

EVALUATING THE EFFECTS OF DEXMEDETOMIDINE ON THE PERFORMANCE OF LEVOBUPIVACAINE IN AXILLARY BRACHIAL PLEXUS BLOCK

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Abstract

Background: Numerous studies have investigated the effects of vasoconstrictors such as dexmedetomidine on peripheral nerve blocks; however, there remains limited understanding regarding the use of dexmedetomidine as an adjunct to levobupivacaine in axillary brachial plexus blocks. The current study aimed to assess the impact of adding dexmedetomidine to levobupivacaine in axillary brachial plexus blocks.

Methods: A total of 50 patients classified as American Society of Anesthesiologists physical status I/II, scheduled for forearm and hand surgery utilizing an axillary block, were included in the study. Patients were randomly assigned to two groups: Group I Levobupivacaine 0.5% 39cc + Dexmedetomidine 1 µg/kg (1cc) = Total volume 40cc. Group II: Levobupivacaine 0.5% 39 cc + Isotonic normal saline (1cc) = Total volume 40 cc. Mean arterial pressure (MAP), heart rate (HR), peripheral oxygen saturation (SpO₂), onset times and durations of sensory and motor blocks, time to first analgesic use, total analgesic consumption, intraoperative verbal analog scale, postoperative visual analog scale (VAS), and side effects were recorded for each patient.

Results: Sensory block onset time was significantly shorter in group D ($P < 0.05$). Group D exhibited significantly longer durations of sensory and motor blocks and time to first analgesic use, with reduced total analgesic requirements ($P < 0.05$). Intraoperative verbal analog scale values at 5 and 10 minutes, as well as postoperative VAS values 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, 1 and 2 hours, etc., were significantly lower in group D ($P < 0.01$). No other side effects were observed in any patients.

Conclusion: In conclusion, the addition of dexmedetomidine in axillary brachial plexus blocks provides effective analgesia with shorter sensory and motor block onset times, prolonged duration, fewer complications, and reduced analgesic requirements.

Keywords: Dexmedetomidine, Levobupivacaine, Brachial Plexus Block.

Introduction

Regional anesthesia techniques play a crucial role in the arsenal of anesthesiologists, and their popularity has been steadily increasing in recent times. These techniques offer a safe and cost-effective alternative, facilitating early ambulation and prolonged postoperative pain relief. [1] By avoiding the side effects associated with general anesthesia, such as the hemodynamic response to laryngoscopy and

tracheal intubation, regional anesthesia, particularly peripheral neural blockade, has become an integral part of comprehensive anesthetic care. Brachial plexus block, a versatile and reliable regional anesthesia technique, involves blocking the roots, divisions, and cords of the brachial plexus. First performed by Halsted in 1884, this technique serves as a valuable alternative to general anesthesia for upper limb surgery, contributing to safety, cost reduction in anesthetic agents decreased pollution in the operating theater, and prolonged postoperative pain relief. The block optimizes surgical conditions by inducing complete muscular relaxation, maintaining stable intraoperative hemodynamic parameters, and producing a sympathetic block, which in turn reduces postoperative pain, vasospasm, and edema. Levobupivacaine, the S (-)-enantiomer of racemic bupivacaine, is preferred for its lower cardiotoxicity while offering similar pharmacology and duration of anesthesia as bupivacaine. [2, 3] However, the effect of plain local anesthetics is short-lived, typically lasting only 6-8 hours. To address this limitation, various adjuvant drugs, such as epinephrine, clonidine, dexmedetomidine, dexamethasone, butorphanol, and buprenorphine, are commonly used alongside local anesthetics in brachial plexus blocks to achieve rapid, dense, and prolonged blocks. Among these, dexmedetomidine, an α_2 -receptor agonist known for its analgesic and sedative properties, exhibits greater selectivity compared to clonidine. While several studies have explored the effects of dexmedetomidine on neuraxial and peripheral nerve blocks, there is limited research on its combination with levobupivacaine for axillary brachial plexus blocks [4-7]. Thus, our study aimed to investigate the impact of adding dexmedetomidine to levobupivacaine for axillary brachial plexus blocks. Our primary outcome measure was the duration of the sensory block, with postoperative analgesia as a secondary outcome. We hypothesized that adding dexmedetomidine would prolong both anesthesia and analgesia durations while reducing onset time.

