ISSN 2515-8260 Volume 09, Issue 07, 2022

COMPARISON BETWEEN FENTANYL AND DEXMEDETOMIDINE AS AN ADJUVANT TO LEVOBUPIVACAINE IN SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK FOR UPPER LIMB SURGERY

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Abstract Background: Ultrasound guided supraclavicular block has emerged as an effective and feasible mode of providing analgesia in upper limb surgery. Participants were allocated to two equal groups of 60 each using a computer generated random number list. Group A patients received 25ml of 0.5% Levobupivacaine with 1mcg/Kg IBW of fentanyl (addressed as LF in the study) and Group B patients received 25ml of 0.5% Levobupivacaine and 1mcg/Kg IBW of Dexmedetomidine (addressed as LD in the study). **Results**: Mean time of onset and completion of the sensory block and motor block was significantly lower in LD group when compared to LF group (p=0.001). Mean total duration of the sensory block and motor block was significantly higher in the LD group when compared to the LF group (p=0.001). **Conclusion**: Ultrasound guided supraclavicular block using dexmedetomidine 1mcg/Kg IBW added to 25ml of levobupivacaine 0.5% in patients undergoing upper limb surgery significantly reduced total analgesic consumption in first 48 hours and provided longer duration of analgesia postoperatively compared to levobupivacaine with fentanyl.

Introduction: Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage (1). Brachial plexus block is a regional anaesthesia technique that is sometimes employed as an alternative or as an adjunct to general anaesthesia for surgery of the upper extremity. The use of ultrasound in the administration of thoracic paravertebral block has greatly reduced the incidence of associated complications. Certain drugs may be used as an adjuvant to local anesthetics to lower the doses of each agent to enhance analgesic efficacy while reducing the incidence of adverse reactions. Levobupivacaine is the S-enantiomer of racemic bupivacaine, a local anaesthetic drug belonging to the amino amide group (2). Levobupivacaine has less cardiovascular and nervous system toxicity than comparable doses of bupivacaine. Dexmedetomidine is a selective alpha2-receptor agonist with sedative, anxiolytic, and antihypertensive properties. Dexmedetomidine as a local anesthetics adjuvant for Brachial

plexus block has been utilized to prolong the duration of the nerve block. Fentanyl , a short acting opioid is widely used as an adjunct to bupivacaine to prolong the duration of sensory and motor blockade and also provide postoperative analgesia (3).

Methodology

Ethics

After obtaining approval from the institutional ethics committee of SGRR university , this prospective, randomized, double-blind trial was carried out by the Department of Anesthesia& Intensive Care .

Inclusion and exclusion criteria

After obtaining written informed consent, 120 ASA (American Society of Anesthesiologists) I/II patients, aged 16-60 years,posted for upper limb surgeryunder supraclavicular block. They were divided into two groups; LF and LD comprising of 60 patients each were enrolled in the study. Patients with history of allergy to local anesthetic, patient's refusal, pregnant or breast feeding females, infection at the site of injection, patients unable to appreciate pain scores, coagulopathy, block failure and partial blocks were excluded from the study.

Randomization

Patients were randomized using coded sealed envelopes computer generated and subsequently participants were allocated to the two groups of 60 patients each. Group A patients received 25ml of 0.5% Levobupivacaine with 1mcg/Kg IBW of fentanyl (LF) and Group B patients received 25ml of 0.5% Levobupivacaine and 1mcg/Kg IBW of dexmedetomidine (LD).

Blinding

All observations of the study were also recorded in a blinded manner. The anaesthesiologist administering the block and observing the effects received serially numbered sealed envelopes indicating the A or B codes for the anaesthetic mixture to be administered. The A and B syringes were loaded with drugs by another anaesthesiologist not involved in administering the injections and in further evaluation of the patients. The allocation sequence was generated by the author entrusted with the statistical analysis.

Procedure

A detailed pre anaesthetic evaluation shall be carried out to rule out the presence of any significant co-morbidity. Patients were given tablet alprazolam 0.5mg and tablet ranitidine150mg, as premedication, night prior to the surgery and was advised a minimum of 8 hrs of fasting. Baseline readings were recorded and an iv access was established. In both the groups, supraclavicular brachial plexus block was performed using 22 gauge needle immediately lateral to the subclavian artery under ultrasound guidance (using a linear probe of 7.5MHz) by the same anaesthesiologist using the same technique. The patient was in supine position and the drug was injected following intermittent negative aspiration. The patients was monitored for heart rate (HR), non-invasive blood pressure (NIBP), mean arterial blood pressure (MAP) at an interval of 5 minutes for first half an hour and thereafter every 15 minutes, intraoperatively. Electrocardiogram (ECG) and oxygen saturation (SPO2) was monitored on a continuous basis. Sensory and motor block evaluation was done every minute after administering the block until complete sensory and motor block or 15 minutes, whichever is earlier. The sensory block was evaluated using the pin-prick method (Hollmen's

Scale). Onset of sensory blockade is defined as the time taken from the completion of injection of the drug (T0) to the time when sensory block begins to be detected i.e a minimum of grade II and the time to complete sensory block was taken from T0 to the achievement of a grade III in the distribution of all the major nerves.

