -adrenoceptor agonist, has been used as an adjuvant during regional and local anesthesia because of rapid onset of action and relatively short half-life up to 2 hours.

Objective of Study: To compare the effects of addition of Dexmedetomidine to Bupivacaine-Lignocaine with Adrenaline combination for Supraclavicular brachial plexus block with regards to onset and duration of sensory block, motor block. Quality of anesthesia, analgesia and Adverse reactions if any after taking written informed consent.

Observations: Onset of sensory as well as motor blockade in Dexmedetomidine group was earlier when compared to plain bupivacaine-lignocaine adrenalin group. The duration of sensory and motor blockade was significantly increased ($p < 0.05$) in Dexmedetomidine group when compared to another group.

With respect to hemodynamic parameters Dexmedetomidine group provided a higher Degree of cardiovascular stability with a lesser incidence of hypotension.

Result: There is earlier onset of action and longer duration of sensory; Motor block and Duration of analgesia (sensory block) was prolonged in dexmedetomidine group. Hence it is

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advisable to add dexmedetomidine as an adjuvant to local anesthetic combinations during supraclavicular block for prolonged anesthesia and to provide better analgesia

Keywords: 0.5% Bupivacaine; 2% lignocaine with adrenaline; Dexmedetomidine; Peripheral nerve stimulator (stimuplex DIG RC); Sensory and motor blockade.

INTRODUCTION

Pain is “an unpleasant sensory or emotional experience associated with actual or potential tissue damage mainly during surgery and post-operative period. Regional anesthesia denotes interruption of pain impulse by physiological blockade at a certain point along with their pathway of transmission in peripheral nerves.

Regional anesthetic techniques have specific advantages both for anesthesia and surgery and it is also useful as analgesic supplements for intra-operative and post-operative period. Regional anesthesia serves an important role in facilitating ambulation by reducing immediate post-operative pain.¹⁰ Uncontrolled pain, nausea and vomiting are common causes for delayed discharge and unanticipated hospital admission.^{11,12}

Supraclavicular Brachialplexus blockade is a time tested technique for upper limb surgeries due to its effectiveness in terms of cost and performance, margin of safety and good post-operative analgesia.¹ The plexus is blocked where it is most compact⁸ i.e. at the middle of brachial plexus, resulting in homogenous spread of anesthetic agent throughout the plexus with a fast onset and complete block action.⁹

An adjuvant is a pharmacological agent that modifies the effect of other agents. Numerous perineural adjuvants have been used with local anesthetics in regional anesthesia in an attempt to optimize block characteristics and improve clinical outcomes.^{13,14} Dexmedetomidine is a selective α_2 -adrenoceptor agonist, Compared with clonidine, dexmedetomidine is about eight times more specific for alpha 2-adrenoreceptors with an $\alpha_2:\alpha_1$ selectivity ratio of 1600:1. These unique properties of dexmedetomidine make it an full agonist agent with sedative and anxiolytic effects.¹¹⁻¹³ The elimination half-life of dexmedetomidine is approximately 2 hours with a rapid distribution half-life being approximately 6 min. It has a rapid onset of action. It undergoes biotransformation in the liver, and the kidney excretes 95% of its metabolites.^{26,27,28}

Duration and quality of motor and sensory blockade is dose dependant.¹ But increasing the doses of this hyperbaric Bupivacaine leads to increased incidences of hypotension, bradycardia and in some cases, respiratory difficulty and cardio-respiratory arrest. In cases of inadvertent intravascular injection of Bupivacaine, it was often fatal and responded poorly to conventional resuscitation methods.^{21,22}

The duration of action of a local anesthetic is proportional to the time the drug is in contact with nerve fibres.¹⁵ For this reason, epinephrine (1:200,000 or 5 $\mu\text{g}/\text{mL}$) is added to local anesthetic solutions to produce vasoconstriction, which limits systemic absorption and maintains the drug concentration in the vicinity of the nerve fibres to be anesthetized. Thus, decreasing the possibility of systemic toxicity.¹⁷ It is necessary to maintain doses of local anesthetic less and the same time increase duration and quality of anesthesia.

