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Efficacy of Dexmedetomidine As an Adjuvant to Ropivacaine Versus Ropivacaine Alone in Ultrasound Guided Axillary Brachial Plexus Block in Upper Extremity Surgeries – A Randomised Controlled Study

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ABSTRACT:

Background: In this study, we wanted to compare the efficacy of dexmedetomidine as an adjuvant to ropivacaine with that of ropivacaine alone, in ultrasound guided axillary brachial plexus block.
Methods: This was a hospital based randomized controlled double blinded study conducted among 68 patients who presented for surgery involving the upper extremities while receiving an axillary brachial plexus block in the Department of Anaesthesiology of a tertiary care centre, after obtaining clearance from Institutional Ethics Committee, and written informed consent from the study participants.
Results: Time of sensory onset and motor onset were statistically significantly higher in cluster R compared to cluster RD (P-value < 0.05). Time of sensory and motor duration, were statistically significantly higher in cluster RD compared to cluster R (P-value < 0.05). The median total rescue analgesia required in 24-hrs, was statistically significantly higher in cluster R when compared to cluster RD (P-value < 0.05).
Conclusion: Adding Dexmedetomidine to Ropivacaine improves post-operative pain relief after ultrasound-guided axillary brachial plexus blocks for upper-extremity procedures.

Keywords: Dexmedetomidine, Ropivacaine, Ultrasound, Axillary Brachial Plexus Block, Upper Extremity Surgeries

1. Introduction

Anaesthesia from a regional block is more targeted, more powerful, and lasts for a longer period of time.[1] Different approaches to the brachial plexus, such as interscalene, supraclavicular, infraclavicular, and axillary, have all been shown to be related with time-efficient anaesthesia, faster recovery, fewer adverse events, better pain relief, and better patient recognition during surgical interventions involving the upper extremities.[2] The axillary brachial plexus block is one of the most popular options due to its convenience, safety, and efficacy.[1] Hirschel initially reported axillary block in nineteen century in 1911, and since then, the procedure and the idea behind axillary block have been refined with the use of various, more modern forms of local anaesthetic medicines. Surgical anaesthesia for the elbow, forearm, and hand can be achieved via an axillary approach by blocking the terminal branches; in addition, an axillary block can induce dermal anaesthesia of the inner upper arm, making it appropriate for torniquet-required operations.[2] The axillary technique has the lowest risk of notable complications and is therefore the safest option. Axillary brachial plexus blocks benefit greatly from ultrasonographic guiding. Compared to the traditional benchmark led technique, ultrasonography is more adapted to the axillary block because of the wide anatomical variability in the location of arterial and neurological systems. Block effective time, success of block rate, initiation time, vascular piercing, and necessary amount of local anaesthetic have all been found to decrease with the use of ultrasonography guidance.[2]

Regional anaesthesia with long acting local anaesthetics is beneficial for effective post-operative pain control.[3] Patient satisfactionssss, post-operative complication, recovery time, rehabilitation time, and overall treatment costs, all may benefit from better pain management after surgery. Ropivacaine and bupivacaine, both are of amino-amide class of local anaesthetic drugs, though they have same mechanism of action as other local anaesthetics. There are some differences in their structural, physiochemical, pharmacokinetic and pharmacodynamic properties. Ropivacaine is pure s enantiomer, whereas bupivacaine is R and S enantiomer of same class. Ropivacaine organically shares similarities with bupivacaine but is less harmful to the heart and nervous system, and blocks sensory nerve fibres more easily than motor ones. Ropivacaine, unlike bupivacaine, which is also used for peripheral nerve blocks, has a secure cardiac function. It is a multi-functional blocker, inhibiting both sensory and motor functions. The effects of local anaesthetic are enhanced by the inclusion of adjuvant, which speeds up the initiation of action, increases the period of effect, and provides post-operative pain relief. When used with a local anaesthetic, an adjuvant can increase the effectiveness of the analgesic effect and shorten the time of onset. Dexmedetomidine is an α-2 adrenergic agonist that is used as an adjuvant to local anaesthetics. In differentiation to clonidine, another α- adrenergic agonist, dexmedetomidine has an affinity for the alpha 2 adrenoreceptor that is eight times higher. It works more quickly, lasts longer, and reduces pain after surgery. Hence, the objective of this research work is to correlate the efficacy of dexmedetomidine as an adjuvant to ropivacaine and ropivacaine alone in ultrasonography guided axillary brachial plexus block.

