Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com/journal/sjams/home

OPEN ACCESS

Anaesthesia

Effect of Adding Dexmedetomidine to Levobupivacaine in Axillary Brachial Plexus Block

Dr. Rinku D Prajapati[1*], Dr. Kirti Kumar S Bagrecha[2], Dr. Bhaarat S Maheshwari[3]

[1]Senior Resident, Department of Anaesthesia, B.J.M.C., Civil Hospital, Ahmedabad, Gujarat, India
[2]Third Year, PG Student, DNB in Radiodiagnosis, Nanavati Hospital, Mumbai, India
[3]Assistant Professor, Department Of Anaesthesia, B. J. M. C., Civil Hospital, Ahmedabad, Gujarat, India

***Corresponding author:** Dr. Rinku D Prajapati
| **Received:** 04.01.2019 | **Accepted:** 13.01.2019 | **Published:** 27.01.2019
DOI: 10.36347/sjams.2019.v07i01.032

Abstract | **Original Research Article**

Background*:** Many studies have described effects of vasoconstrictors as dexmedetomidine on peripheral nerve blocks, to date there is limited knowledge available on the study of dexmedetomidine adjunct to levobupivacaine in axillary brachial plexus block. ***Aims and Objectives: The aim of our study was to see the effects of adding dexmedetomidine to levobupivacaine in an axillary brachial plexus block. ***Objectives:*** To compare the onset and duration of motor and sensory block, requirements of any analgesics, compications if any and general vitals**.** ***Materials and Methods:*** A total of 60 patients of American Society of Anesthesiologists physical status I/II scheduled to undergo forearm and hand surgery, in which an axillary block was used, were enrolled. The patients were randomly divided into 2 groups: in group L patients (n = 30), an axillary block was performed with 39 mL levobupivacaine 0.5% plus 1 mL of isotonic sodium chloride. In group D patients (n = 30), an axillary block was performed with 39 mL levobupivacaine 0.5% and 1 mL dexmedetomidine 1 $\mu g/kg^{-1}$ plus isotonic sodium chloride. Then mean arterial pressure (MAP), heart rate (HR), peripheral oxygen saturation (Spo_2), sensory and motor block onset times and block durations, time to first analgesic use, total analgesic need, intraoperative verbal analog scale, postoperative visual analog scale (VAS) data, and side effects were recorded for each patient. ***Results****:* Sensory block onset time was shorter in group D ($P < 0.05$). Sensory and motor block duration and time to first analgesic use were significantly longer in group D ($P < 0.05$), and the total need for analgesics was lower in group D ($P < 0.05$). Intraoperative 5- and 10-minute verbal analog scale values and postoperative VAS value at 12 hours were significantly lower in group D ($P < 0.05$). Intraoperative MAP and HR values, except at 5 minutes and postoperatively at 10 and 30 minutes and 1 and 2 hours and so on, were significantly lower in group D ($P < 0.01$). No any other side effects were not seen in any patients. ***Conclusion****:* We conclude that adding dexmedetomidine in axillary brachial plexus block provides good analgesia with shorter onset of sensory and motor and long lasting effects with lesser complications and reduced the dose or requirements of analgesic.

Keywords: vasoconstrictors, dexmedetomidine, levobupivacaine, brachial plexus block.

INTRODUCTION

Regional anaesthesia techniques are an important part of the armamentarium of an anaesthesiologist. Regional anaesthesia has been increasing in popularity in recent years. It provides a safe and low cost technique with advantage of early ambulation and prolonged postoperative pain relief. It avoids unwanted effects of anaesthetic drugs used during general anaethesia, pressure response of laryngoscopy and tracheal intubation. Peripheral neural blockade remains a well accepted component of comprehensive anaesthetic care.

Brachial plexus block is a versatile and reliable regional anaesthesia technique**.** It is a block of roots, divisions and cords first performed by Halsted in 1884. It provides a useful alternative to general anaesthesia for upper limb surgery by being safe, decreasing the cost of anaesthetic agents, decrease operation theatre pollution and with an advantage of prolonged post-operative pain relief. The block achieves ideal operating conditions by producing complete muscular relaxation maintaining stable intraoperative haemodynamic parameters and the associated sympathetic block. The sympathetic block decreases post-operative pain, vasospasm and oedema.

Levobupivacaine is the S (_)-enantiomer of racemic bupivacaine; it has less cardiotoxicity compared with bupivacaine [1, 2] and its pharmacology

and duration of anesthesia are similar to those of bupivacaine [2].