AIMS AND OBJECTIVE

To compare the effects of addition of Dexmedetomidine to Bupivacaine-Lignocaine with adrenaline combination for Supraclavicular brachial plexus block. The effects will be studied in terms of:

1. Onset of sensory and motor blockade
2. Duration of sensory and motor blockade
3. Hemodynamic effect
4. Quality of anesthesia
5. Vas score
6. Complications/side-effects if any

MATERIALS AND METHODS

Prospective, randomized, clinical study designed to evaluate and compare the effects of addition of Dexmedetomidine to Bupivacaine-Lignocaine with adrenaline combination for Supraclavicular brachial plexus block was conducted on 80 patients undergoing elective upper limb surgery.

Inclusion Criteria: All patients of ASA **grade I and II**, undergoing elective surgeries.

Exclusion Criteria: Patients having deformities and infection at the site of block.

Patients having bleeding disorders/coagulation abnormalities/raised intra cranial pressure.

Patients who fail to achieve desired sensory and motor blockade were excluded from the study.

The study protocol was approved by Hospital Ethics committee and Ethical Clearance was obtained from the institution for the study. Written informed consent was obtained. Pre-operative preparation and optimization of the patients were done as per protocol.

A prospective randomized comparative study was carried out in eighty patients of either sex

(18-60 yrs) allocated in one of two parallel groups containing 40 patients each.

Group I: Patients receiving 0.5% bupivacaine (15ml) + 2% lignocaine with Adrenaline (15ml) + normal saline (0.5ml).

Group II: Patients receiving 0.5% bupivacaine (15ml) +2% lignocaine with Adrenaline (15ml) + Dexmedetomidine (0.5ml).

0.5% bupivacaine, 2% lignocaine with adrenaline, dexmedetomidine, peripheral nerve stimulator (stimuplex DIG RC) were used in the study.

Pre-operative Preparation: Patients who are fulfilling all inclusion and exclusion criteria were explained about the study and were invited to participate in the study. All the patients underwent through pre-anesthetic evaluation on the day prior to surgery. A careful history and a thorough general and systemic examination were carried out including airway and the surface anatomy where the block was going to be given, and the procedure to be carried out was explained. They were informed about development of paresthesia and the motor twitch produced by nerve stimulator and vas score. Patients were reassured to alleviate their anxieties. They were investigated for routine blood and ECG, X-ray, chest. All Patients were kept nil per oral as per the fasting guidelines. All of them received Tab. Alprazolam 0.5 mg and Tab. Ranitidine 150 mg night before the surgery. Written informed consent taken. Operation theatre was prepared with routine equipment's as well as for emergency resuscitation in case of failed block or toxic reactions occurring during the procedure.

After shifting the patient to operation theatre, IV access was obtained on the forearm with 18 Gauge IV canula and IV infusion started with Ringer Lactate. Patients were monitored for heart rate (HR), non-invasive blood pressure (NIBP), percentage oxygen saturation (SpO₂). Patients were premedicated with Inj. Glycopyrrolate 0.004mg/kg IV, Inj. Ranitidine 1 mg/kg IV, Inj. Ondansetron 0.08 mg/kg IV and Inj. Fentanyl 2 µg/kg IV.

Patient was made to lie supine with head turned opposite to side of intended block and arm adducted & pulled down gently. A small pillow or folded sheet was placed below the shoulder to make the anatomical landmarks more prominent like 1 cm above the midpoint of clavicle and pulsations of subclavian artery palpable in supraclavicular fossa.

Skin wheal is raised using 1ml of 2% lignocaine solution subcutaneously. The tip of index finger was rested in supraclavicular fossa directly over the arterial pulsation. A 22 gauge, 50mm (stimuplex,

B Braun) needle attached to peripheral nerve stimulator was held in right hand and patient was instructed not to move as soon as he felt a "tingle" or "electric shock like sensation" going down his arm. The needle was inserted through skin and advanced slowly downward (caudal) rolled slightly inward (medially) and slightly backward (posteriorly). A nerve stimulator was used to locate the brachial plexus. The location endpoint was a distal motor response, i.e. the movement of the fingers and the thumb with an output current of 0.5 mA. During injection of the drug solution, negative aspiration done every 5 ml to avoid intravascular injection. Plexus block considered successful when at least two out of the four nerve territories (ulnar, radial, median, and musculocutaneous) effectively blocked for both sensory and motor block.

Sensory block (four nerve territories) assessed by pin prick test using a 3-point scale: 0=normal sensation, 1=loss of sensation of pin prick (analgesia), and 2=loss of sensation of touch (anesthesia).

