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Dr. Upasana Bezbaruah
Senior Resident, Dr. Baba Saheb Ambedkar Medical College, New Delhi, India

Dr. Abhijit Khaund
Senior Consultant, Department of Anaesthesiology, Jaipur Golden Hospital, New Delhi, India

Corresponding Author:
Dr. Upasana Bezbaruah
Senior Resident, Dr. Baba Saheb Ambedkar Medical College, New Delhi, India

Comparison of intravenous and perineural dexmedetomidine as an adjunct to levobupivacaine in supraclavicular brachial plexus block: A prospective randomised study

Dr. Upasana Bezbaruah and Dr. Abhijit Khaund

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Abstract
Introduction: Dexmedetomidine, an selective alpha-2 agonist, has been proposed as a safe and effective adjunct capable of extending the duration of a single-shot block. The present study aimed to investigate the efficacy of IV dexmedetomidine in improving the duration and quality of ultrasound guided brachial plexus block as compared to perineural use of dexmedetomidine as adjunct.
Material and Methods: This was a randomized and double blind prospective study. 70 patients undergoing unilateral upper limb surgery under supraclavicular brachial plexus block were inducted. All the patients received 20 ml infusion of either the study drug or placebo as per group allocation over 20 minutes just prior to execution of brachial plexus block.
Results: Mean duration of onset of sensory and motor block in both the groups were found to be similar (p=0.692). Both groups showed longer onset time for motor blockade as compared to onset time of sensory block. Perineural group showed significantly longer sensory & motor block as compared to DIV group. The time point for demand for first rescue analgesia, perineural group showed considerably longer duration of analgesia than group DIV.
Conclusion: Dexmedetomidine (0.5 mcg/kg body weight) administered either perineurally or as IV bolus at the time of execution of brachial plexus block can considerably prolong both sensory and motor blockade duration without much influence on duration of onset of block. Perineural dexmedetomidine provides longer duration period of analgesia than intravenous route. But IV dexmedetomidine provides better intraoperative sedation and patient comfort as compared to equivalent perineural dose.

Keywords: Dexmedetomidine, perineural, intravenous, efficacy, brachial plexus block

Introduction
Upper limb surgeries are mostly performed under peripheral blocks such as brachial plexus blocks. Peripheral nerve blocks not only provide intraoperative anaesthesia but also extend analgesia in the post-operative period without any systemic side-effects [1]. Supraclavicular brachial plexus block has been the choice of anaesthesia for upper limb surgeries over the past several decades. Over the years an array of techniques and newer drugs with higher safety profiles have been introduced, which has led to decreased mortality and morbidity in patients and at the same time eased the life of clinicians [2].
Dexmedetomidine, an selective alpha-2 agonist, has been proposed as a safe and effective adjunct capable of extending the duration of a single-shot block. Hyperpolarization-activated cation currents normally bring neurons back to the resting potential and normal functional activity during the refractory phase in an action potential. It has been postulated that by blocking these currents, dexmedetomidine can accentuate inhibition of neuronal conduction and produce analgesia [3]. A meta-analysis demonstrated that dexmedetomidine in combination with local anaesthetics increases postoperative analgesia for around [5]. hours. However, there are higher risks of intraoperative hypotension and bradycardia [4].
Perineural dexmedetomidine when added to levobupivacaine has shown to potentiate its effects, providing better quality of anaesthesia and postoperative analgesia [2]. Currently available literature does not confirm the superiority of either perineural or IV use of dexmedetomidine upon each other while used as adjunct. But utility of IV dexmedetomidine as a premedication and intraoperative sedation agent along with regional blocks is well

established. So, if its efficacy in influencing block quality and enhancing analgesic property of LA can be confirmed, IV dexmedetomidine would be the definite choice as adjunct. Thus, the current study was designed to evaluate the efficacy of IV dexmedetomidine in positively influencing supraclavicular brachial plexus block profile as compared to that of perineural use as mixture with local anaesthetic.

Material and methods Study design
Prospective randomized double-blind trial.

Study duration: The study was conducted for a duration of 22 months i.e., January 2019 to October, 2020.

Study population
Subjects planned for unilateral upper limb surgery under supraclavicular brachial plexus block who met the inclusion criteria.