Material and Methods

This cross-sectional study was conducted in the Department of Anesthesiology, Prathima Institute of Medical Sciences, Naganoor, Karimnagar. Institutional Ethical Approval was obtained for the study. Written consent was obtained from all the participants of the study after explaining the nature of the study in the vernacular language. A total of 50 patients were evenly divided into two groups.

Inclusion Criteria:

1. Patients provided written informed consent.
2. Patients aged 18-65 years of either sex.
3. Patients with ASA grade I or II.
4. Elective and emergency surgeries.
5. Unilateral upper limb surgeries.

Exclusion Criteria:

1. Age < 18 years.
2. Patients with ASA grade III, IV, or V.
3. Patients refusing to provide consent.
4. Patients with hypersensitivity to local anesthetic drugs.
5. Patients with hemodynamic instability.
6. Patients with local infection or inflammation.
7. Patients with coagulopathy.
8. Patients with neuropathies.
9. Unconscious patients.

Procedure: All patients underwent pre-anesthetic checkup, and routine and specific investigations were documented. Patients fasted for six hours before surgery. Standard monitors such as ECG, NIBP, and pulse oximeters were applied, and baseline parameters including pulse, blood pressure, respiratory rate, and SpO₂ were recorded. Intravenous lines were secured, and intravenous fluids were initiated. Pre-

medication was administered to all patients, including Inj. Midazolam 2 mg IV slowly, Inj. Glycopyrrolate 4 µg/kg IV, and Inj. Ondansetron 60 µg/kg IV.

Technique: The patient was positioned supine, with the arm forming a 90-degree angle with the trunk and the forearm forming a 90-degree angle with the upper arm. A needle puncture was performed while identifying the axillary artery with two fingers, and the drug was injected. Patients were randomly allocated to two groups: Group I: Levobupivacaine 0.5% 39cc + Dexmedetomidine 1 µg/kg (1cc) = Total volume 40cc. Group II: Levobupivacaine 0.5% 39 cc + Isotonic normal saline (1cc) = Total volume 40 cc.

Observations: Patients were monitored for sensory blockade onset, duration, and intensity, motor blockade onset and duration, hemodynamic parameters, intraoperative complications, postoperative analgesia, and postoperative complications. Sensory blockade onset and duration were assessed using atraumatic pin prick tests and graded accordingly. Motor blockade was evaluated using the Modified Lovett rating scale. Hemodynamic parameters were recorded at regular intervals. Postoperative pain was assessed using the VAS score. Patients were observed for any postoperative complications. The two groups were compared for the duration of analgesia, and postoperative complications were noted.

Statistical analysis: All the available data was refined and uploaded to an MS Excel spreadsheet and analyzed by SPSS version 15 in Windows format. All the continuous variables were denoted as mean, standard deviations, and percentages, and categorical variables were denoted as p values, and p values of < 0.05 were considered as significant.

Results

Table 1 provides patient and surgical characteristics for the Axillary Brachial Plexus Block. Sex (male/female): Group I had 21 male and 4 female patients, while Group II had 22 male and 3 female patients. This indicates a slightly higher proportion of male patients in both groups. Age, years: The mean age in Group I was 37.5 years with a standard deviation of 5.5 years, while in Group II, it was 38.2 years with a standard deviation of 6.5 years. The patients in both groups were relatively close in age, with Group II having slightly older patients on average. Height, cm: The mean height in Group I was 166.54 cm with a standard deviation of 7.75 cm, while in Group II, it was 165.33 cm with a standard deviation of 10.54 cm. There was a minor difference in height between the two groups, with Group I, having slightly taller patients on average. Weight, kg: The mean weight in Group I was 60.27 kg with a standard deviation of 7.9 kg, while in Group II, it was 62.24 kg with a standard deviation of 8.4 kg. Group II had slightly heavier patients on average compared to Group I.