Motor block determined by thumb abduction (radial nerve), thumb adduction (ulnar nerve), thumb opposition (median nerve), and flexion of elbow (Musculocutaneous nerve) according to the modified Bromage scale (18 scale) on a 3 points:

- **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 finger.

Both sensory and motor blocks assessed at 2, 5 minutes, then every 5 min for first 30 minutes and then at 45, 60, 90, and 120 min; and then hourly till the end of surgery even after the completion of surgery, until they had resolved.

Assessment of complete recovery of both sensory and motor blockade will be done for at least 12 hrs. post-operatively.

The time taken for the procedure, the onset of sensory blockade & motor blockade was noted. Intra-operatively, hemodynamic were monitored at regular intervals. Following completion of surgery, the patients were monitored to assess the quality and duration of post-operative analgesia. Thus, the patients were asked to classify analgesia as no pain, mild pain, moderate pain or severe pain every hour for the first 6 hours and then again at 8, 10 & 12 hrs. At the time of each subsequent assessment, patients were observed and/or questioned about any

subjective and/or objective side effects (sedation, nausea, vomiting or respiratory depression, neurological injury).

Defenitions of Parameters



Fig. 1: Brachial plexus block with the help of nerve stimulator.

- *Onset of sensory blockade:* defined as interval between the time of injection of test drug to reduction of pain at the site of surgery or loss of sensation to cold at the site of surgery.
- *Onset of motor blockade:* defined as interval between time of injection of drug to development of motor weakness in the blocked limb.
- *Duration of analgesia:* defined as interval between onset of analgesia/sensory blockade to the time patient first complains of pain at wound site.
- *Duration of motor blockade:* defined as the interval between the onset of motor blockade to the time patient first experiences movement of the blocked limb.
- *Failure of block:* it is defined as inadequate or patchy analgesia even after 30 mins of the drug administration. Depending on the effectiveness of the block the patient was being administered sedative & analgesic in the form of IV midazolam & Injection Fentanyl. Incase of complete failure general anesthesia was administered.
- *Totally effective:* when the procedure is completed without the need of supplementation/analgesia.
- *Partially effective:* when there is need of supplementary analgesia. We administered injection fentanyl 1µg/kg.

STATISTICAL ANALYSIS

Results were statistically analyzed using association among study and control group with the chi-square and fisher exact test. Non-parametric values were analyzed using student t-test Qualitative data is presented with the help of frequency and percentage table. Quantitative data is presented with the help of Mean, Standard deviation, Median and IQR. p value less than 0.05 is taken as significant level.

OBSERVATION AND RESULTS

The prospective, randomized, comparative study was conducted on 80 patients aged between 18-60 years posted for upper limb surgeries. Patients are divided into two group to compare the effects of addition of Dexmedetomidine to Bupivacaine-Lignocaine with Adrenaline combination for Supraclavicular brachial plexus block in terms of onset & duration of sensory & motor blockade respectively, quality of block, hemodynamic changes & complications.

Group I: Patients receiving 0.5% bupivacaine (15ml) + 2% lignocaine with Adrenaline (15ml) + normal saline (0.5ml).

Group II: Patients receiving 0.5% bupivacaine (15ml) +2% lignocaine with Adrenaline (15ml) + Dexmedetomidine (0.5ml)

There were no clinical or statistically significant differences in the demographic profile of patients in either group. The average age was 36.93 ±10.413 yrs in group I, and 37.70±13.591 yrs in group II.

The average weights of the patients were 71.23±2.465 kgs in group I and 71.15 ±2.348 in group II respectively. There was no significant difference in age and weight between the two group with p > 0.05 which was statistically not significant.

Table 1: Comparison of age and weight distribution between the two groups

	Group	Group I	Group II	P Value
Age	Mean	36.93	37.70	0.775
	SD	10.413	13.591	
Weight	Mean	71.23	71.15	0.890
	SD	2.465	2.348	

Gender Distribution

Table 2: Gender distribution in two groups

-		Group I	Group II	P-Value
Sex	Male	22	26	0.361
	Female	18	14	

Both the study groups are comparable in terms of gender as shown in the table.

Onset of Motor blockade

Table 4: Onset of sensory block in the two groups

-	Group	Group I	Group II	P Value
Onset of sensory blockade (min)	Mean	13.05	9.03	0.000
	SD	1.260	0.920	

Onset of Sensory blockade.