Aims and Objectives

- To evaluate the post-operative analgesia with dexmedetomidine as an adjuvant to ropivacaine versus ropivacaine alone.
- To evaluate the effect of dexmedetomidine as an adjuvant to ropivacaine to Ropvacaine alone in ultrasound-guided axillary brachial plexus block with respect to onset of sensory and motor block.

- To evaluate duration of sensory and motor blockade with dexmedetomidine as an adjuvant to ropivacaine to Ropvacaine alone in ultrasound-guided axillary brachial plexus block.

2. Methods

This was a hospital based randomized controlled double blinde study conducted amongst 68 patients who presented for surgery involving the upper extremities while receiving an axillary brachial plexus block to the Department of Anaesthesiology of Tertiary Care Centre, after obtaining clearance from Institutional Ethics Committee and written informed consent from the study participants.

Inclusion Criteria

- American Society of Anaesthesiologists (ASA) physical status I/II
- Age above 18 years up to 70 years
- Patients posted for upper extremity surgeries
- Body mass index (BMI) of < 30 kg/m2.

Exclusion Criteria

- H/o allergy to study drug.
- Patient not willing to participate.

Statistical Methods

- Results for continuous variables were provided as probability standard deviation (SD) across two research groups, whereas data on categorical variables were presented as n (percent of instances).
- Chi-square or fisher's exact probability test for 2 x 2 contingency tables was used to examine whether or not there was a statistically notable variation in the allocation of categorical variables between the two study groups. The statistical significance of the difference between the both groups' probabilities on continuous variables was examined using the independent sample t test.
- Before using t test to study variables, we first ensured that they satisfied the assumption of normality. Without normality, we utilised non-parametric tests that were designed specifically to determine whether or not there were probability full differences between the groups.
- The threshold for statistical significance was set at a P value of less than 0.05. Hypothesis were developed using two-tailed alternatives to the null hypothesis (hypothesis of no difference).
- All of the information was analysed statistically using SPSS for Windows (version 22.0, IBM).

3. Results

	Cluster R (n = 34)		**Cluster RD (n = 34)**		**P-Value**
Time of Onset (Min)	Probability	SD	Probablity	SD	
Sensory onset	20.65	1.55	16.94	1.41	0.001^{***}
Motor onset	24.38	1.10	20.56	1.31	0.001^{***}
Values are probability and SD, P-value by independent sample t test. P-value < 0.05 is considered to be statistically notable. ***P – value < 0.001.					
Inter-cluster Differentiation of Probability Time of Sensory and Motor Onset					
Table 1					

Allocation of probability time of sensory onset was notably higher in cluster R compared to cluster RD (P-value < 0.05). Allocation of probability time of motor onset was notably higher in cluster R compared to cluster RD (P-value < 0.05). Hence, this was found to be statistically significant.

	Cluster R (n = 34)		**Cluster RD (n=34)**		**P-Value**
Time Duration (Min)	Probability	SD	Probability	SD	
Sensory duration	440.15	18.03	661.32	38.66	0.001***
Motor duration	346.91	16.24	508.53	40.33	0.001***
Values are probability and SD, P-value by independent sample t test. P-value < 0.05 is considered to be statistically notable. ***P-value < 0.001.					
Inter-cluster Differentiation of Probability Time of Sensory and Motor Duration					
Table 2					

Allocation of probability time of sensory duration is notably higher in cluster RD compared to cluster R (P-value < 0.05). Allocation of probability time of motor duration is notably higher in cluster RD compared to cluster R (P-value < 0.05). Hence, this was found to be statistically significant.

