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A RANDOMISED CONTROLLED TRIAL TO STUDY THE EFFECT OF ADDITION OF LIGNOCAINE VERSUS DEXMEDITOMIDINE ON BLOCK CHARACTERISTICS WITH BUPIVACAINE IN ULTRASOUND GUIDED INFRACLAVICULAR BLOCK

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ABSTRACT

Background: A randomised, double blinded trial was designed to study the effect of addition of dexmedetomidine versus lignocaine to bupivacaine for infraclavicular block with the primary objective of comparing onset time of block and duration of post operative analgesia as secondary objective. **Materials & Methods:** Under ultrasonic guidance, the point of needle puncture was identified and 2 ml of Inj. Lidocaine 2% was infiltrated in the proposed needle tract. The nerve bundle was identified and drug infiltrated in aliquots around each nerve bundle9 according to the groups as proposed in the study.

Group B: 35 ml bupivacaine 0.375% + 1 ml Normal Saline

Group BL: 25 ml bupivacaine 0.375%+ 10 ml lignocaine 2% + 1 ml Normal Saline

Group BD: 35 ml bupivacaine 0.375% + 1 mcg/ kg dexmedetomidine in 1 ml Normal Saline.

Onset of sensory and motor blockade, haemodynamic parameters and side effects were monitored. Time of completion of block was taken as time 0 and all durations were measured thereon. Patients were assessed for loss of sensation to blunt pin prick over C5-T1 dermatomes at every 1 minute for 15 minutes and motor block every 1 minute for 15 minutes. Sensory block was measured by Modified Hollmen score and motor block was assessed using the modified Bromage Scale. Time of onset of sensory block (grade 1) and motor block (Bromage 2) were noted. **Results:** The demographic parameters and preoperative haemodynamics were statistically comparable. The systolic and diastolic blood pressures were statistically lower in group containing dexmedetomidine (BD).The mean heart rate in these groups was also statistically lower. The addition of dexmedetomidine to bupivacaine (BD) provides a statistically significant increase in the duration of analgesia as compared to the addition of lidocaine (BL) ($p<0.001$). The bupivacaine and lidocaine group (BL) had similar duration of analgesia as plain bupivacaine (9.24±3.6 hrs vs 10.22±3.29 hrs.) (p-0.831). **Conclusion:** With a longer duration of analgesia in post operative period. There should be minimum risk of toxicity and haemodynamic alterations. A prolonged motor blockade is undesirable. Addition of dexmedetomidine to bupivacaine provides similar reduction in onset time as addition of lidocaine with a superior duration of post operative analgesia.

KEYWORDS: USG Guided Block, Regional Anaesthesia, Dexmeditomidine, Lignocaine, Bupivacaine.

INTRODUCTION

Infraclavicular block under the guidance of USG is emerging as a safer approach by providing uniform distribution of drugs in closely clustered cords of brachial plexus.[1] Bupivacaine, a long acting local anaesthetic with slow onset and lignocaine, a short acting drug with faster onset, are among the preferred drugs routinely used in regional anaesthesia.[2,3] Endorsed by literature, a mixture of these two is frequently used to improve characteristics of regional block and post operative analgesia.[4] However, these mixtures may predispose the patients to toxicity as it is difficult to calculate the safe dose of local anaesthetic mixture and these may have unpredictable pharmacodynamics due to variable final concentration of each drug.

Further research introduced adjuvants in regional anaesthesia[5,6] to improve block characteristics and prolong the duration of analgesia. Dexmedetomidine, an alpha 2 agonist, potentiates the effect of local anaesthetics through and produces peripheral analgesic effects.[7] There is ample research to support dexmedetomidine as an adjuvant to local anaesthetic agents, hastening the onset, prolonging the duration of

blockade and post operative analgesia. However, the use of adjuvants may also pose clinical and medicolegal challenges due to the administration through off label route use. In addition, the long term effects of the drug are unknown.

Literature search reveals studies comparing block characteristics using addition of adjuvant to a single local anaesthetic or a mixture of local anaesthetics. However, it is not known whether addition of local anaesthetic or an adjuvant will provide superior brachial plexus anaesthesia and analgesia. Therefore, a randomised, double blinded trial was designed to study the effect of addition of dexmedetomidine versus lignocaine to bupivacaine for infraclavicular block with the primary objective of comparing onset time of block and duration of post operative analgesia as secondary objective.

