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Original Research Article

A Comparative Study of Dexmedetomidine and Clonidine as an Adjuvant to Bupivacaine in Ultrasound-Guided Supraclavicular Brachial Plexus Block

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Abstract:

Background: For upper limb surgeries, ultrasound-guided brachial plexus block is the preferred technique. Adding adjuvants to peripheral nerve blocks is common to enhance their analgesic effectiveness and duration. In this study, we compared the analgesic effects of dexmedetomidine 1µg/kg and clonidine 1µg/kg as adjuvants to a low volume of bupivacaine in ultrasound-guided supraclavicular brachial plexus block.

Methods: A prospective, randomized controlled, double-blind study was conducted after obtaining permission from the institutional ethics committee. We included 40 ASA grade I and II patients, aged 18 to 60 years, who were scheduled for upper limb orthopedic surgery. Group D (Dexmedetomidine group) received 20 ml of bupivacaine along with dexmedetomidine (10 ml of 0.5% bupivacaine + 1µg/kg of dexmedetomidine, diluted with 0.9% NS to 20 ml). Group C (Clonidine group) received 20 ml of 0.25 bupivacaine along with clonidine (10 ml of 0.5% bupivacaine + 1µg/kg of clonidine, diluted with 0.9% NS to 20 ml) in the ultrasound-guided supraclavicular brachial plexus block.

Results: The mean age of Group C, receiving bupivacaine with clonidine, had a mean age of 37.5 ± 10.55 years, while Group D, receiving bupivacaine with dexmedetomidine, had a mean age of 35.81 ± 8.55 years. The average time for the onset of sensory block in group C was 12.22 minutes, while in group D, it was 9.55 ± 1.2 minutes. The mean time of onset of motor block in group C was 14.2 ± 1.56 minutes and in group D it was 11.9 ± 0.88 minutes no instances of hypotension or bradycardia were observed in either group.

Conclusion: The addition of dexmedetomidine to bupivacaine 0.25% has been found to significantly prolong the pain-free period, duration of motor blockade, and sensory blockade when compared to clonidine or the control group. This combination offers the advantage of maintaining hemodynamic stability while keeping the patient calm. Ultrasound-guided supraclavicular block using a low volume of bupivacaine with 1µg/kg dexmedetomidine resulted in adequate blockade and provided effective postoperative analgesia.

Keywords: Adjuvant, Bupivacaine, Clonidine, Dexmedetomidine, Clonidine, sensory and motor blockade.

Introduction

Ultrasound-guided peripheral nerve block (USG) is an emerging technique rapidly gaining popularity compared to traditional methods like peripheral nerve stimulators and paraesthesia. [1] This approach not only reduces the risk of nerve injury associated with blind techniques but also decreases the required dose of a local anesthetic to block the plexus effectively. Among various nerve blocks, the supraclavicular nerve block offers consistent and time-efficient anesthesia for the entire upper extremity. [2]Alpha-2 adrenergic receptor agonists have attracted attention due to their sedative, analgesic, and cardiovascular stabilizing effects, leading to reduced anesthetic requirements. [3] When concurrently injected with local anesthetics, these agonists are believed to enhance nerve block characteristics through mechanisms such as local vasoconstriction, facilitation of C-fiber blockade, or spinal actions via axonal transport or diffusion along the nerve.[3] Two such alpha-2 adrenergic agonists, clonidine and dexmedetomidine, have shown potent central and peripheral antinociceptive properties. Clonidine acts on alpha-2 adrenoceptors located on primary afferent terminals, contributing to analgesia. [4] Dexmedetomidine, a selective alpha-2 adrenoceptor agonist, has been used as an adjuvant in regional and local anesthesia. [5, 6] While some studies support its efficacy and safety, others have reported varying analgesic effects. [7, 8]In this study, we aimed to compare the analgesic effects of dexmedetomidine and clonidine, as well as a control group, when added to bupivacaine 0.25% in a dose

of 1 μg/kg for an ultrasound-guided supraclavicular brachial plexus block.