Follow up

Total duration of analgesia was taken from the time of complete sensory block to the request of first rescue analgesic or a numeric pain rating scale ≥4. Pain was assessed regularly every 30 min for the first 3 hours and then every 3 hourly for the next 12 hours.The duration of motor block was assessed at T0 , every minute for 15 minutes after administering the block or until complete motor block is attained, whichever is earlier. Thereafter every 30 minutes for first 3 hours and then 3rd hourly for next 12 hours by asking the patient to flex his arm and forearm. The time when the patient can flex his arm and forearm completely was recorded and taken as cessation of the motor block effect. Duration of motor block is defined as the time interval between the drug administration and the recovery of complete motor power of the upper limb. Injection diclofenac sodium aqueous 75mg intravenous was given when the numeric pain rating score is ≥4. The time between the end of local anaesthetic administration and first rescue analgesic administration was recorded as the duration of analgesia.

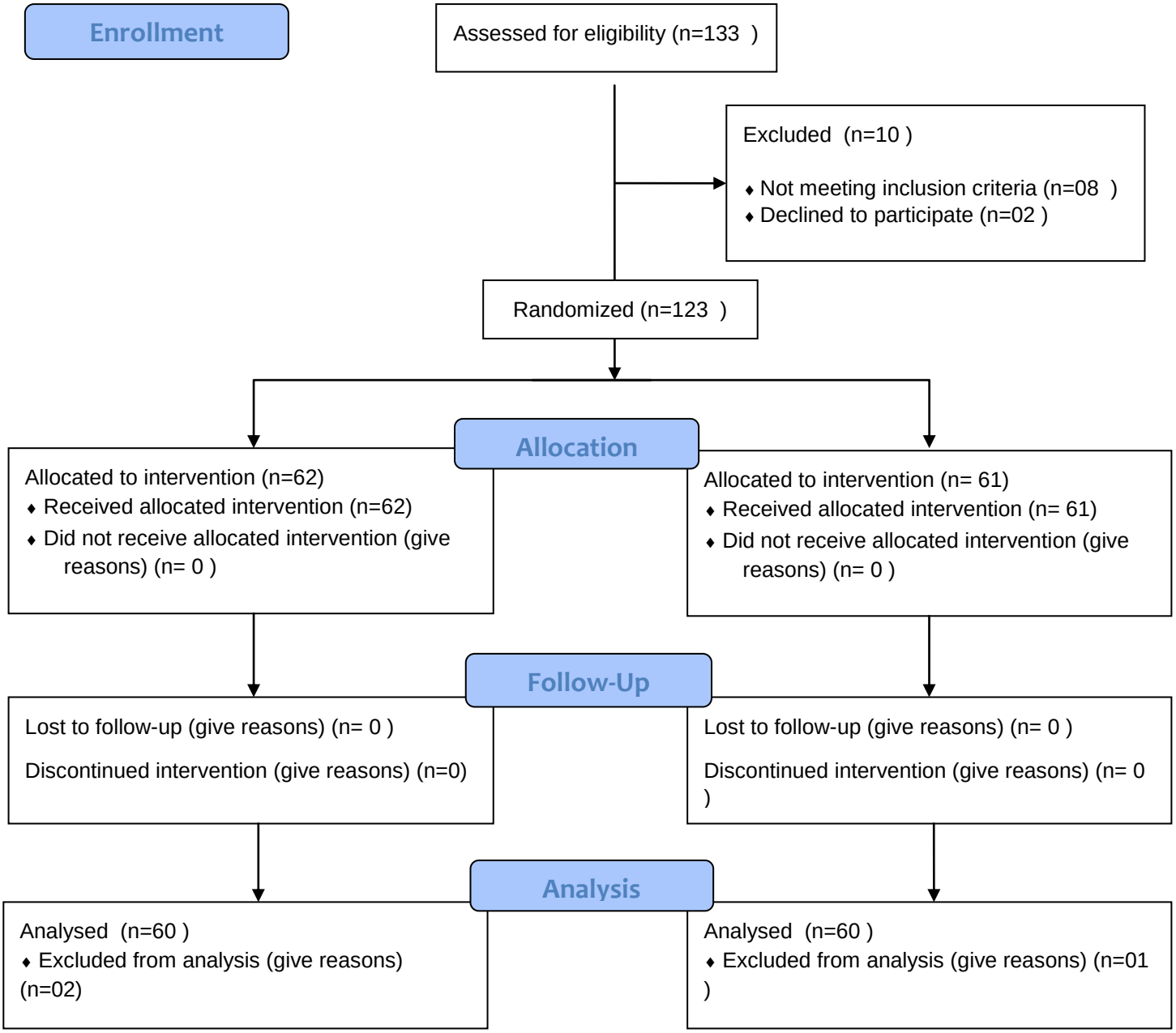
Statistical Analysis

To estimate the sample size, the study conducted by Manbir Kaur et al in 2011 was taken as the reference. The power of a test (1-β) is approximately equal to $\beta = \Phi [-z\alpha/2 + (\Delta\sqrt{n}/\sigma)]$,where Δ denotes the expected mean difference, n denotes the sample size, σ denotes the standard deviation of the difference, α denotes the level of significance, Φ denotes the ordinate of standard normal distribution. Keeping an alpha error of 0.005 and power of 0.8, the estimated sample size (n) was 80 with 40 patients in each group. Data was recorded in a master chart in MS Excel program. Data collected was analysed using Statistical Product for Social Sciences (SPSS) Version 20.0. Continuous variables were presented as mean ± SD, qualitative variables were described as number (percentage). Normally distributed data was compared using independent t-test. Chi-square test and student t-test was applied as appropriate. The p-value was determined to evaluate the level of significance. The statistical test was considered significant at p-value.