MATERIALS AND METHOD

After the approval from scientific and ethics committees (BPSGMCW/RC243/IEC/17), a randomised, double-blinded trial was conducted at a rural tertiary care hospital. The trial is registered with CTRI, trial number CTRI/2017/12/011001.

After thorough pre anaesthetic check up and written informed consent, 87 patients of ASA grade I to III, in the age group 18-65 years posted for surgeries of arm around and distal to the elbow were recruited for this study. Patients were randomly distributed into four groups by closed envelope method. Both the patient and the observer were blinded to the study group.

Patient unwillingness, existing chronic diseases and coagulation disorders, known history of allergy, pregnancy and morbid obesity were exclusion criteria for the study.

All the patients were kept fasting for 6 hours prior to surgery. An IV line was secured in the unaffected limb and injection Ringer lactate was infused at the rate calculated by Holiday-Segar[8] formula in the pre-operative room. After shifting the patients to the operation theatre, vital parameter monitoring was initiated and premedication given with injection midazolam 0.03mg/kg IV.

After standard aseptic precautions, ultrasonography (USG) was conducted using linear transducer of Sonosite™ micromax® ultrasound machine with frequency of 5-13 Hz, in parasagittal orientation placed over coraco-clavicular groove in supine position. Under ultrasonic guidance, the point of needle puncture was identified and 2 ml of Inj. Lidocaine 2% was infiltrated in the proposed needle tract. The nerve bundle was identified and drug infiltrated in aliquots around each nerve bundle[9] according to the groups as proposed in the study.

1. Group B: 35 ml bupivacaine 0.375% + 1 ml Normal Saline
2. Group BL: 25 ml bupivacaine 0.375%+ 10 ml lignocaine 2% + 1 ml Normal Saline
3. Group BD: 35 ml bupivacaine 0.375% + 1 mcg/ kg dexmedetomidine in 1 ml Normal Saline.

Pulse rate, non-invasive blood pressure, oxygen saturation (SpO_2) were monitored throughout the procedure and recorded at every 5 minutes interval. Oxygen was supplied via face mask. In case of any adverse drug reaction or if patient's safety was compromised, the randomisation codes were broken and necessary measures to ensure patient safety were carried out.

Onset of sensory and motor blockade, haemodynamic parameters and side effects were monitored. Time of completion of block was taken as time 0 and all durations were measured thereon. Patients were assessed for loss of sensation to blunt pin prick over C5-T1 dermatomes at every 1 minute for 15 minutes and motor block every 1 minute for 15 minutes.

Sensory block was measured by Modified Hollmen score and motor block was assessed using the modified Bromage Scale. Time of onset of sensory block (grade 1) and motor block (Bromage 2) were noted.

In case of inadequate sensory blockade in any one nerve distribution even 30 mins after the administration of block, injection fentanyl 2mcg/kg was given. The patients were observed for pain till 10 min after administering fentanyl. If patient complained of pain in two or more nerve distributions or even 10 mins after injecting fentanyl, then block was considered as failure, general anaesthesia was given and patients excluded from trial.

In case the surgical incision had to be extended beyond the coverage of infraclavicular block, field block was given with 10 ml of 2 % lidocaine. Surgery was allowed to begin once full surgical anaesthesia (complete sensory block at C5-T1 dermatomes) was established.

Patients were observed intra-operatively for adverse drug reactions, hypotension, bradycardia etc.

Post operatively, haemodynamic parameters, nausea, vomiting, paraesthesia and pain (using Visual Analogue Scale) were monitored for a period of 24 hours at intervals of 1,2,3,4,6,8,12,18 and 24 hour. Analgesia was provided with inj. PCM 1g iv when patients complained of pain (VAS>4).

STATISTICAL METHODS

Sample size was calculated based on previous similar studies.[10-12] The superiority margin was taken at 180 min and expected difference at 191 minutes. With the power of study being 90% and alpha error at 5%, the sample size was calculated to be 28 patients in each

group i.e. a total of 84 patients. To account for dropouts, 87 patients were recruited for the study.