	Cluster R (n = 34)		**Cluster RD (n = 34)**		**P-Value**
Parameter	Median	Min - Max	Median	Min - Max	
Total rescue analgesia (mg)	1050.00	1050 – 1050	50.00	0 – 1050	0.001***
Values are median and min - max, P-value by Mann-Whitney U test. P-value < 0.05 is considered to be statistically notable. ***P-value < 0.001.					
Inter-cluster Differentiation of Median Total Rescue Analgesia Required in 24-hours					
Table 3					

Allocation of median total rescue analgesia required in 24-hours is notably higher in cluster R compared to cluster RD (P-value < 0.05). Hence, this was found to be statistically significant.

4. Discussion

Bernucci F, Gonzalez A,Finlayson R et al.[4] in 2012 conducted research comparing ultrasound-guided axillary brachial plexus blocks administered using percutaneous catheters versus perineural catheters. Success rates and overall anaesthesia-related timeframes are similar for the ultrasound-guided perivascular and perineural axillary brachial plexus block. Since it requires fewer needle passes and less time to conduct than ultrasound-guided axillary brachial plexus block, the perivascular method is a convenient option.

Ranganath A, Srinivasan K K, Iohom G et al. in 2014 among the several approaches to axillary brachial plexus block (ABPB), including paraesthesia-seeking, nerve-stimulating, perivascular, and trans-arterial procedures, ultrasonography guided ABPB was carried out. They found that, among the four methods for blocking the brachial plexus, ultrasound-guided axillary brachial plexus block was the easiest and safest. Using ultrasound significantly increases the success rate, shortens the onset time, and decreases the volume of local anaesthetic medication needed for effective block.

Also Liu FC et al.[5] conducted research comparing ultrasound-guided axillary brachial plexus block versus nerve stimulator-guided axillary brachial plexus block for effectiveness. They came to the conclusion that ultrasound-guided axillary brachial plexus block was superior to conventional techniques in terms of both the quality and safety of the sensory and motor

blockades it produced. Our research required an axillary brachial plexus block, thus we opted to employ ultrasound to accomplish this.

Gaurav Kuthiala et. al.[6]Compared to bupivacaine and its congener levobupivacaine, ropivacaine has similar efficacy and effects when used for peripheral nerve blocks, the authors write. Thus, we assumed that ropivacaine was employed in our experiment.

Shailendra Modak et. al.[7] as a result, ropivacaine 0.5 % is a secure replacement for bupivacaine 0.5 % in the supraclavicular block. In addition, the onset or duration effects of the block were not enhanced by increasing the concentration of ropivacaine from 0.5 % to 0.75 %, as found by Stephen M. Klein et. al.[8] As a result, a ropivacaine concentration of 0.5 % was used for this investigation.

Mamta Chadha et. al.[9] sensory and motor block onset times for 20 mL and 35 mL of 0.5 % ropivacaine for supraclavicular brachial plexus block for upper limb surgery were found to be comparable.

AnuKewlani et al.[10] ultrasound-guided costo-clavicular block: Determining the median effective volume of 0.5 % ropivacaine. They determined that a costoclavicular block guided by ultrasonography is likely to be successful with a 19-ml dosage of 0.5 % ropivacaine, allowing for safe and sufficient surgical anaesthetic. So, we decided to use 19 ml volume of 0.5 % ropivacaine concentration for our study.