The mean time of onset of sensory blockade in **Group I** was 13.05 ± 1.260 mi. In **Group II** it was 9.03 ± 0.920 min. There is significantly delayed onset of sensory blockade in group I which is statistically significant.

Duration of Sensory blockade

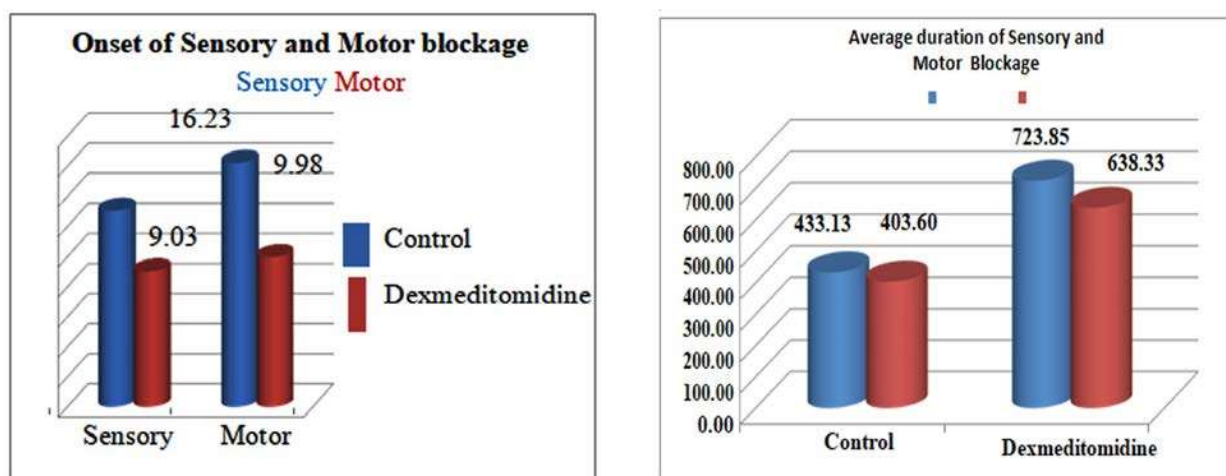


Fig. 2: BAR Diagram of Onset of sensory and motor block in Dexmedetomidine and control groups

Table 5: Duration of sensory blockade in the two groups

Group	Group I	Group II	P Value
Mean (min)	433.13	723.85	0.000
SD	16.396	11.021	

In **group, I** the mean duration of sensory blockade was 433.13 ± 16.396 min and in **group II** 723.85 ± 11.021 min. The duration of sensory blockade was shorter in **group I** when compared to **group II** and was statistically significant.

Duration of motor blockade**Table 6:** Duration of motor blockade in the two groups

Group	Group I	Group II	P Value
Mean (min)	403.60	638.33	0.000
SD	15.979	13.327	

In **group I** the mean duration of motor blockade was 403.60±15.979 min where as in **group II** it was 638.33±13.327 min. The duration of motor blockade was shorter in **group I** when compared to **group II** & it was statistically significant

Haemodynamic Parameters**Table 7:** Pulse Rate /Systolic BP /Diastolic BP in the two groups