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Non-normally distributed quantitative variables were summarized by median and inter-quartile range (IQR).

For normally distributed Quantitative parameters the mean values were compared between study groups using Independent sample t-test (2 groups) / ANOVA (>2 groups). For non-normally distributed Quantitative parameters, Medians and Inter-quartile range (IQR) were compared between study groups using Mann Whitney U test (2 groups) / Kruskal Wallis test (> 2 groups). The change in the quantitative parameters, before and after the intervention was assessed by paired t-test (In case of two time periods) or one way repeated measures ANOVA (In case of comparison across more than 2 time periods). If statistically significant difference was found in ANOVA, appropriate post-hoc test (LSD/ Bonferroni) was used to assess statistical significance of pair wise comparisons. Categorical outcomes were compared between study groups using Chi square test P value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.

RESULT

A total of 84 patients were included in the analysis; as due to poor visualisation of structures, infra-clavicular block could not be administered to three patients who were excluded from the study. In three cases the surgical anaesthesia was inadequate and these were conducted under general anaesthesia. The final statistical analysis was carried out for 81 patients. Among these, 10 patients required supplementation with fentanyl. Surgical incision was extended beyond the blockade coverage and field block for T2 dermatome had to be given in 4 patients.

Table 1: Comparison of demographic and haemodynamic parameters across the study groups (n=81).

Parameter	Group			p-value
	B(n=27)	BD(n=27)	BL(n=27)	
Age(Years) Mean± std	30.96 ± 12.55	33.63 ± 15.3	32.3 ± 13.19	0.819
Weight(Kg) Mean± std	64.74 ± 9.67	63.26 ± 12.82	65.63 ± 11.52	0.607
Gender				
Male	23 (85.2%)	20 (74.1%)	24 (88.9%)	Not significant
Female	4 (14.8%)	7 (25.9%)	3 (11.1%)	
Baseline heart-rate				
HR (bpm)	81.19±16.53	83.26±11.4	83.93±15.49	0.230
Systolic blood pressure				
Preop	127.85±7.98	131.22±12.37	128.3±13.82	0.704
Intraop 10 min	124.48±7.2	120.54±10.15	125.59±10.66	0.023*
20 min	123.15±9.21	116.27±11.2	125.74±13.82	0.001*
30 min	122.52±8.79	117.54±11.31	122.85±10.15	0.002*
60 min	122.22±8.74	116.58±9.55	123.33±8.94	<0.001*
90 min	120.48±8.66	116.04±9.65	122.42±10.89	0.047*
Post op 0 hr	119±7.78	113.74±9.45	120.19±10.39	0.004*
12 hr	119.37±8.56	117.85±10.78	121.89±9.6	0.035*
Diastolic blood pressure				
Preop	77.48±9.35	80.3±8.63	77.93±10.09	0.525
Intraop 10 min	76.37±7.69	71.85±10.38	76.26±10.73	0.032*
20 min	75.3±8.36	68.74±9.77	76.3±9.59	0.004*
30 min	74.93±7.27	71.3±9.79	75.07±9.22	0.001*
60 min	73.22±8.61	70.3±8.55	74.3±9.83	0.017*
90 min	73.43±8.65	70.17±9.53	74.54±8.63	0.026*
Post op 0 hr	71.96±8.03	68.48±8.8	72.19±8.95	0.020*
12 hr	70.89±8.7	71.04±6.89	73.63±8.39	0.065

As shown in table 1, the demographic parameters and preoperative haemodynamics were statistically comparable. The systolic and diastolic blood pressures were statistically lower in group containing dexmedetomidine (BD).The mean heart rate in these groups was also statistically lower. (Fig: 2).