Table 1: Patient and surgical characteristics Axillary Brachial Plexus Block

Variable	Group I (Levobupivacaine 0.5% + Dexmedetomidine 1 µg/kg)	Group II (Levobupivacaine 0.5% + Isotonic saline)
Sex (male/female)	21/4	22/3
Age, years	37.5 ± 5.5	38.2 ± 6.5
Height, cm	166.54 ± 7.75	165.33 ± 10.54
Weight, kg	60.27 ± 7.9	62.24 ± 8.4
ASA status, I/II	20/5	19/6
Duration of surgery, min	86.24 ± 25.64	84.33 ± 27.91

ASA status, I/II: In Group I, 20 patients were classified as ASA status I and 5 patients as ASA status II. In Group II, 19 patients were classified as ASA status I and 6 patients as ASA status II. Both groups had a similar distribution of ASA status, indicating a relatively balanced mix of patients with different levels of physical health. Duration of surgery, min: The mean duration of surgery in Group I was 86.24

minutes with a standard deviation of 25.64 minutes, while in Group II, it was 84.33 minutes with a standard deviation of 27.91 minutes. The duration of surgery was comparable between the two groups, with Group II having a slightly shorter average duration. No significant differences between the two groups were found.

Table 2 presents the characteristics of the block in two groups: Group I, receiving Levobupivacaine 0.5% + Dexmedetomidine 1 µg/kg, and Group II, receiving Levobupivacaine 0.5% + Isotonic saline. It also includes the p-values indicating the statistical significance between the two groups.

Table 2: Block Characteristics between the groups

	<i>Group I (Levobupivacaine 0.5% + Dexmedetomidine 1 µg/kg)</i>	<i>Group II Levobupivacaine 0.5% + Isotonic saline</i>	<i>P values</i>
Sensory block onset time, min(Mean ± SD)	9.06± 3.12	12.01 ± 2.19	0.004
Motor block onset time, min(Mean ± SD)	13.97 ± 3.74*	17.91 ± 3.97	0.034
Duration of sensory block, min(Mean ± SD)	951.63 ± 75.89	595.10 ± 61.92	0.001
Duration of motor block, min(Mean ± SD)	872 ± 54.12	580.21.90 ± 49.57	0.012
Time to first analgesic, min(Mean ± SD)	1027.31 ± 65.47	651.63 ± 35.34	0.019
Total analgesic need	0	10	0.001

Sensory block onset time, min (Mean ± SD): The mean onset time for the sensory block was significantly shorter in Group I (9.06 ± 3.12 min) compared to Group II (12.01 ± 2.19 min) with a p-value of 0.004. This indicates that the addition of dexmedetomidine resulted in a faster onset of sensory block. Motor block onset time, min (Mean ± SD): The mean onset time for the motor block was also significantly shorter in Group I (13.97 ± 3.74 min) compared to Group II (17.91 ± 3.97 min) with a p-value of 0.034. This suggests that the addition of dexmedetomidine accelerated the onset of motor block as well. Duration of sensory block, min (Mean ± SD): Group I had a significantly longer duration of sensory block (951.63 ± 75.89 min) compared to Group II (595.10 ± 61.92 min) with a p-value of 0.001. This implies that dexmedetomidine prolonged the duration of the sensory block. Duration of motor block, min (Mean ± SD): Similarly, Group I exhibited a significantly longer duration of motor block (872 ± 54.12 min) compared to Group II (580.21.90 ± 49.57 min) with a p-value of 0.012. This indicates that dexmedetomidine extended the duration of the motor block. Time to first analgesic, min (Mean ± SD): The time to the first analgesic requirement was significantly longer in Group I (1027.31 ± 65.47 min) compared to Group II (651.63 ± 35.34 min) with a p-value of 0.019. This suggests that patients in Group I experienced prolonged analgesia compared to Group II. Total analgesic need: Group I had a total analgesic need of 0, indicating that none of the patients required additional analgesics, while Group II had a total analgesic need of 10. The difference between the two groups was statistically significant with a p-value of 0.001, indicating that the addition of dexmedetomidine significantly reduced the need for analgesics. Overall, these findings demonstrate that adding dexmedetomidine to Levobupivacaine in axillary brachial plexus block resulted in a faster onset of sensory and motor blocks, prolonged duration of the block, delayed requirement for analgesics, and reduced total analgesic need compared to using Levobupivacaine alone with isotonic saline.