Effect of simple anesthetic solution i.e. plain local anasthetics is short lived and often lasting only for 6-8 hours. So nowadays different drugs have been used as an adjuvant with local anesthetics in brachial plexus block to achieve quick, dense and prolonged block. Drugs like epinephrine, clonidine, dexmedetomidine, dexamethasone, butorphanol, buprenorphine are commonly being used along with local anesthetics for this purpose. Moreover, dexmedetomidine is α2-receptor agonist that has more selectivity than clonidine and has analgesic and sedative properties [5, 6]. Although several studies have described the effects of dexmedetomidine on neuroaxial and peripheral nerve blocks [7-9]. Up to date, there is only one study available, performed by Esmaoglu *et al.*, [10] on the effect of adding dexmedetomidine to levobupivacaine for an axillary brachial plexus block.

In this study, we aimed to investigate the effects of adding dexmedetomidine to levobupivacaine for an axillary brachial plexus block. The primary outcome of our study was the duration of sensory block, and the secondary outcome was postoperative analgesia. We hypothesized that adding dexmedetomidine will prolong the duration of anesthesia and analgesia with a shorter onset time.

MATERIALS AND METHODS

After obtaining approval from institutional ethical committee and written informed valid consent, a study of 50 patients of either sex, ASA-I/II in the age group of 18-65 years was conducted in B.J. Medical, Civil hospital, Ahmedabad.

Study design

- A Randomized, Prospective and Double-Blind Comparative study was done.
- 50 patients were divided into two equal groups.

Inclusion criteria

- Written informed consent given by patient & relatives
- Patients Aged 18-65 years of either sex
- ASA grade I, II
- Elective and emergency surgeries
- Unilateral upper limb surgeries

Exclusion criteria

- Age < 18 years
- ASA grade III, IV, V
- Patient refusing to give consent
- Patient having hypersensitivity to local anaesthetic drug
- Hemodynamic instability
- Local infection / inflammation
- Patients having coagulopathy
- Patient having neuropathies
- Unconscious patient

- All the patients underwent a pre anaesthetic checkup before surgery and all the routine and specific investigations were noted.
- The patients were kept electively nil per oral for 6 hours before surgery
- On the day of surgery, written informed valid consent was taken and prior to operation patients were explained about the procedure.
- Standard monitors like ECG, NIBP, and pulse oximeters were applied and patient's baseline parameters like pulse, blood pressure, respiratory rate, SpO2 were recorded.
- Intravenous line secured in all the patients and intravenous fluid started.
- **Pre-Medication**: to all patients.

  Inj.Midazolam 2 mg i.v. slowly &
  Inj.Glycopyrrolate 4 µg /kg i.v.
  Inj.Ondansetron 60 µg /kg i.v.

Technique

- The patient is placed supine, with the arm forming 90 degree angle with the trunk, and the forearm forming a 90 degree angle with upper arm. This position allows the anaesthesiologist to stand at the level of patient's upper arm and palpate the axillary artery. A line should be drawn tracing the course of the artery from mid axilla to the lower axilla, overlying this line, the index and third fingers of the anesthesiologist's left hand are used to identify the artery and minimize the amount of subcutaneous tissue overlying the neurovascular bundle. In this manner, the anaesthesiologist can develop a sense of the longitudinal course of the artery, which is essential for performing an axillary block.
- Needle puncture: while the axillary artery is identified with two fingers, the needle and syringe are inserted .After the needle is positioned, the drug is injected.
  - According to the drug administered the patients were randomly allocated to 2 groups39
    - **Group D:** Levobupivacaine 0.5% 39 cc + Dexmedetomidine 1 µg /kg (1 cc) = Total volume 40 cc
    - **Group L:** Levobupivacaine 0.5% 39 cc + Isotonic normal saline (1 cc) = Total volume 40 cc
  - During the conduct of block and thereafter, the patient was observed vigilantly for any complications of the block and for the toxicity of the drugs injected.

Prevention of deleterious effects

Following precautions were taken during conduct of the block:

- Repeated aspiration before injection to prevent intravascular spread.
- Injection would be stopped immediately if early signs of toxicity appeared.

Parameters to be observed

All the following parameters were observed at 5 minutes interval for 15 minutes, then 15 minutes interval for 30 minutes , then 30 minute interval for 60 minutes, then 1 hourly for 2 hours, then 2 hrly for 12 hrs and then at 16th hour.

Sensory blockade

- Onset of Sensory block was assessed every 2 min **by atraumatic pin prick test** in the areas innervated by radial, ulnar, and median nerves and compared with the same stimulation on contralateral hand.
- Sensory blockade was **graded** as
- grade 0(no block): normal sensitivity
- grade 1(onset):reduced sensitivity compared with same territory in contralateral upper limb
- grade 2(partial): analgesia or loss of sharp sensation of pinprick
- grade 3(complete): anaesthesia or loss of sensation to touch
- **Onset time** was defined as time taken from drug injection to complete abolition of sensation (sensory score 2). 40
- **Duration of sensory block** was defined as time from onset of block to complete return of parasthesia (sensory score 0).