Material and Methods

This prospective randomized controlled study was conducted in the Department of Anesthesiology, Prathima Institute of Medical Sciences, Naganoor, Karimnagar. Institutional Ethical approval was obtained for the study. Written permission was obtained for the study from all the participants after explaining the nature of the study in vernacular language.

Inclusion criteria

1. Upper limb orthopedic surgeries
2. ASA grade – I & II 2.
3. Age between 18 - 55yrs
4. Males and Females
5. Voluntarily willing to participate in the study

Exclusion criteria

1. Patients with complications like severe anemia, hypovolemia, septicemia, and shock.
2. Known case of hypersensitivity reaction to clonidine or dexmedetomidine.
3. Bleeding disorders or on anticoagulant therapy
4. Local infection at the site of puncture.

A detailed history and examination of the patient were performed, and all the required investigations were done. Randomization in this study was achieved using a computer-generated randomized number table. Each random number was sealed in an opaque envelope, and one of the investigators opened it just before the block to determine the assigned study drug/combination. The observer anesthesiologist conducting the block was kept blind to the administered test drug/combination. Patients were informed about the 11-point Verbal Rating Score (VRS) one day before the surgery, where 0 indicates no pain, and 10 represents the worst imaginable pain. All patients were premedicated with oral alprazolam 0.25 mg the night before and on the morning of the surgery. According to the assigned random number, patients were allocated to one of the three groups: Group D (Dexmedetomidine group) received an ultrasound-guided supraclavicular brachial plexus block with 20 ml of 0.25% bupivacaine + 1μg/kg of dexmedetomidine (10 ml of 0.5% bupivacaine + 1μg/kg of dexmedetomidine, diluted to a total of 20 ml with 0.9% normal saline). Group C (Clonidine group) received an ultrasound-guided supraclavicular brachial plexus block with 20 ml of 0.25% bupivacaine + 1μg/kg of clonidine (10 ml of 0.5% bupivacaine + 1μg/kg of clonidine, diluted to a total of 20 ml with 0.9% normal saline). Surgery was done under the supraclavicular approach of the brachial plexus block. Patients were positioned in the supine position with their heads turned away from the side to be blocked. Heart rate, systolic and diastolic blood pressure, and SpO2 were recorded at one-minute intervals for ten minutes after the administration of the supraclavicular block. Subsequently, these parameters were recorded at ten-minute intervals until the end of the surgery and then at intervals of 0, 1, 2, 4, 8, 12, 18, and 24 hours after surgery. The ultrasound-guided supraclavicular brachial block was performed with strict aseptic precautions, using a 22 G echogenic needle and an 8-12 Hz linear probe with an ultrasound machine. Data were collected at 5-minute intervals for the first 30 minutes, followed by 45-minute, 60-minute, and 30-minute intervals until the surgery was completed. Afterward, sensory block assessment was performed for each nerve using ice to test for cold sensation, comparing the anesthetized arm with the contralateral arm in the dermatomes corresponding to the median nerve, ulnar nerve, radial nerve, and musculocutaneous nerve until the complete blockade was achieved.

The sensory block was graded as follows:

Grade 1: No difference between the two sides.
Grade 2: Some difference between the two sides, but a cold sensation is still sensed in the blocked arm.
Grade 3: Complete sensory loss on the anesthetized limb.

Motor block assessment was conducted based on specific movements: thumb abduction (radial nerve), thumb adduction (ulnar nerve), thumb opposition (median nerve), and flexion of the elbow (musculocutaneous nerve). The modified Bromage Scale was used, with onset considered as grade 2 and peak motor block at grade 3.

The motor block was graded as follows:

Grade 1: Normal motor function with full flexion and extension of elbow, wrist, and fingers.
Grade 2: Reduced motor strength with the ability to move fingers only.
Grade 3: Complete motor block with an inability to move fingers.

The pain-free period was defined as the time interval between the administration of the test drug and the first demand for rescue analgesia in minutes, and it was recorded. Pain assessment was conducted intraoperatively using the Verbal Rating Scale (VRS) every 15 minutes and continued for 24 hours at intervals of 0, 1, 2, 4, 8, 12, 18, and 24 hours after surgery.