Time	-	Pulse Rate	-	-	Systolic BP	-	-	Diastolic BP	-
Basal	82.28 ± 9.218	81.03± 9.088	0.543	130.73 ± 11.916	130.15 ± 11.939	0.83	84.08 ± 7.043	83.08 ± 7.276	0.534
2 min	85.98 ± 8.853	82.53± 8.048	0.072	131.40 ± 11.743	130.08 ± 10.166	0.591	84.33 ± 6.833	82.93 ± 6.203	0.34
5 min	88.38 ± 8.860	80.10 ± 7.675	0	131.50 ± 10.715	127.30 ± 9.704	0.07	83.95 ± 6.790	81.10 ± 5.982	0.05
10 min	88.10 ± 7.899	78.43 ± 7.510	0	130.53 ± 10.175	124.15 ± 9.119	0.004	82.30 ± 6.446	78.08 ± 5.269	0.002
15 min	85.70 ± 7.978	76.68 ± 7.195	0	127.85 ± 10.88	121.50 ± 8.555	0.005	80.55 ± 6.950	76.28 ± 5.472	0.003
20 min	83.08 ± 7.188	74.90 ± 6.964	0	126.65 ± 10.561	119.68 ± 8.574	0.002	78.88 ± 7.809	74.53 ± 5.139	0.004
25 min	80.13 ± 6.940	73.45 ± 6.935	0	126.03 ± 10.299	117.30 ± 8.456	0	78.53 ± 7.500	72.75 ± 4.824	0
30 min	77.53 ± 7.016	71.65 ± 6.530	0	125.90 ± 11.043	115.13 ± 8.668	0	77.95 ± 8.025	70.98 ± 5.423	0
45 min	75.50 ± 6.965	70.18 ± 6.234	0.001	125.50 ± 11.200	113.18 ± 8.348	0	78.33 ± 8.194	69.33 ± 4.96	0
60 min	74.58 ± 6.621	69.18 ± 6.365	0	126.35 ± 9.875	112.50 ± 7.978	0	78.73 ± 7.977	68.83 ± 5.017	0
90 min	72.43 ± 5.505	68.13 ± 6.035	0.001	127.10 ± 10.553	113.28 ± 6.691	0	78.63 ± 7.645	69.33 ± 3.938	0
120 min	73.03 ± 4.902	67.38 ± 5.405	0	127.38 ± 10.567	112.90 ± 6.234	0	79.85 ± 6.904	70.05 ± 3.063	0

Pulse Rate (Beats Per Min)/Systolic BP /Diastolic BP

Mean pulse rate decreases in both groups after 5 minutes, but decreases significantly in **group II** than **group I**. Respiratory rate in both groups are similar, there is no respiratory depression in both groups.

Mean systolic BP decreases in **group I** and **II**. After 20 minutes, there was statistically significant decrease in BP in **group II** compared to **Group I**.

Mean Diastolic BP decreases in **group I** and **II**. After 10 minutes, there was statistically significant decrease in mean diastolic BP in **group II** compared to **Group I**.

Table 8: Mean Respiratory rates in Dexmedetomidine and control groups

-	Group I	Group II	P value
Basal	12.58 ± 1.083	12.53 ± 1.086	.837

2 min	12.58 ± 1.083	12.58 ± 1.086	.837
5 min	12.60 ± 1.081	12.55 ± 1.085	.837
10 min	12.58 ± 1.130	12.53 ± 1.109	.842
15 min	12.13 ± 1.090	12.30 ± 1.114	.480
20 min	11.73 ± 1.062	12.00 ± 1.109	.261
25 min	11.55 ± 1.061	11.85 ± 1.075	.213
30 min	11.50 ± 1.038	11.68 ± 1.023	.450
45 min	11.45 ± 1.011	11.50 ± 1.038	.828
60 min	11.58 ± 1.130	11.58 ± 1.035	1.000
90 min	11.98 ± 0.947	11.63 ± 1.079	.127
120 min	11.90 ± 0.900	11.75 ± 1.104	.507