Motor blockade

- By asking the patient to elevate the arm while keeping elbow straight (superior trunk) and at the hand by grip strength (middle and inferior trunk) which were graded as follows:-

Motor block evaluated by Modified 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

- **Onset time** was defined as time taken from drug injection to complete motor block (motor grade score 0).
- **Duration of motor blockade** was defined as time taken from complete motor blockade to restoration of movements of forearm (grade 6).

Hemodynamic parameters

- Intra-operative Pulse, Blood pressure, Respiratory rate, SPo2 were recorded at regular intervals as shown in proforma.

Intra-op complications

- Patients were observed for any systemic side effects like bradycardia, hypotension, nausea, vomiting, pruritus etc. 41

Post-operative analgesia

- Intensity of post-operative pain was evaluated using **VAS Score** (visual analogue scale) with grade 0 (no pain) to 10 (worst pain). Pain score were noted post-operatively at 30 mins, 60 min and then 2 hourly interval till 16 hrs. Time noted when patient regain VAS score of 4. Analgesia was considered satisfactory if the score was 3 or less. If VAS score was more than 4, analgesia was judged unsatisfactory and RESCUE ANALGESIA was administrated in form of inj. Diclofenac sodium 1.5 mg/kg i.v..
- Evaluation was stopped and time for need of first analgesia was noted.

Both groups were compared for duration of analgesia.

Duration of postoperative analgesia = Time from onset of sensory blockade to time when patient VAS score > 4 (four).

Post-operative complications

- Patients were observed for any complications like
- Local : Haematoma / Infection/ Neuropathy
- Systemic: Neurotoxicity/ cardio toxicity/ pneumothorax
- Miscellaneous.
- Tourniquet inflation and deflation time and duration of surgery were noted.

Comparison between two groups

Both groups were compared for

- Onset of sensory block (time taken from drug injection to complete ablation of sensation (sensory score 3).
- Onset of motor block (Time taken from drug injection to complete motor block (motor grade score 0).
- Duration of sensory block (time from onset of block to complete return of parasthesia (sensory score 0).
- Duration of motor block (Time taken from complete motor blockade to restoration of movements of forearm (grade 6).
- Duration of Post-operativer analgesia (Time from onset of sensory blockade to time when patient VAS score > 4 (four).

Statistical analysis

- All the data was filled in proforma and was statistically analysed by using.

"Unpaired student t- test"

- P value was calculated with the help of ©2013 GRAPH PAD SOFTWARE.

p value was applied as follows:

- If $p > 0.05$, it means that there is no significant difference between means of two groups studied.
- If $p < 0.05$, it indicates that the data is significant at 5% level of significance (i.e out of 100, in 95 cases there is a significant difference).

RESULTS

Table-1: There were no significant differences in patient and surgery characteristics between the 2 groups: Patient and surgical characteristics

	Group L (n = 30)	Group D (n = 30)
Sex (male/female)	22/8	23/07
Age, y	39.67 ± 14.44	38.83 ± 14.31
Height, cm	165.22 (7.32)	168.36 (8.14)
Weight, kg	61.27± 8.41	61.00 ±10.57
ASA status, I/II	16/14	15/15
Duration of surgery, min	84.60 ± 34.83	85.70 ± 35.37

Values shown for age, height, weight, and duration of surgery values are mean (SD), and the values shown for sex and American Society of Anesthesiologists (ASA) class are the number of patients.