A special mode of action characterises dexmedetomidine. It triggers activity in the locus ceruleus.[11] The sedative and hypnotic effects are the consequence of presynaptic activation of alpha-2 aadrenoceptors in the locus ceruleus.[12] Alpha-2 adrenoceptors are key regulators of nociceptive neurotransmission, and stimulating them stops the spread of pain signals, resulting in analgesia. When alpha-2 receptors are activated post-synaptically in the central nervous system, it slows the heart rate, producing bradycardia.[13]

By 2010 Esmaoglu et al.[14] Dexmedetomidine was found to increase the duration of levobupivacaine-induced axillary brachial plexus block.

Tripathi et al.[15] in 2016 brachial plexus block for upper limb surgery, comparing the effects of bupivacaine with and without the addition of dexmedetomidine and clonidine. They determined that dexmedetomidine not only speeds up the onset of sensory and motor block, but also boosts anaesthesia and analgesia quality and lengthens the duration of anaesthesia and analgesia.

Bangera A, Manasa M, Krishna P et al.[1] in 2016 examined axillary brachial plexus block with and without dexmedetomidine and ropivacaine. They determined that adding dexmedetomidine to ropivacaine sped up the onset of anaesthesia and prolonged the relief of pain. In addition, it provides a safe and reliable method of anaesthetic for forearm and/or hand procedures, as well as excellent hemodynamic stability and post-operative analgesia.

Therefore, in our experiment, we added ropivacaine with dexmedetomidine as an adjuvant.

Gupta et al.[16] found that 5.0 μg of dexmedetomidine combined by ropivacaine intrathecally causes satisfactory relief of pain.

Keplinger M et al.[17] in his study used 20 to 150 μg/kg dose of dexmedetomidine for peripheral nerve block, but it results in high rate of side effects such as decrease heart rate and sedation. However, with 1 μg/ kg of dexmedetomidine, they observed less side effects and better pain relief. Hence, for our study we opted for 1 μ/kg dose of dexmedetomidine.

This study was done on 68 individuals scheduled for upper extremity operative procedure by axillary brachial plexus block at a tertiary care center who were randomized equally into two clusters, 34 patients gets USG guided 19 ml of 0.5% ropivacaine and 1 ug/kg dexmedetomidine (Cluster RD) (study Cluster) and 34 received USG guided 19 ml of 0.5 % ropivacaine and 1 ml of normal saline cluster R (control Cluster). The clusters were approximated with respect to age, gender, BMI, ASA, and hemodynamic parameters, which shows no statistically notable variant among the two clusters.

Visual Analogue Scale

VAS is a scale with markings from zero to ten with zero being no pain to 10 being the extreme pain. Preoperatively all the participants were taught about VAS and its use in analysing pain. In this study, we found the allocation of probability pain score (VAS) at 3.5 hr, 4 hr, and 6 hr in cluster R (control cluster) were 0.62 +/- 0.74, 1.59 +/- 1.13, 3.38 +/- 0.89 and cluster RD (study cluster) were 0.00 +/- 0.00, 0.26 +/- 0.57, 1.32 +/- 1.32 and is notably higher in cluster R (control cluster) compared to cluster RD (study cluster) (P-value < 0.005).

The probable explanation of better analgesia in the dexmedetomidine group (group RD) is because of the dexmedetomidine which induces vasoconstriction via α2 adrenoceptor, causing vasoconstriction around the site of injection, delaying the absorption of local anaesthetic drug and hence prolonging its effect.

Sane et al.[18] pain scores on a visual analogue scale (VAS) were reported to be 0.633, 2.633, 3.313, 6.017, and 5.11 in the control cluster (getting just bupivacaine) and 0.47, 1.14, 3.23, 5.12, and 3.92 in the intervention cluster (receiving bupivacaine plus dexmedetomidine). This difference in patient pain assessment was significant over all research hours in the intervention cluster, with a two-way repeated-measure ANOVA test yielding a P-value of 0.001.

Modh DB et al.[19] cluster NS (got 10 ml lignocaine 2 % + 20 ml bupivacaine 0.5 % + 1 ml normal saline) had significantly higher VAS scores than cluster D (received 10 ml lignocaine 2 % + 20 ml bupivacaine 0.5 % + 1 g/kg of dexmedetomidine) did after surgery.