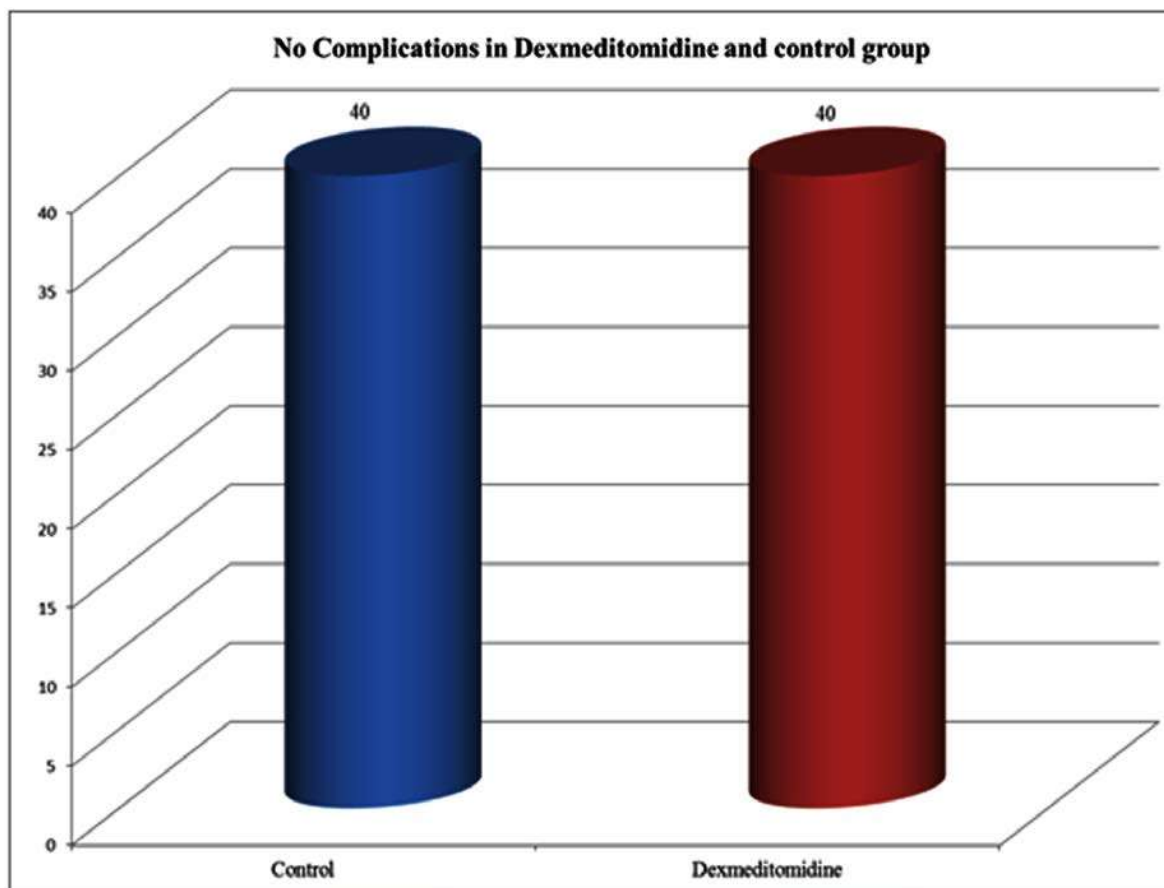


Fig. 3: Respiratory rate in both groups are similar, there is no respiratory depression in both groups

Mean Respiratory Rate (RR) in two Groups

COMPLICATIONS

Group I and II patients were observed for intra-operative and post-operative complications which include pain, nausea/vomiting, respiratory changes, SPO₂ less than 90%, hypotension, bradycardia. There is no significance difference, and no any complication in both groups.

DISCUSSION

Peripheral nerve blocks are cost effective anesthetic techniques used to provide good quality anesthesia and analgesia while avoiding airway instrumentation and hemodynamic consequences of general anesthesia. Patient satisfaction, a growing demand for cost effective anesthesia and a favourable post-operative recovery profile have resulted in increased popularity for regional techniques.

Brachia I plexus block is widely used in our practice for elective forearm and hand surgeries. It provides good intra-operative and post-operative analgesia. Various approaches like supraclavicular, interscalene, infraclavicular and axillary have been used for blocking the brachial plexus. Supraclavicular approach has rapid onset of action as compared to others.^{1,2,3,8}

Evolution of Supraclavicular Brachial Plexus Block²⁴

In 1911-1912, Kulenkampff described the first percutaneous supraclavicular approach.

He pointed out that above the clavicle the plexus lies under the skin as it passes over the first rib and accessible to a percutaneous technique. The midpoint of clavicle and the subclavian artery provided a constant landmark, most frequently at the point where external jugular vein intersects the clavicle.