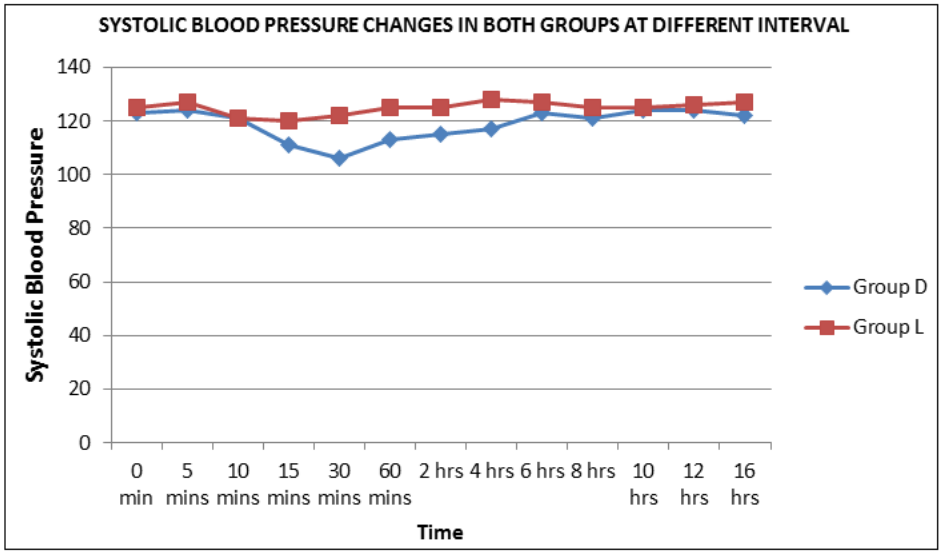
Table-2: Block Characteristics

	Group L (n = 30)	Group D (n = 30)
Sensory block onset time, min(Mean ± SD)	11.93 ± 2.65	9.23± 2.54*
Motor block onset time, min(Mean ± SD)	17.30 ± 4.20	14.67 ± 3.98*
Duration of sensory block, min(Mean ± SD)	596.00 ± 61.92	950.67±78.88*
Duration of motor block, min(Mean ± SD)	576.90 ±54.48	867±73.33*
Time to first analgesic, min(Mean ± SD)	657.93 ± 47.81	1029.55 ± 95.87*
Total analgesic need	10	0*

All values except total analgesic need data are mean (SD). The value shown for total analgesic need data is the number of patients.

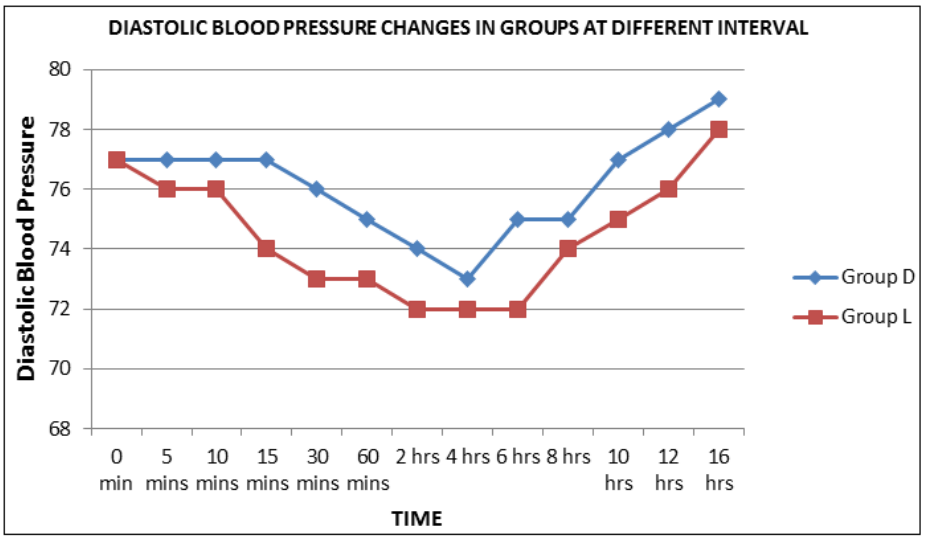
***P* < 0.05 compared with group L.**

Sensory block onset time was shorter in group D ($P < 0.05$). Sensory and motor block duration and time to first analgesic use were significantly longer in group D ($P < 0.01$), and the total need for analgesics was also lower in group D ($P < 0.05$).



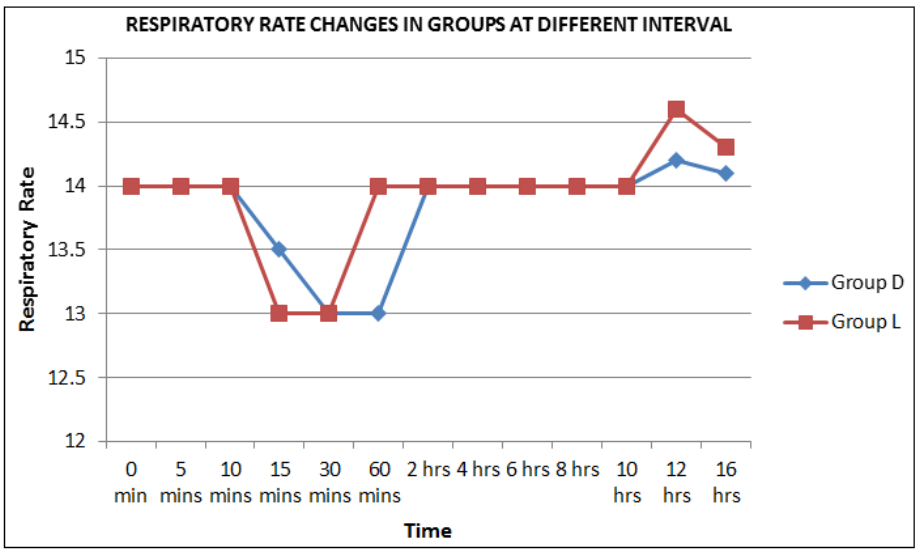
Graph-1: Systolic Blood Pressure Changes in Both Groups at Different Interval

Graph-1 shows systolic blood pressure in mm of Hg at different time interval. There was no significant difference in the mean systolic blood pressure in both groups at any point of observation.