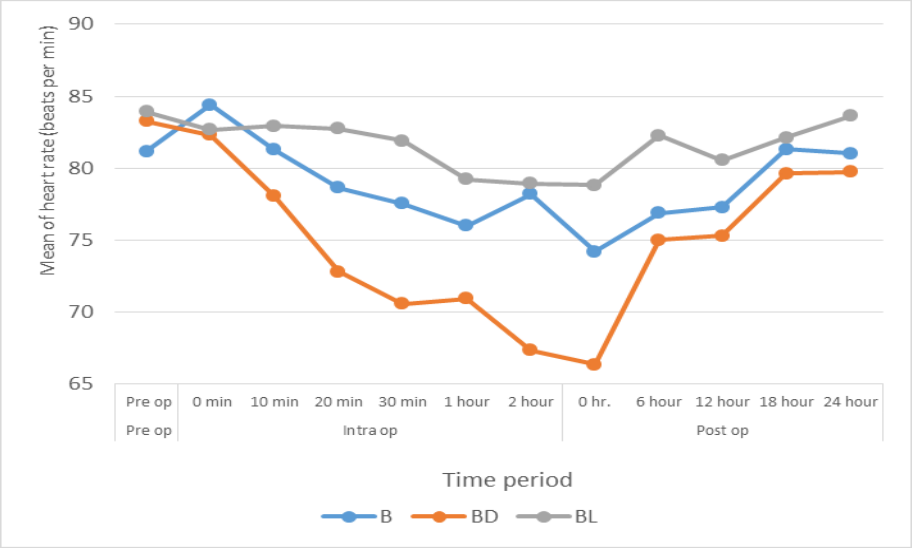

Fig. 1: Trend line diagram for comparison of mean heat rate across the study groups (n=81).

Table 2: Comparison of mean Onset and duration of sensory and motor block and duration of post operative analgesia across the study groups (n=81).

			p value	
	PARAMETERS	**Mean ±std**	**vs BD**	**vs BL**
B	Onset of sensory block (minutes)	10.07±3.35	**<0.001**	**<0.001**
	Onset of motor block (minutes)	13.36±4.17	**<0.001**	**<0.001**
	Duration of analgesia (hours)	11.96±3.6	**<0.001**	**0.831**
BD	Onset of sensory block (minutes)	5.48±2.95		**0.304**
	Onset of motor block (minutes)	7.81±4.13		**0.631**
	Duration of analgesia (hours)	16.87±2.88		**<0.001**
BL	Onset of sensory block (minutes)	4.7±2.49		
	Onset of motor block (minutes)	8.04±4.55		
	Duration of analgesia (hours)	11.76±4.12		

As depicted in table 2, the reduction in onset (sensory and motor) achieved by adding lignocaine to bupivacaine (BL) was statistically comparable to use of dexmedetomidine as an adjuvant (BD) (p value 0.304).

The addition of dexmedetomidine to bupivacaine (BD) provides a statistically significant increase in the duration of analgesia as compared to the addition of lidocaine (BL) (p<0.001). The bupivacaine and lidocaine group (BL) had similar duration of analgesia as plain bupivacaine (9.24±3.6 hrs vs 10.22±3.29 hrs.) (p-0.831).

Table 3: comparison of side effects across the groups.

	B	**BD**	**BL**
Bradycardia (HR<60, requirement of atropine)	Nil	2	Nil
Hypotension	Nil	Nil	Nil
Nausea/ vomiting	Nil	Nil	Nil
Prolonged sensory/ motor blockade (≥24 hrs.)	Nil	Nil	Nil

There were no significant side effects like hypotension, pneumothorax, nausea and vomiting. Sensory and motor blockade for around 24 hours was seen in 1 patient of group BLD. Bradycardia (HR<60 bpm) requiring intervention with inj. Atropine was encountered in 2 patients in group BD.

DISCUSSION

In our study, we observed that addition of dexmedetomidine and lidocaine provided a similar reduction in the onset time of sensory and motor blockade. Though, a mixture of lidocaine and bupivacaine had a faster onset as compared to bupivacaine alone, it had no distinctive advantage when the duration of blockade and post operative analgesia were compared.

In our study, majority of cases achieved adequate surgical anaesthesia. We encountered technical difficulty in muscular patients due to increased depth of area of interest and there was increased vasculature of the muscle. However, as observed by Alan Macfarlen et-al

(2009)[13], placement of a crescent of local anaesthetic around and posterior to the axillary artery provided a reliable blockade in obese and muscular patients even if the plexus could not be easily visualized.