Inclusion and exclusion criteria
Patients of either gender in the age group of 20 to 70 years with ASA grade of 1 & 2 who have consented for participation were included. Patients who had bleeding disorders/on anticoagulant therapy, prior history of brachial plexus injury, peripheral neuropathy, failed block, pregnant women and ASA grade 3 & 4 were excluded.

Sample size calculation and group division
Assuming a mean postoperative analgesia free period of dexmedetomidine IV as 520 mins and dexmedetomidine perineurally as 660 mins with inferiority margin of 65 minutes, type 1 error of 5% and power of 80%, the optimum sample size was calculated as 32 subjects in each study group. Dexmedetomidine intravenous group (DIV) received 0.5 mcg/kg body weight as an 20 ml of IV infusion 20 minutes prior to brachial plexus block and 5ml of normal saline as placebo was added to 20ml of 0.5% levobupivacaine at the time of giving brachial plexus block. In the other group (DP), patients received placebo which was given as 20 ml of IV infusion prior to brachial plexus block and 0.5mcg/kg body weight of dexmedetomidine diluted to 5 ml volume was mixed with 20 ml of 0.5% levobupivacaine for inducing brachial plexus block.

Randomization and blinding
Block randomization was done by sealed envelope method in block sizes of 4, 6 and 8. Stacks of identical opaque sealed envelopes containing either 4, 6 or 8 in number were created as per block size. In each block an equal number of envelopes contained either A or B labels where one label represents IV dexmedetomidine group and the other label represents Perineural group. Once a patient gave consent to enter the trial, an envelope was opened randomly from the chosen block and the patient was offered the allocated group. Neither the observer nor the patient were aware of which label represented which group making the study double blinded.

Study variables: Sensory and motor blockade assessed using modified Bromage scale. The duration of onset of sensory & motor blockade, duration of sensory and motor block was also observed. The time taken from administering the brachial plexus block till the time of demand of first rescue dose of analgesia (duration of post operative analgesia) was noted. Other parameters such as hemodynamic trends (heart rate, systolic and diastolic blood pressure) and intraoperative sedation scores by Ramsay sedation scale were also recorded.

Statistical analysis
The data was entered in Microsoft excel spreadsheet and analyzed using SPSS software version for Windows. Categorical data were represented as frequency and proportions whereas continuous data were presented as mean and standard deviation. Test of normality was assessed by Kolmogorov Smirnov test. Independent sample t-test was used to compare continuous data (Mann Whitney test where normality was violated). Chi-square test was used to see association between nominal variables. Point of statistical significance was considered when p-value was less than 0.05.

Results
Our study was conducted on 70 patients who underwent supraclavicular brachial plexus block with levobupivacaine along with either perineural (Group DP n=35) or intravenous dexmedetomidine (Group DIV, n=35). Mean age of both groups was similar (p=0.103) with maximum subjects falling in age category of 31-50 years (Table 1). Mean weight were 65.91±10.74 kg and 67.51±9.29 kg in intravenous and perineural group respectively with no significant difference (p=0.666).
Majority of the surgeries performed pertained to Radius and Ulna bone (65.71% and 54.28%) in DIV and DP group respectively. The mean duration of surgery in intravenous and perineural group were 102.86±31.86 and 106.29±35.47 minutes which was not statistically significant (p=0.671). Table 2 is showing the block parameters with their comparison in two study groups.

Table 1: Demographic variables with comparison among study groups

Variable	Category	DIV	DP	p-value*
Age	Upto 30 years	10 (28.5%)	7 (20%)	0.564
	31-40 years	7 (20%)	12 (34.3%)	
	41-50 years	8 (22.8%0	5 (14.3%)	
	51-60 years	6 (17.1%)	8 (22.8%)	
	61-70	4 (11.4%)	3 (8.6%)	
Gender	Female	13 (37.1%)	10 (28.6%)	0.445
	Male	22 (62.9%)	25 (71.4%)	
ASA grade	I	25 (71.4%)	25 (71.4%)	1.00
	II	10 (28.6%)	10 (28.6%)	

*Chi-square test

Table 2: Comparison of duration of sensory and motor block between DIV and DP groups.