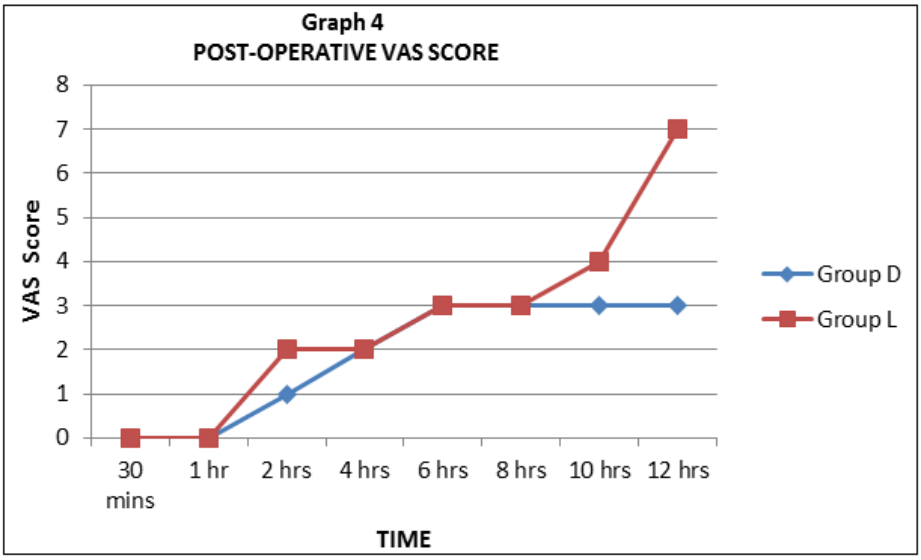
Graph-2: Diastolic Blood Pressure Changes in Groups at Different Interval

Graph-2 shows changes of diastolic blood pressure in mm of Hg at different time interval. There was no significant difference in the mean diastolic blood pressure in both groups at any point of observation.



Graph-3: Respiratory Rate Changes in Groups at Different Interval

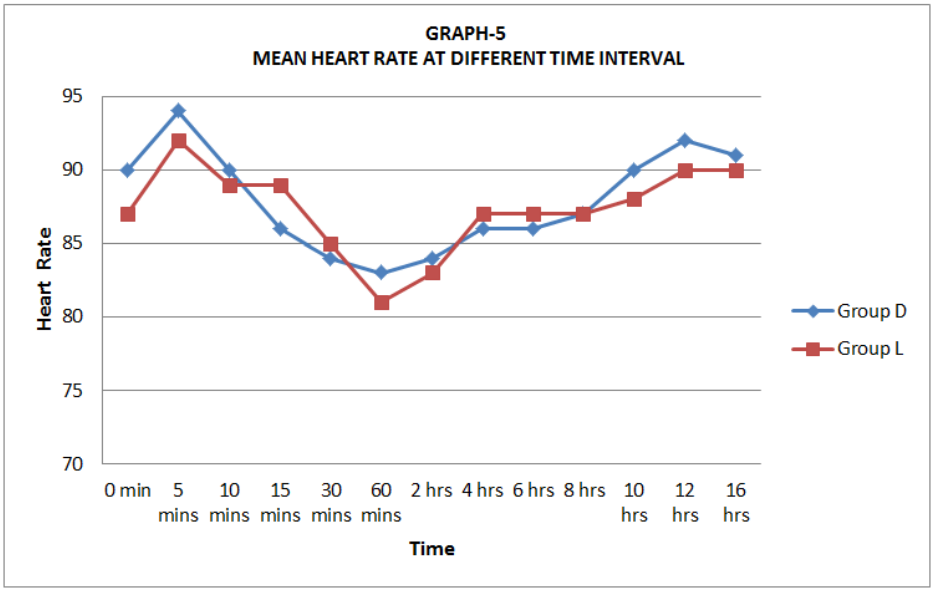
Graph-3 Shows Respiratory rate per minute in both groups at different time intervals and which was statistically not significant.



Graph-4: Post-Operative Vas Score

Graph-4 shows there was Mean significant difference in both groups in Post-operative VAS score.