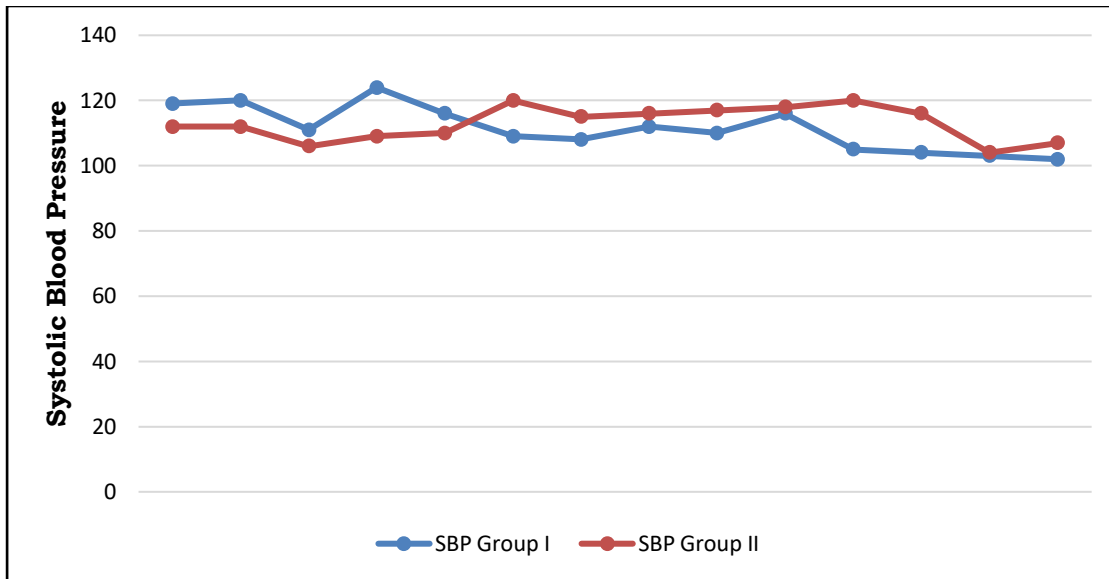


Figure 1: Systolic Blood Pressure Changes in both groups at different Intervals

Figure 1 illustrates the systolic blood pressure measured in millimeters of mercury (mmHg) at various time intervals. There were no notable discrepancies observed in the average systolic blood pressure between both groups at any observed time point.