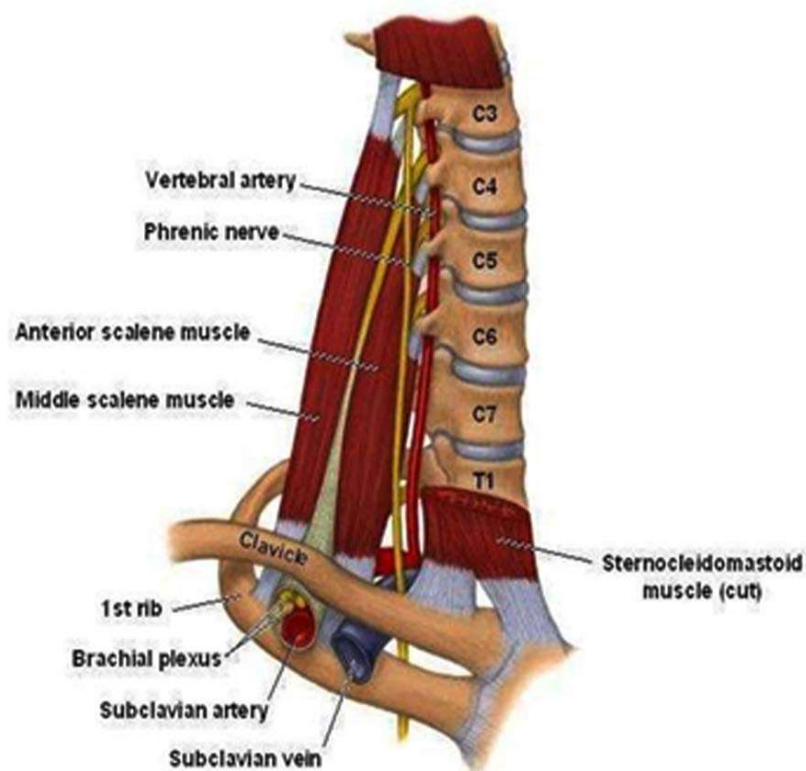


Fig. 4: Relations of brachial plexus

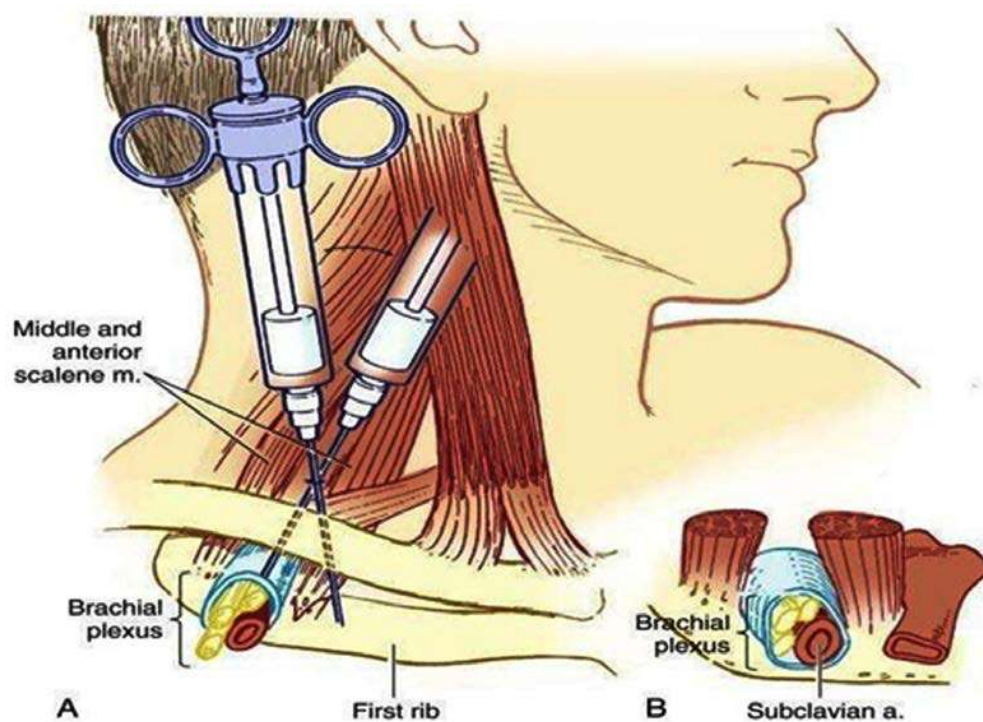


Fig. 5: Arrangement of nerve trunks in relation to landmarks used

In its passage from the cervical transverse processes to the first rib, the plexus is "sandwiched" between the anterior and middle scalene muscles and invested in the fascia of those two muscles. As the plexus cross the first rib, the three trunks are 'stacked' one on top of the other vertically. This block is usually given after eliciting paresthesia and muscle twitch with peripheral nerve stimulator.^{4,6} Paresthesia elicited serve two purposes.^{24,25} (1) It indicates that the point of the needle is in contact with the nerve to be blocked *i.e.* an optimal position for injection of local anesthetic. (2) It also serves as a warning, indicating a risk for nerve injury.