Rescue analgesic was administered when VAS sacore was equal to or greater than 4 in form of Inj. Diclofenac 1-2 mg/kg i.v.



Graph-5: Mean Heart Rate at Different Time Interval

Graph-5 shows mean heart rate per minute at different time interval. There was no statistically significant difference in heart rate in both groups at any point of observation.

DISCUSSION

Although general anaesthesia continues to be used for most of the surgical procedures, regional anaesthesia has been increasingly become popular in recent years.

Regional anaesthesia provides improved satisfaction and cause less cognitive impairment and less immunosuppression compared to general anesthesia (particularly in elderly patients). Peripheral nerve blocks offer an excellent alternative for patients in whom postoperative nausea and vomiting are a problem or who are at risk for development of malignant hyperthermia or who are hemodynamically compromised or too ill to tolerate general anesthesia.

Brachial plexus block is a versatile and reliable regional anaesthetic technique and a suitable alternative to general anaesthesia for upper limb surgeries. The brachial plexus block consists of injecting local anaesthetic drugs in the fascial spaces surrounding the nerve plexus, there by blocking the autonomic, sensory and motor fibres supplying the upper extremity. It is a

simple, safe and effective technique of anaesthesia having distinct advantages over general and intravenous regional anaesthesia.

There are different approaches to block the brachial plexus.

- The Supraclavicular approach provides the most complete and reliable anaesthesia as it provides anaesthesia of the entire upper extremity in the most consistent, time efficient manner of many brachial plexus techniques.
- The Axillary approach provides smaller area of anaesthesia than supraclavicular, tendency to produce "patchy" blocks and low overall success rate and increased incidence of tourniquet pain during prolonged surgery.
- The Interscalene approach is difficult to master as there is high degree of intrathecal, epidural and intra-arterial injection. It also causes phrenic nerve and recurrent laryngeal nerve paralysis along with Horner‟s syndrome.

Out of these three approaches, we had selected axillary approach. We designed a randomized, prospective comparative study to compare effects of levobupivacaine along with dexmedetomidine and levobupivacaine along with isotonic normal saline on onset and duration of sensory and motor block and duration of postoperative analgesia in axillary brachial plexus block.

This study was conducted in 60 patients of varying age and sex belonging to ASA grade I and II for upper limb surgeries.

Patients were divided into 2 groups
In Group D Inj. levobupivacaine 0.5% 39 cc +dexmedetomidine 1 µg /kg (1cc)
In Group L Inj. levobupivacaine0.5% 39 cc + isotonic normal saline (1cc) was injected.

Out Of various local anaesthetics used for brachial plexus block, bupivacaine is the most commonly administered long acting drug but in large doses, it causes cardiac depression and central nervous system toxicity. A newer long acting local anaesthetic drug levobupivacaine has a better safety profile compared to bupivacaine as it has less cardiac depression and central nervous system toxicity; potential clinical advantage during neural blockade when large volumes are used.

The hypothesis of this study was that adding 1 µg /kg dexmedetomidine to 39 mL levobupivacaine 0.5% for an axillary brachial plexus block shortens the sensory block onset time, prolongs sensory and motor block duration and time to first analgesic use, and decreases the total analgesic requirement with no side effects.

To date, there has been an increasing use of some adjuncts (eg, opioids, α2- adrenoreceptor agonists) to local anesthetics to improve the block quality in peripheral nerve blocks. It was suggested in some studies that the addition of 2 agonists to local anesthetics in peripheral nerve blocks improved the block quality and extended the block duration [4, 9-12]. The mechanism of action of α2-adrenoceptor agonists in peripheral nerve blocks is not understood fully. The most probable mechanisms include vasoconstriction, central analgesia, and anti-inflammatory effects [9-12]. Conversely, in some previous studies [13-16], in which clonidine was used as the adjuvant, no prolongation or improvement was reported.

Dexmedetomidine is a more selective α2 agonist than clonidine. Many studies evaluated the effects of dexmedetomidine on neuroaxial and peripheral nerve blocks [7, 17, 18] and dexmedetomidine was reported to be safe and effective in these studies. In a study that compared the effects of adding either isotonic normal saline or dexmedetomidine to levobupivacaine during a Bier's block, it was found that adding dexmedetomidine improved the quality of anesthesia and analgesia more than the addition of isotonic normal saline [19]. Kol *et al*., [20] compared the effects of adding dexmedetomidine and lornoxicam to prilocaine in a Bier block and reported that adding dexmedetomidine had shortened the sensory block onset time and prolonged the sensory block recovery time more than lornoxicam.

In 2 other studies, a dexmedetomidine–lidocaine mixture was used to provide a Bier block and was found to improve the quality of anesthesia and reduce postoperative analgesic requirement [17, 18].