Sedation level was evaluated using the Modified Ramsay Sedation Scale every 15 minutes, with the following grades:

Grade 1: Wide awake
Grade 2: Drowsy
Grade 3: Asleep but arousable with verbal stimulus
Grade 4: Arousable with mild physical stimulus
Grade 5: Not arousable with mild physical stimulus

Intravenous diclofenac 75 mg was administered in 100 ml of normal saline as an infusion when the VRS score was greater than 3. The total requirement of rescue analgesia was recorded after the 24-hour study period. The block was considered a failure if there was inadequate sensory and motor blockade beyond 30 minutes following its administration. In the event of block failure, additional drug infiltration was administered in the block, or general anesthesia was used to complete the surgical procedure. Time 0 was considered when the patient was transferred to the postanesthetic care unit (PACU). If the heart rate dropped below 50 bpm or decreased by 20% compared to the baseline, an injection of atropine was administered. Furthermore, a 3mg bolus of injection mephenteramine was given if the systolic blood pressure or mean arterial pressure decreased to less than 20% of the baseline value.

Results

A total of 40 patients, both male and female, aged between 18 and 55 years, who were scheduled for upper limb surgeries and were undergoing supraclavicular brachial plexus block, were included in this study. The primary objective of the study was to compare the effectiveness of dexmedetomidine (1µg/kg) with clonidine (1µg/kg) as adjuvants to bupivacaine (0.25%) for brachial plexus block.

Table 1:Mean age Distribution between the two groups

Group	Mean±SD	T value	P value
Group D	35.81 ± 8.55	0.65	0.13
Group C	37.5 ± 10.55		

The minimum age of the patient was 18 years, and the max-age was 55 yrs. The mean age of the patient in group C was 37.5 ± 10.55 years and group B was 35.81 ± 8.55.

Table 2: **Showing the onset of sensory block in minutes**

Group	Mean±SD	T value	P value
Group D	9.55 ± *1.2*	7.37	0.01*
Group C	12.22 ± *2.30*		

* Significant

The average time for the onset of sensory block in group C was 12.22 minutes, while in group D, it was 9.55 ± 1.2 minutes. The statistical analysis, using the student's unpaired 't-test, revealed that the time of onset of sensory block in group D was significantly faster compared to group C, with a p-value of 0.01. These significant differences are displayed in Table 2.

Table 3: **Showing the onset of Motor block in minutes**

Group	Mean±SD	T value	P value
Group D	11.9±*0.88*	6.94	0.01*
Group C	14.2 ±*1.56*		

* Significant

The mean time of onset of motor block in group C was 14.2± 1.56 minutes and in group D it was 11.9±0.88 minutes. The p values were found to be 0.01 and significant depicted in Table 3.

Table 4: **Showing the duration of sensory block in hours**

Group	Mean ± SD	T value	P value
Group D	9.14 ± 0.69	9.987	0.01*
Group C	7.12 ± 0.75		

* Significant

Both groups of patients were monitored for 24 hours, and the moment they requested rescue analgesics was recorded. The average duration of the sensory block in group C was 7.12 ± 0.75 hours, while in group D, it was 9.14 ± 0.69 hours. It was determined that the duration of the sensory block in group D was significantly shorter than in group C ($p < 0.01$) given in Table 4.

Table 5: **Showing the duration of motor block in hours**

Group	Mean ± SD	T value	P value
Group D	8.62 ± 0.57	8.912	0.01*
Group C	6.77 ± 0.71		

* Significant

The mean duration of the motor block in group C was 6.77 ± 0.71 hours and similarly the mean duration of the motor block in group D was 8.62 ± 0.57 the p-value was found to be 0.01 and significant given in Table 5.