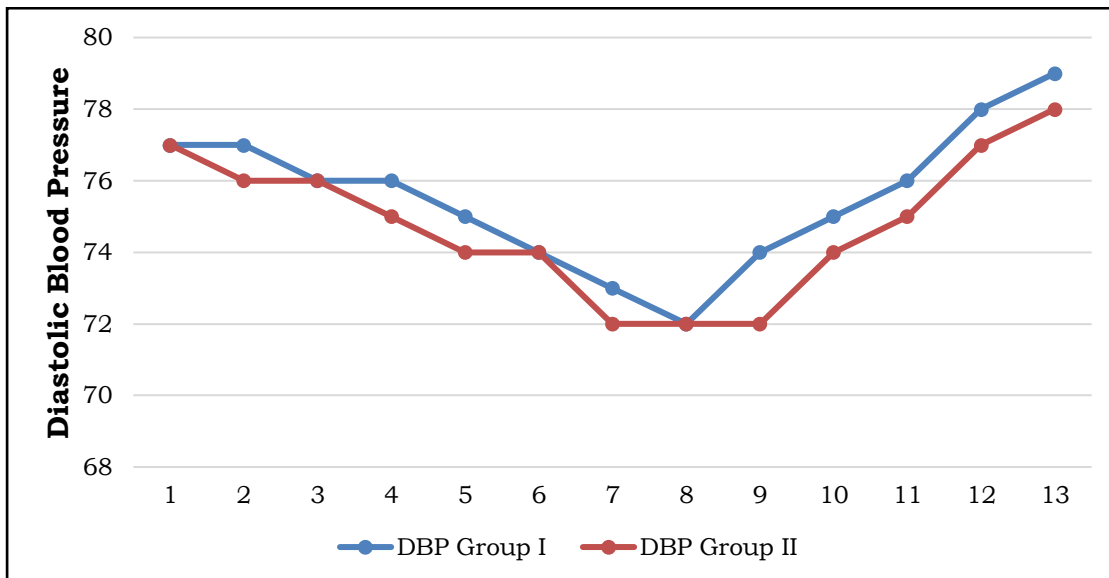


Figure 2: Diastolic Blood Pressure changes in groups at different interval

Figure 2 depicts the alterations in diastolic blood pressure measured in millimeters of mercury (mmHg) across different time intervals. No notable variance was observed in the average diastolic blood pressure between both groups at any observed time point. The respiratory rates between the two groups remained from 13 – 15 and no significant differences were observed between the groups.

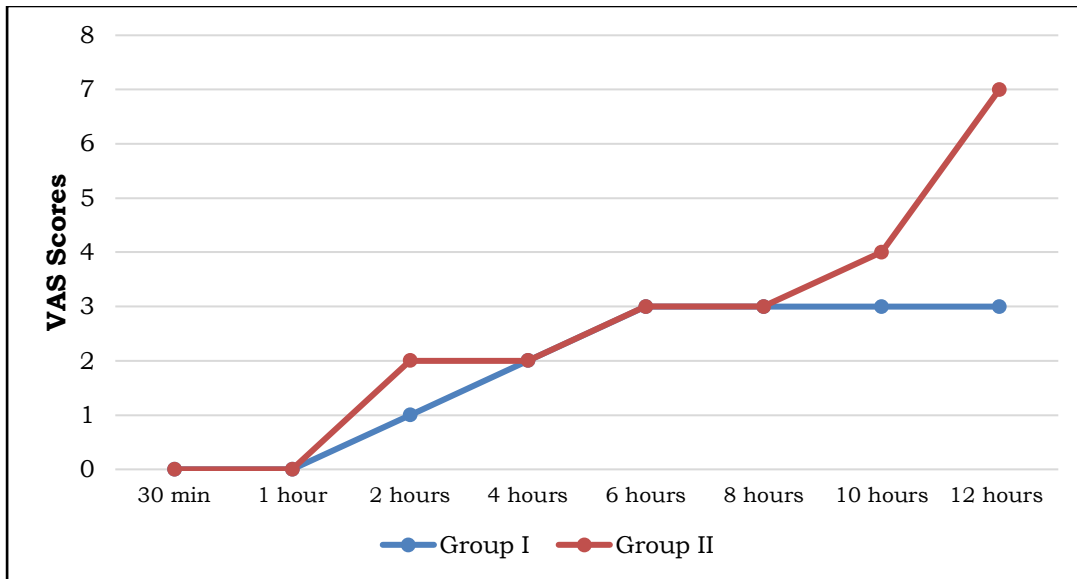


Figure 3: Post-Operative VAS Score

Figure 3 illustrates a notable difference in the mean postoperative Visual Analog Scale (VAS) scores between both groups. Rescue analgesia was provided when the VAS score reached or exceeded 4, in the form of intravenous administration of Injection Diclofenac at a dosage of 1-2 mg/kg.