Bajwa *et al.*, [21] had compared dexmedetomidine and clonidine in epidural anesthesia and concluded that dexmedetomidine is a better neuraxial adjuvant compared with clonidine for providing an early onset of sensory analgesia and prolonged postoperative analgesia.

Our knowledge is limited to only one study performed by Esmaoglu *et al.*, [10] to evaluate the effects of dexmedetomidine in axillary brachial plexus blocks.

Esmaoglu *et al*., [10] divided 60 patients who had been scheduled to undergo forearm and hand surgery using an axillary block into 2 groups. They administered 0.5% 40 mL levobupivacaine plus 1 mL saline solution in 1 group and 0.5% 40 mL levobupivacaine plus 100 g dexmedetomidine in other group. Their study differs from our study in the dexmedetomidine dose that we used (1 µg /kg dexmedetomidine). Esmaoglu *et al*., [10] found that adding dexmedetomidine to levobupivacaine for an

axillary brachial plexus block shortens both the sensory and motor block onset time, extends the block duration, and the analgesia period. There was no shortening of the motor block onset time in our study in contrast to the study by Esmaoglu *et al*., [10]. They also indicated that dexmedetomidine may lead to bradycardia which did not occur in our study which is another point on which our study differs. We thought that the different results of the study by Esmaoglu et al, such as the shortened motor block onset time and the occurrence of bradycardia, in contrast to those of our study, could be related to their use of the higher dexmedetomidine dose of 100 µg in all patients. According to demographic data**,** all patients in our study were demographically similar in both groups. There were no statistically significant intergroup variations regarding age, body weight, and gender distribution.

Duration of surgery was also similar in both groups and statistically not significant ($p>0.05$). In present study, onset of sensory block was rapid with Group D as compared to Group L. The mean onset time was 9.23± 2.54 min in group D while it was 11.93 ± 2.65 min with group L and the difference was statistically significant ($p<0.05$).Onset of motor block was also rapid with Group D as compared to Group L. The mean onset time was 14.67 ± 3.98 min in group D while it was 17.30 ± 4.20 min with group L and the difference was statistically significant ($p<0.05$) which is the same in the study, done by Esmaoglu *et al.*, [10]. In our study, duration of sensory block was significantly longer with Group D as compared to Group L. The mean duration of sensory block was 950.67±78.88 min group D while it was 596.00 ± 61 min with group L and the difference was statistically significant ($p<0.05$).

The duration of motor block was significantly shorter with Group L as compared to Group D. The mean duration of 81 motor block was 867±73.33min in group D while it was 576.90 ±54.48 min with group L and the difference was statistically significant ($p<0.05$).Results of our results were similar in study by Kenan Kaygusuz *et al*., [6] in 2012. They observed longer duration of sensory blockade and motor blockade with Inj. levobupivacaine 0.5% 39 cc + dexmedetomidine 1 µg /kg(1cc) as compared to Inj. levobupivacaine0.5% 39 cc + isotonic normal saline (1cc) was injected.

In our study, duration of post-operative analgesia was significantly longer with Group D as compared to Group L. They observed that duration of analgesia was prolonged with Ropivacaine (682.8 ± 152.4 mins) than with Bupivacaine (641 ± 76.6 mins) In our study, the intra operative Pulse rate, Blood pressure remained stable without any significant fluctuation in both groups.

No significant intra-operative and post-operative complications like pneumothorax, intra-arterial or intravascular placement of drug, nausea, vomiting, pruritus, neurotoxicity or cardiotoxicity were found in either group that indicates that there is no significant difference in study done by Esmaoglu *et al*., [10].

CONCLUSION

We conclude that adding dexmedetomidine for an axillary brachial plexus block in a dose of 1 µg /kg improves the block quality by shortening the sensory block onset time, increasing the sensory and motor block duration, and increasing the interval to the first analgesic use with no side effects. We also conclude that adding dexmedetomidine to axillary brachial plexus block may decrease postoperative total analgesic use. So it's a good alternative additive for axillary brachial plexus block.