Many substances have been added to local anesthetic agents in an attempt to prolong their duration of action. Among them addition of Dexmedetomidine is α_2 receptor agonist and its α_2/α_1 selectivity is 8 times more than clonidine. Presynaptic activation of α_2 adrenoceptor in central nervous system (CNS) inhibits the release of norepinephrine, terminating the propagation of pain signals and their post synaptic activation inhibits sympathetic activity, thereby decreasing HR and BP. High selectivity for α_2 receptors mediates analgesia, sedation, and anxiolysis.

We have investigated the effect of adding dexmedetomidine 9 to bupivacaine-lignocaine adrenalin for supraclavicular brachial plexus block, our primary end point was to find out the onset time and duration of motor and sensory blocks, hemodynamic stability and post-operative analgesia.¹¹⁻¹³ We conducted studies on eighty patients with demographic data in terms of age, weight and sex being similar in both the groups. The data collected was analyzed for statistical significance by student 't' test and Chi-Square test.

In our study the mean onset of sensory and motor blockade in Dexmedetomidine group was 9.03 and 9.98 minutes respectively. The mean time of onset of sensory and motor blockade in group I was 13.05 and 16.23 respectively the results of our study showed that addition of Dexmedetomidine as an adjuvant significantly enhanced the onset of both sensory and motor blockade.

The duration of sensory and motor blockade was significantly increased ($p < 0.05$) in Dexmedetomidine group when compared to other group. In our study the mean duration of sensory and motor blockade in Dexmedetomidine group was 723.85 and 638.33 minutes respectively and in control group was

433.13 and 403.60 minutes respectively. It shows addition of dexmed significantly enhanced duration of block. ($p < 0.05$).

Effects on hemodynamic parameters including pulse rate, systolic BP (SBP), diastolic BP (DBP) monitored at 0, 2, 5, 10, 15, 20, 25, 30, 45, 60, 90 and 120 minutes. When the percentage changes in the HR, SBP, and DBP were compared from 0-5 min up to 0-120 min, they came out to be highly significant ($P < 0.001$) in dexmedetomidine group. But there was no incidence of hypotension or bradycardia in both groups. There were no changes in respiration in both groups. **Group I and II**, patients were observed for intra-operative and post-operative complications which include pain, nausea/vomiting, respiratory changes, SPO_2 less than 90%, hypotension, bradycardia. There was no incidence of complications in both groups. Supraclavicular brachial plexus block is a very popular mode of anesthesia for various upper limb surgeries, due to its effectiveness in terms of cost and performance, margin of safety and good post-operative analgesia.¹

Supraclavicular approach gives the most effective block for upper extremity and is carried out at the level of trunks of brachial plexus. The plexus is blocked where it is most compact *i.e.* at the middle of brachial plexus, resulting in homogenous spread of anesthetic agent throughout the plexus with a fast onset and complete block action.

A variety of adjuvants has been studied for brachial plexus blockade due to delayed onset of sensory and motor blockade, shorter duration of blockade for prolonged surgery and to increase post-operative analgesia. To overcome this drawback following were tried like, addition of enzymes, buffered and carbonated solutions, opioids, vasoconstricting agents, alkalization and warming up of local anesthetic solutions and potentiation of blockade by pain and muscular exercise. Dexmedetomidine, a selective α_2 -adrenoceptor agonist, has been used as an adjuvant during regional and local. Anesthetic procedures, such as subarachnoid, epidural, and caudal injections.

CONCLUSION

Our study compared the effects of addition of Dexmedetomidine to Bupivacaine-Lignocaine with Adrenaline combination for Supraclavicular

brachial plexus block with plain Bupivacaine-Lignocaine with adrenaline from our study it was concluded that.

The onset of sensory and motor blockade was early in dexmedetomidine group when compared to control group:

- The duration sensory and motor blockade was prolonged in dexmedetomidine group when compared to another group.
- Duration of analgesia (sensory block) was prolonged in dexmedetomidine group.
- Enhancement of onset time and prolongation of duration and good post-operative analgesia, the lack of significant side effects and hemodynamic stability makes dexmedetomidine an attractive choice as an adjuvant for supraclavicular brachial plexus block.
- In this modern era of anesthesia which demands greater need of comfort, stress free anesthetic and surgical techniques, introduction of dexmedetomidine as an adjuvant to bupivacaine-lignocaine adrenaline solution might go a long way in the advancement of anesthetic procedures.

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