Akhondzadeh et al.[20] found a statistically significant difference between the two clusters in the VAS pain levels after surgery when comparing lidocaine alone to lidocaine + dexmedetomidine in ultrasound guided supraclavicular block (P - 0.001). After comparing pain ratings with and without dexmedetomidine, they discovered that lidocaine alone cluster was more effective.

NazaninHashemi et al.[21] discovered that VAS scores at 4, 8, and 24 hours post-op for the dexmedetomidine cluster were 1.20.4, 2.90.5, 3.90.5, 4.60.5, respectively; and that scores at the same time points for the fentanyl cluster were 2.40.6, 3.60.5, 4.50.5, 4.70.5. Significantly higher VAS scores poor cluster performance in terms of dexmedetomidine (P 0.001). Our findings mirrored those of the previous study.

First Rescue Analgesia Duration

Time to first rescue analgesia, or VAS > 422, is defined as the amount of time between block performance and the initial request for analgesia. Allocation of probability time for first rescue analgesia was determined to be 8 +/- 2.31 hours in cluster R (control cluster) and 13.05 +/- 2.40 hours in cluster RD (study cluster), with the latter value being statistically significantly greater (P 0.05).

Reason being the dexmedetomidine stimulates alpha-2 adrenoceptors, which is an important modulator of nociceptive neurotransmission that terminates the propagation of pain signals leading to analgesia. Also dexmedetomidine induces vasoconstriction via α2 adrenoceptor, causing vasoconstriction around the site of injection, delaying the absorption of local anaesthetic drug therefore prolonging its analgesic effect. Therefore the first rescue analgesia duration was more in the study group (group RD).

Similar findings were reported by Sane et al.[18] who determined that the average time from the onset of pain and the first request for analgesia was 308 109. 14 minutes in the control cluster and 458 205. 43 minutes in the intervention cluster. When comparing the intervention and control clusters, a statistically significant difference (p = 0.001) was found in the time between the patient's initial request for analgesia and its receipt.

Cluster D (levobupivacaine and dexmedetomidine) had a significantly longer duration to first analgesic usage compared to cluster L (levobupivacaine; P 0.01), as determined by research by K. Kaygusuz et al.

BangeraA et al. Analgesia lasted for a clinically significant 764.38 110.275 minutes after using ropivacaine plus dexmedetomidine, but only 576.88 76.306 minutes when using ropivacaine alone. In the same vein, our research also came to a similar conclusion.

Total Rescue Analgesia Required in 24-Hours

Total rescue analgesia required is described as the number and dose of analgesics required in the first 24 hours of post-operative period.[22] In this study, we found the allocation of median total rescue analgesia (Inj tramadol 50 mg and inj Paracetamol 1000 mg) required in 24-hrs in cluster R (control cluster) is 1050.00 mg and in cluster RD (study cluster) is 50.00 mg and is notably higher in cluster R compared to cluster RD (P-value < 0.05). Because dexmedetomidine is more selective α-2 agonist which has been added to local anaesthetic agents for axillary brachial plexus block as dexmedetomidine is eight times more specific for α-2 adrenoreceptor with α-2: α-1 selectivity ratio of 1620:1, compared with 200:1 for clonidine, especially for the 2a subtype which makes dexmedetomidine more effective than clonidine for analgesia.[23] A similar finding was given by Sojitra et al.[24] that Probability total analgesic requirement (inj. Diclofenac sodium) was notably less in 48 hours after performing axillary block in cluster 1 (Dexmedetomidine cluster), was 250 ± 35.95 mg as compared to cluster 2 (Control cluster) was 405 ± 42.24 mg. ($p < 0.01$).