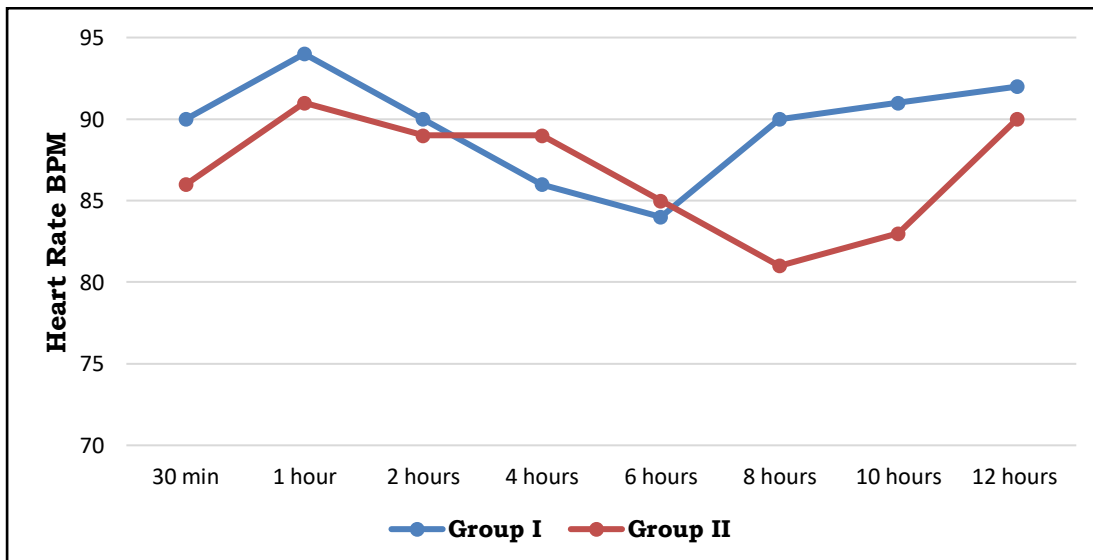


Figure 4: Showing the heart rate recorded in two groups

Discussion

Although general anesthesia continues to be used for most surgical procedures, regional anesthesia has increasingly become popular in recent years. Regional anesthesia provides improved satisfaction and causes 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 who are at risk for the 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 anesthetic technique and a suitable alternative to general anesthesia for upper limb surgeries. The brachial plexus block consists of injecting local anesthetic drugs in the fascial spaces surrounding the nerve plexus, thereby blocking the

autonomic, sensory, and motor fibers supplying the upper extremity. It is a simple, safe, and effective technique of anesthesia having distinct advantages over general and intravenous regional anesthesia.

There are different approaches to blocking the brachial plexus. The Supraclavicular approach provides the most complete and reliable anesthesia as it provides anesthesia of the entire upper extremity in the most consistent, time-efficient manner of many brachial plexus techniques. The Axillary approach provides a smaller area of anesthesia than supraclavicular, the tendency to produce "patchy" blocks, and low overall success rate, and an increased incidence of tourniquet pain during prolonged surgery. The Interscalene approach is difficult to master as there is a 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 selected the axillary approach. We designed a randomized, prospective comparative study to compare the 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 on 50 patients of varying ages and sexes belonging to ASA grades I and II for upper limb surgeries. Out of various local anesthetics 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 anesthetic drug levobupivacaine has a better safety profile compared to bupivacaine as it has less cardiac depression and central nervous system toxicity; a potential clinical advantage during neural blockade when large volumes are used. This study hypothesized 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 increasing use of some adjuncts (eg, opioids, α_2 -adrenoceptor agonists) to local anesthetics to improve the block quality in peripheral nerve blocks. It was suggested in some studies that the addition of α_2 agonists to local anesthetics in peripheral nerve blocks improved the block quality and extended the block duration [8-12]. The mechanism of action of α_2 -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 α_2 agonist than clonidine. Many studies evaluated the effects of dexmedetomidine on neuroaxial and peripheral nerve blocks [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, 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] 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 Esmoğlu *et al.*, [10] to evaluate the effects of dexmedetomidine in axillary brachial plexus blocks. Esmoğlu *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 µg dexmedetomidine in another group. Their study differs from our study in the dexmedetomidine dose that we used (1 µg/kg dexmedetomidine). Esmoğlu *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 Esmoğlu *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, [10] 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 the present study, the onset of sensory block was rapid in Group I as compared to Group II. The mean onset time was 9.23 ± 2.54 min in group I while it was 11.93 ± 2.65 min in group L and the difference was statistically significant ($p<0.05$). The onset of motor block was also rapid with Group I as compared to Group L. The mean onset time was 14.67 ± 3.98 min in group I while it was 17.30 ± 4.20 min in 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, the duration of sensory block was significantly longer with Group I as compared to Group II. The mean duration of sensory block was 950.67 ± 78.88 min in group I while it was 596.00 ± 61 min in group II and the difference was statistically significant ($p<0.05$).