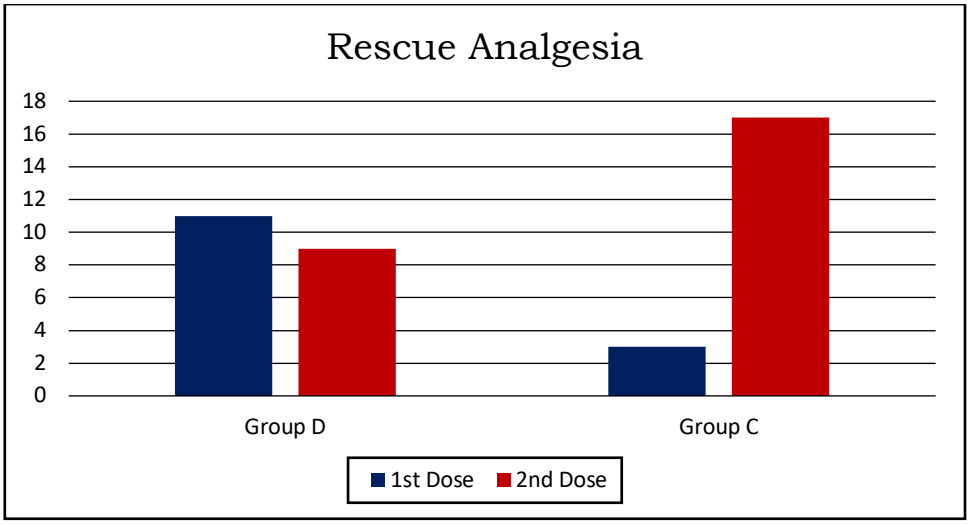

Figure 1: Comparison of rescue analgesia required in two groups

In group C 20% of cases required one dose of rescue analgesic and 80% of cases required 2 doses of analgesic within 24 hours. Similarly, in group D 55% of cases required one dose of analgesic, and 45% required a second dose of analgesic within 24 hours. The statistical comparison between the two revealed p values were (<0.05) and significant depicted in Figure 1.

Table 6: Comparison of sedation scores between the two groups

Sedation scores	Group D	Group C
2	4 (20%)	16 (80%)
3	16 (80%)	4 (20%)
Total	20 (100%)	20 (100%)
Mean ± SD	3.0 ± 0.45	2.0 ± 0.5
P value	0.047*	

* Significant

In group C, 80% of patients exhibited a sedation score of 2, while 20% of patients had a sedation score of 3. On the other hand, in group D, 20% of patients had a sedation score of 2, and 80% of patients had a sedation score of 3. The difference in sedation scores between the two groups was determined to be statistically significant by using the student's unpaired 't-test (p<0.047) given in Table 6. Patients were closely monitored for potential side effects, including hypotension and bradycardia, in both groups. However, no instances of hypotension or bradycardia were observed in either group. Only one patient experienced minimal pneumothorax, but it was diligently managed by following up with a chest X-ray, and the pneumothorax gradually resolved over time.

Discussion

The brachial plexus provides only short-term post-operative analgesia, even when longer-acting local anesthetic agents like bupivacaine are used. To extend the duration of analgesia, various adjuvants such as opioids, midazolam, neostigmine, etc., have been investigated. Among the newer drugs, clonidine, and dexmedetomidine have shown promising results in producing anti-nociception when administered intrathecally and epidurally. [9]In light of these findings, this study aimed to assess the effectiveness of dexmedetomidine compared to clonidine as an adjuvant to bupivacaine in the brachial plexus block. The study evaluated parameters such as onset time, duration of analgesia, and sedation. Additionally, hemodynamic variables and the number of rescue analgesics required within the first 24 hours after the procedure were also investigated. The study comprised a total of 40 patients aged between 18 and 55 years, with 20 patients in each group. Group C, receiving bupivacaine with clonidine, had a mean age of 37.5 ± 10.55years, while Group D, receiving bupivacaine with dexmedetomidine, had a mean age of 35.81 ± 8.55years. Therefore, both groups were similar in terms of age. The main findings of the study are the combination of bupivacaine and dexmedetomidine led to a significantly faster onset of sensory block and motor block when compared to the combination of bupivacaine and clonidine. The onset of sensory block was 12.22 ± 2.30 minutes in group C and 9.55

± 1.2 minutes in group D. Similarly, the onset of motor block was 14.2 ± 1.56 minutes in group C and 11.9 ± 0.88 minutes in group D.