Onset of Sensory and Motor Block

A sensory block's onset is the point in time between the commencement of the block and the point at which it is fully resolved. Start of muscle is the amount of time that passes between when the last dose of local anaesthetic is given and full motor blockade. Cluster R (the control group) had an allocation of the probability time of sensory beginning of 20.65 +/- 1.55 minutes, whereas cluster RD (the study group) had an allocation of 16.94 +/- 1.41 minutes, a statistically significant difference (P0.05). Cluster R's (the control cluster) allocation of probability time of motor initiation is significantly greater than cluster RD's (the study cluster) at 24.38 +/- 1.10 (P 0.05) The sensory and motor onset was significantly early in Group RD (study group). because the direct action of dexmedetomidine on the nerve, by enhancing activity-dependent hyperpolarisation generated by the Na/K pump during repetitive stimulation, increases the threshold for initiating the action potential causing slowing or blockage of conduction, which results in faster onset of action. In a similar vein, Manasa et al. showed that the onset time of upper extremity sensory block in the intervention cluster RD was shorter than in the cluster R, with the difference being statistically significant (p 0.001). More importantly, the R cluster had a statistically significant (p 0.001) earlier onset time for motor block in the upper extremities compared to the RD cluster. Bangera A et al. Cluster RD (the study cluster) had a significantly (p 0.001) earlier sensory (16.13+/- 4.001 min) and motor (18+/- 3.889 min) onset than cluster R (the control cluster), where these times were 20.5+/- 3.889 min and 23.13+/- 3.337 min, respectively. Our research yielded similar findings. Dai w et al.[25] In addition, a research was conducted to evaluate the efficacy and safety of adding dexmedetomidine to ropivacaine for a brachial plexus block. The research included a pooled analysis of data from randomised trials. Dexmedetomidine was reported to speed up the onset of sensory and motor block compared to ropivacaine alone. Significant (P 0.05) in the statistical sense. NazaninHashemi et al.[21]observed that the onset to onset of sensory block (min) was 8.7±0.8 and time to achieve motor block (min) was 11.8±1.2 which was notably early in 0.5% ropivacaine plus dexmedetomidine cluster compared to 0.5 % ropivacaine plus fentanyl cluster. That is the dexmedetomidine shortened the time to onset of sensory ($P = 0.001$) and motor block ($P = 0.001$). Similar results were found in our study.

Duration of Sensory and Motor Blockade

The length of a sensory block is measured from the moment it begins to the moment it is fully resolved. How long a motor block lasts measures the length of time that passes between the onset of a full motor block and the return of full hand and forearm function. 27. Cluster R (the control cluster) had an allocation of probability time of sensory length of 440.15 +/- 18.03 minutes, whereas cluster RD (the study cluster) had a value of 661.32 +/- 38.66 minutes; this difference was statistically significant (P 0.05). In a related study, Manasa et al. also came to a similar conclusion. Upper-extremity sensory block lasted 494.3870.64 minutes in the R cluster and 677.2599.664 minutes in the RD cluster. The RD cluster had a significantly longer average anaesthetic time than the R cluster did (p 0.001). Duration of motor block was much shorter in the R cluster (526.2570.229) than in the RD cluster (712.8889.32), with the difference being statistically significant (p0.001). Bangera A et al. Cluster RD had a sensory block that lasted 677.25 99.64 minutes, whereas cluster R's lasted 494.38 70.64 minutes. Cluster RD had significantly longer sensory block times compared to cluster R (P 0.001). Cluster RD had a motor block that lasted 712.88 89.32 minutes, whereas cluster R's was 526.25 70.229 minutes. Statistical analysis showed that the longer length of motor block in cluster RD compared to cluster R was statistically significant (P - 0.001). Our research yielded similar findings.

5. Conclusion

To conclude, we found that adding dexmedetomidine to ropivacaine improved post-operative pain relief after ultrasound-guided axillary brachial plexus blocks for upper-extremity procedures; this combination is now under standard practise.

6. References

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