Variable	Type	DIV (mean ± sd)	DP (mean ± sd)	P-value*
Duration of onset of block	Sensory	580.86±61.76	642.29±71.09	0.0003
	Motor	548.86±59.74	623.43±74.63	<0.001
Duration of block	Sensory	580.86±61.76	642.29±71.09	0.0003
	Motor	548.86±59.74	623.43±74.63	<0.001

*Independent t-test

Duration of post-operative analgesia between the two groups were 592.86±63.18 minutes and 687.71±71.66 minutes in DIV and DP groups respectively (p=<0.001). Sedation levels were compared between the two groups on Ramsay sedation scale which were found similar at baseline, 30 minutes, 60 minutes, 2 hours and 3 hours. Consumption of Midazolam was lower in DIV group (1.06±0.55) as compared to DP group (2.14±0.73) which was statistically significant (p=<0.001). The comparison of heart rate, systolic and diastolic blood pressure were similar at various time intervals in both study groups.

Adverse events reported were bradycardia, hypotension, and sedation which were comparable in both groups. There were no adverse events in DIV (74.29%) and DP (88.57%) groups.

Discussion

Many studies have independently confirmed the early onset and prolongation of the block along with extension of postoperative analgesia when dexmedetomidine is used perineurally with local anaesthetics as well as with intravenous route. 3-7 Based on the evidence, although some are contradictory, it was hypothesised that dexmedetomidine when administered intravenously can influence the quality of upper limb block in a comparable way to perineural administration.

Distribution of cases across different age bands showed no statistically significant difference (p=0.564). The relatively higher prevalence of trauma in the younger age group was reflected in the age wise composition of study groups.

Regarding duration of onset of both motor and sensory blockade, both the groups show longer onset time for motor blockade as compared to sensory block. Study by Somsunder *et al*. reported shorter time period for both sensory and motor blocks as compared to results of current study. The early onset time could be explained by the larger volume of drug (30 ml) as well as mixture of drugs (2% lignocaine, 10 ml & 0.5% Levobupivacaine, 20 ml) along with higher dose of dexmedetomidine (1 mcg/kg) used for the block [2]. Kathuria *et al*. contradicts these findings and claims through their randomized trial of year 2015 that the sensory and motor block onset was significantly quicker in perineural use of dexmedetomidine as compared to its IV use [6].

In the perineural group, both the sensory block and motor blockade time was considerably high with statistical significance. Studies conducted by Modh *et al*., Das *et al*. and Grajala *et al*. observed similar results [8, 9, 10]. The current study found that mean duration of first demand for analgesia in the postoperative period was significantly higher in the perineural group as compared to intravenous group. This finding is being validated by several studies earlier also [6, 8, 9, 10].

Present study also aimed to assess the contribution of dexmedetomidine to patient comfort by monitoring the level of sedation during surgery. Sedation offered by dexmedetomidine mimics NREM sleep and the patient appears to be deeply sedated but easily arousable as in natural sleep. This is desirable for all surgeries conducted under regional anaesthesia.

IV dexmedetomidine provided sedation and comfort to the patients which was not obvious with perineural administration of similar dose. We could compare our findings with the study of Somsunder *et al.* [2], where they used 1 mcg/kg of dexmedetomidine to levobupivacaine in supraclavicular brachial plexus block both IV and perineurally. The level of sedation was more in IV group when compared with perineural group. The average sedation score (Ramsay Sedation Scale) was observed to be 3.83±0.55 in the intravenous group and 2.38±0.35 in the perineural group.

The current study had some limitations. Smaller sample size and generalizability of dexmedetomidine effect in other peripheral nerve blocks merits the need of larger studies and other nerve block surgeries. Also, the possibility of chronic or rebound pain was also not evaluated the present study.

Conclusion

The study concludes that IV dexmedetomidine administered at the time of execution of brachial plexus block significantly prolongs both motor and sensory block duration as compared to blocks without adjunct. But the magnitude of extension of block duration is less as compared to perineural administration of dexmedetomidine in similar dose. Both the interventions provided long duration of postoperative analgesia. Intravenous dexmedetomidine also provided better intraoperative sedation and patient comfort. In overall, IV dexmedetomidine as adjunct can provide comparable block duration and postoperative analgesia as perineural dexmedetomidine used at the same dose, with the added advantage of better intraoperative sedation.

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