REFERENCES

1. Kopacz DJ, Allen HW. Accidental intravenous levobupivacaine. Anesthesia & Analgesia. 1999 Oct 1;89(4):1027.
2. Foster RH, Markham A. Levobupivacaine: a review of its pharmacology and use as a local anaesthetic. *Drugs*. 2000;59:551-579.
3. Duma A, Urbanek B, Sitzwohl C, Kreiger A, Zimpfer M, Kapral S. Clonidine as an adjuvant to local anaesthetic axillary brachial plexus block: a randomized, controlled study. British journal of anaesthesia. 2004 Oct 29;94(1):112-6.
4. Kapral S, Gollmann G, Waltl B, Likar R, Sladen RN, Weinstabl C, Lehofer F. Tramadol added to mepivacaine prolongs the duration of an axillary brachial plexus blockade. Anesthesia & Analgesia. 1999 Apr 1;88(4):853-6.
5. Masuki S, Dinenno FA, Joyner MJ, Eisenach JH. Selective α2-adrenergic properties of dexmedetomidine over clonidine in the human forearm. Journal of applied physiology. 2005 Aug;99(2):587-92.
6. Kaygusuz K, Gokce G, Gursoy S, Ayan S, Mimaroglu C, Gultekin Y. A comparison of sedation with dexmedetomidine or propofol during shockwave lithotripsy: a randomized controlled trial. Anesthesia & Analgesia. 2008 Jan 1;106(1):114-9.
7. Kanazi GE, Aouad MT, Jabbour-Khoury SI, Al Jazzar MD, Alameddine MM, Al-Yaman R, Bulbul M, Baraka AS. Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anaesthesiologica Scandinavica. 2006 Feb;50(2):222-7.
8. Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, Murshidi MM, Ammari BA, Awwad ZM, Al-Edwan GM, Ramsay MA. Effect of dexmedetomidine added to spinal bupivacaine for urological procedures. Saudi medical journal. 2009;30(3):365-70.

9. Obayah GM, Refaie A, Aboushanab O, Ibraheem N, Abdelazees M. Addition of dexmedetomidine to bupivacaine for greater palatine nerve block prolongs postoperative analgesia after cleft palate repair. European Journal of Anaesthesiology (EJA). 2010 Mar 1;27(3):280-4.
10. Esmaoglu A, Yegenoglu F, Akin A, Turk CY. Dexmedetomidine added to levobupivacaine prolongs axillary brachial plexus block. Anesthesia & Analgesia. 2010 Dec 1;111(6):1548-51.
11. Singelyn FJ, Gouverneur JM, Robert A. A minimum dose of clonidine added to mepivacaine prolongs the duration of anesthesia and analgesia after axillary brachial plexus block. Anesthesia & Analgesia. 1996 Nov 1;83(5):1046-50.
12. Singelyn FJ, Dangoisse M, Bartholomee S, Gouverneur JM. Adding clonidine to mepivacaine prolongs the duration of anesthesia and analgesia after axillary brachial plexus block. Regional anesthesia. 1992;17(3):148-50.
13. Gaumann D, Forster A, Griessen M, Habre W, Poinsot O, Santa Della D. Comparison between clonidine and epinephrine admixture to lidocaine in brachial plexus block. Anesthesia and analgesia. 1992 Jul;75(1):69-74.
14. Sia S, Lepri A. Clonidine administered as an axillary block does not affect postoperative pain when given as the sole analgesic. Anesthesia & Analgesia. 1999 May 1;88(5):1109-12.
15. Erlacher W, Schuschnig C, Orlicek F, Marhofer P, Koinig H, Kapral S. The effects of clonidine on ropivacaine 0.75% in axillary perivascular brachial plexus block. Acta anaesthesiologica scandinavica. 2000 Jan;44(1):53-7.
16. Culebras X, Van Gessel E, Hoffmeyer P, Gamulin Z. Clonidine combined with a long acting local anesthetic does not prolong postoperative analgesia after brachial plexus block but does induce hemodynamic changes. Anesthesia & Analgesia. 2001 Jan 1;92(1):199-204.
17. Memis D, Turan A, Karamanloglu B, Pamukçu Z, Kurt I. Adding dexmedetomidine to lidocaine for intravenous regional anesthesia. Anesthesia & Analgesia. 2004 Mar 1;98(3):835-40.
18. Esmaoglu A, Mizrak A, Akin A, Turk Y, Boyaci A. Addition of dexmedetomidine to lidocaine for intravenous regional anaesthesia. European journal of anaesthesiology. 2005 Jun;22(6):447-51.
19. Abosedira MA. Adding clonidine or dexmedetomidine to lidocaine during Bier's block: a comparative study. J Med Sci. 2008 Nov 1;8(7):660-4.
20. Kol IO, Ozturk H, Kaygusuz K, Gursoy S, Comert B, Mimaroglu C. Addition of dexmedetomidine or lornoxicam to prilocaine in Intravenous regional anaesthesia for hand or forearm surgery. Clinical drug investigation. 2009 Feb 1;29(2):121-9.
21. Bajwa SJ, Bajwa SK, Kaur J, Singh G, Arora V, Gupta S, Kulshrestha A, Singh A, Parmar SS, Singh A, Goraya SP. Dexmedetomidine and clonidine in epidural anaesthesia: A comparative evaluation. Indian journal of anaesthesia. 2011 Mar; 55(2):116.