The duration of the motor block was significantly shorter with Group L as compared to Group I. The mean duration of 81 motor blocks was 867 ± 73.33 min in group I while it was 576.90 ± 54.48 min in group L and the difference was statistically significant ($p<0.05$). The results of our study were similar to the study by Kenan Kaygusuz et al., [6] in 2012. They observed a longer duration of sensory blockade and motor blockade with Inj. levobupivacaine 0.5% 39 cc + dexmedetomidine 1 µg/kg(1cc) as compared to Inj. Levobupivacaine 0.5% 39 cc + isotonic normal saline (1cc) was injected. In our study, the duration of postoperative analgesia was significantly longer with Group I as compared to Group II. They observed that the duration of analgesia was prolonged with Ropivacaine (682.8 ± 152.4 mins) than with Bupivacaine (641 ± 76.6 mins) In our study, the intraoperative Pulse rate and blood pressure remained stable without any significant fluctuation in both groups. No significant intra-operative and post-operative complications like pneumothorax arterial or intravascular placement of drug, nausea, vomiting, pruritus, neurotoxicity, or cardiotoxicity were found in either group indicating that there is no significant difference in a 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 the axillary brachial plexus block may decrease postoperative total analgesic use. So, it's a good alternative additive for axillary brachial plexus block.

References

1. Hutton M, Brull R, Macfarlane AJR. Regional anesthesia and outcomes. *BJA Educ.* 2018 Feb;18(2):52-56.
2. Bajwa SJ, Kaur J. Clinical profile of levobupivacaine in regional anesthesia: A systematic review. *J Anaesthesiol Clin Pharmacol.* 2013 Oct;29(4):530-39.
3. Foster RH, Markham A. Levobupivacaine: a review of its pharmacology and use as a local anesthetic. *Drugs.* 2000; 59:551-79.
4. Bhatnagar S, Mishra S, Madhurima S, Gurjar M, Mondal AS. Clonidine as an analgesic adjuvant to continuous paravertebral bupivacaine for post-thoracotomy pain. *Anaesth Intensive Care.* 2006; 34:586–91.
5. Gabriel JS, Gordin V. Alpha 2 agonists in regional anesthesia and analgesia. *Curr Opin Anaesthesiol.* 2001; 14:751–53.
6. El-Hennawy AM, Abd-Elwahab AM, Abd-Elmaksoud AM, El-Ozairy HS, Boulis SR. The addition of clonidine or dexmedetomidine to bupivacaine prolongs caudal analgesia in children. *Br J Anaesth.* 2009; 103:268–74.

7. Marhofer D, Kettner SC, Marhofer P, Pils S, Weber M, Zeitlinger M. Dexmedetomidine as an adjuvant to ropivacaine prolongs peripheral nerve block: A volunteer study. *Br J Anaesth.* 2013; 110:438–42.
8. Kapral S, Gollmann G, Walzl 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):853-56.
9. Esmoğlu A, Yegenoğlu F, Akin A, Turk CY. Dexmedetomidine added to levobupivacaine prolongs axillary brachial plexus block. *Anesthesia & Analgesia.* 2010 Dec 1;111(6):1548-51.
10. Obayah GM, Refaie A, Aboushanab O, Ibraheem N, Abdelaziz 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):280-84.
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, Poinot 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):53-57.
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):199-04.
17. Memis D, Turan A, Karamanoglu B, Pamukçu Z, Kurt I. Adding dexmedetomidine to lidocaine for intravenous regional anesthesia. *Anesthesia & Analgesia.* 2004 Mar 1;98(3):835-40.
18. Esmoğlu A, Mizrak A, Akin A, Turk Y, Boyaci A. Addition of dexmedetomidine to lidocaine for intravenous regional anesthesia. *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):660-64.
20. Kol IO, Ozturk H, Kaygusuz K, Gursoy S, Comert B, Mimaroglu C. Addition of dexmedetomidine or lornoxicam to prilocaine in Intravenous regional anesthesia for hand or forearm surgery. *Clinical drug investigation.* 2009 Feb 1;29(2):121-29.
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 anesthesia: A comparative evaluation. *Indian Journal of anesthesia.* 2011 Mar; 55(2):116.