Previously, clonidine was primarily used for its antihypertensive properties. Its central effects are mediated through α2-adrenoceptors located at the locus coeruleus and the dorsal horn of the spinal cord. However, the specific peripheral effects of clonidine are less apparent due to the absence of these adrenoceptors on the axon of normal peripheral nerves. [10]The action of clonidine in peripheral nerve blocks involves four proposed mechanisms. Firstly, it may induce centrally mediated analgesia. Secondly, it may exert vasoconstrictive effects through α2β adrenoceptor receptors. Thirdly, it can directly act on the peripheral nerve. Lastly, it may attenuate the inflammatory response. [11]The direct impact of clonidine on the nerve can be better understood by referencing a study conducted by Dalle et al. [12] They suggested that clonidine enhances activity-dependent hyperpolarization generated by the Na/K pump, thereby increasing the threshold for initiating the action potential. This process leads to a slowing or blockage of nerve conduction.

In their meta-analysis of randomized controlled studies, DM Popping et al. [13] demonstrated that the positive impact of clonidine on the duration of analgesia was observed across all tested local anesthetics. Another study conducted by Brumett et al. [6] revealed that dexmedetomidine increases the duration of bupivacaine anesthesia and analgesia without causing any nerve damage. Histopathological evaluation of the nerve axons in both the control and combination groups showed normal results. In a separate study, the analgesic effect of peripheral perineural dexmedetomidine, when added to ropivacaine, prolonged the duration of analgesia through the enhancement of the hyperpolarization-activated cation current. This enhancement prevents the nerve from returning to its resting membrane potential from a hyperpolarized state, thereby inhibiting subsequent firing. [6] Clonidine also inhibits compound action potentials (CAPs), but its maximum effect was only around 20%.

Esmaoglu et al. [14] conducted a study where they combined dexmedetomidine with levobupivacaine for axillary block, and their findings demonstrated that this combination resulted in a shortened onset time for both sensory and motor blocks, as well as an extended duration of the block and postoperative analgesia. This effect might be attributed to a reduction in norepinephrine release, leading to α2 receptor-independent inhibitory effects on nerve fiber action potential. Similarly, our study also revealed faster onset times for sensory and motor blocks in group D compared to group C, and this difference was statistically significant. Moreover, the duration of analgesia was significantly prolonged in group D compared to group C. In our investigation, we compared the effects of adding clonidine (Group BC, 1 μg/kg) and dexmedetomidine (Group D, 1 μg/kg) to bupivacaine in brachial plexus block. The results indicated that all patients in both groups were comparable concerning their demographic profiles. Additionally, with these doses, the patients in both groups maintained stable hemodynamics throughout the study.

In Group D, none of the patients required intraoperative sedation, and they remained comfortable throughout the surgery with easily arousable sedative effects. This can be attributed to the possibility of some systemic absorption of the drug. α2 agonists induce sedation through their central action, inhibiting the release of substance P at the level of the dorsal root neuron and activating α2 adrenoreceptors in the locus coeruleus. Based on the findings of this study, we propose that dexmedetomidine can be safely utilized in combination with local anesthetics for peripheral nerve blocks. Nevertheless, further trials are necessary to determine the precise dosage and potential neurotoxic effects on human nerves.

Conclusion

The addition of dexmedetomidine to bupivacaine 0.25% has been found to significantly prolong the pain-free period, duration of motor blockade, and sensory blockade when compared to clonidine or the control group. This combination offers the advantage of maintaining hemodynamic stability while keeping the patient calm. Ultrasound-guided supraclavicular block using a low volume of bupivacaine with 1μg/kg dexmedetomidine resulted in adequate blockade and provided effective postoperative analgesia. Additionally, this approach minimizes the side effects that could arise from using high volumes and doses of bupivacaine. Therefore, incorporating dexmedetomidine as an adjuvant to bupivacaine in ultrasound-guided blocks proves beneficial for both intraoperative and postoperative analgesia. This combination can be especially advantageous for long regional surgeries requiring ultrasound-guided blocks.

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