Most studies on brachial plexus block have been conducted using 30-40 ml of drug solution.[14] Dual guidance with ultrasound and peripheral nerve stimulator enhances the efficacy and nerve blockade can be achieved with a lower drug volume.[15] In our study, we administered 36 ml of drug solution in all groups under Usg guidance.

Delay in onset is a limiting factor for long acting anaesthetic agents. Both lignocaine and dexmedetomidine have been found to accelerate the onset of sensory as well as motor blockade when added to a long acting local anaesthetic.[16,17] Lidocaine has intrinsic vasodilator activity resulting in greater absorption of local anaesthetic mixture and decreasing the onset time. On the other hand, the action of dexmedetomidine is mediated by its action on the α2 receptors to produce faster sensory and motor blockade. On comparing BL versus BD, our results demonstrated that both lignocaine and dexmedetomidine provided similar improvement in onset time of bupivaciane brachial plexus block (BL VS BD, p-0.132) yet, the duration of analgesia was significantly prolonged by addition of dexmedetomidine to bupivacaine when compared with addition of lignocaine ($p<0.005$).

Post operative analgesia has been found to be prolonged by 8 hrs in supraclavicular and 4 hours in interscalene block by addition of dexmedetomidine to bupivacaine.[18,19] In a dose of 1 mcg/kg, dexmedetomidine produces minimal sympatholysis and sedation.[20] In our study, addition of dexmedetomoidine to bupivacaine provided analgesia for an average duration of 16 hours. None of the patients in our study exhibited excessive sedation or required supplemental oxygen therapy.

Though we did not encounter any episode of significant hypotension, the mean heart rate and blood pressure were statistically lower in dexmedetomidine containing group (BD). The incidence of bradycardia was 4 out of 27 patients in group BD. Out of these, 2 patients required treatment with inj. Atropine.

Duration of peripheral nerve block depends on the dose of local anaesthetic, lipid solubility and degree of protein binding. Though, lignocaine added to bupivacaine increases the duration of post-operative analgesia by altering the lipid solubility[21], in our study duration of post operative analgesia was statistically comparable in groups B and BL (p-0.803). This may be attributable to lower concentration of bupivacaine in BL versus B and BD groups. Though we did not encounter any adverse effects, there are documented case reports of toxicities after administration of even modest amounts of local anaesthetic combinations.[22,23] These mixtures tend to have unpredictable pharmacodynamics and the risk of toxicity is higher. The rate of absorption of drug depends on the route of injection. Since brachial plexus is a highly vascular area, the risk of inadvertent intravascular injection and systemic absorption is high. In absence of additional data, the toxicities for the drug mixture should be considered additive.

An ideal anaesthetic solution should provide rapid onset of sensory and motor blockade along with a longer duration of analgesia in post operative period. There should be minimum risk of toxicity and haemodynamic alterations. A prolonged motor blockade is undesirable. Addition of dexmedetomidine to bupivacaine provides similar reduction in onset time as addition of lidocaine with a superior duration of post operative analgesia. The risk of local anaesthetic toxicity out-weighs the risk of sympatholysis when comparing the side effects of the two combinations. Even though the long term effects of addition of adjuvant are unknown and the off label route use of dexmedetomidine poses medico-legal challenges, the safety profile and supporting data suggest addition of dexmedetomidine as a better alternative to addition of lidocaine for hastening the onset time and prolonging the duration of analgesia.

LIMITATIONS

The limitation of our study includes use of a standardised volume of drug (36 ml), with different final concentration in all groups. We also found that within the groups, the duration of analgesia was longer in patients with lower BMI. Moreover, administration of rescue therapy may have confounded the intensity of pain and duration of post operative analgesia. Over and above, the superior results of BD versus BL may be attributed to higher concentration of bupivacaine in BD group.

FURTHER RESEARCH

Addition of lignocaine and dexmedetomidine to compare the effects on block characters can be studied with same concentration of bupivacaine in both the groups.

CONCLUSION

Addition of lignocaine to bupivacaine hastens the onset of sensory and motor blockade in infrclavicular block akin to addition of dexmedetomidine with added benefits of increased duration of sensory and motor blockade; longer post operative analgesia and decreased analgesic requirement in post operative period.

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