Results

A total number of 120 patients aged 16- 60 years belonging to ASA PS I and II, scheduled for upper limb surgery using ultrasound guided supraclavicular brachial plexus block. They were divided in two groups LD and LF with 60 patients each. The following observations were made. The onset and duration of action of both the groups were comparable. The baseline demographic parameters did not differ significantly between the two groups.

CONSORT Flow Diagram



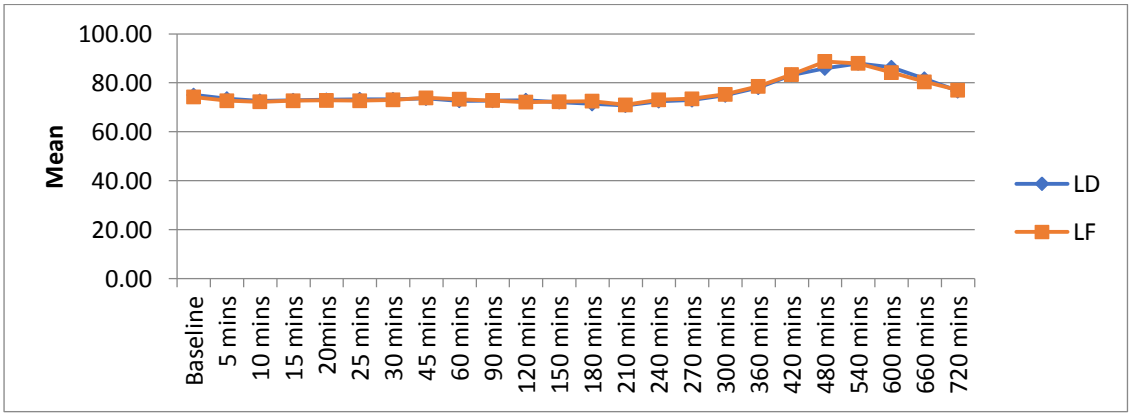
Comparison of mean onset, completion and duration of motor block and sensory block between the two groups.

In Minutes	LD		LF		p-value
	Mean	SD	Mean	SD	
(Sensory) Time of onset	6.57	1.36	9.62	1.69	0.001
Time of completion	19.43	1.52	23.15	1.80	0.001
Total duration	625.92	36.19	509.00	33.13	0.001

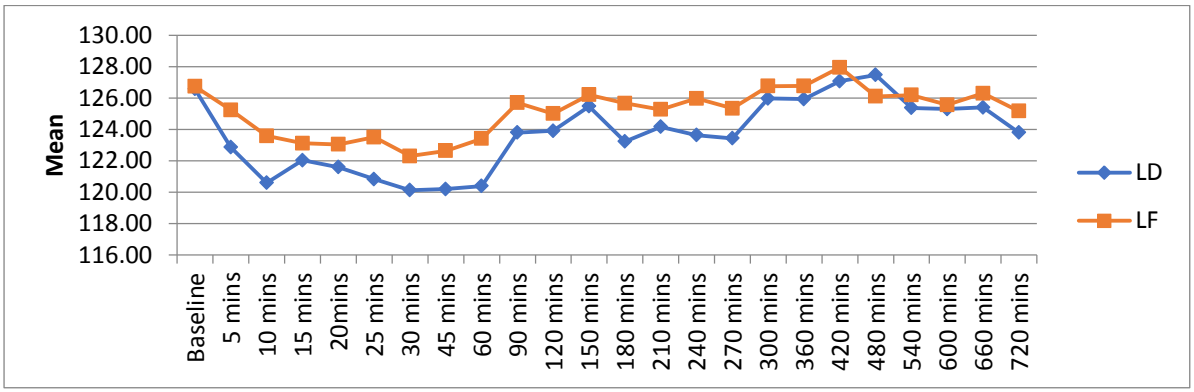
(Motor) Time of onset	8.87	1.53	12.08	1.80	0.001
Time of completion	21.83	2.43	26.03	1.89	0.001
Total duration	609.67	38.73	493.33	33.51	0.001

Mean time of onset and completion of the sensory block was significantly lower in LD group (6.57 ± 1.36 and 19.43 ± 1.52) when compared to LF group (9.62 ± 1.69 and 23.15 ± 1.80) (p=0.001), The mean total duration of the sensory block was significantly higher in the LD group (625.92 ± 36.19) when compared to the LF group (509.0 ± 33.13) (p=0.001).

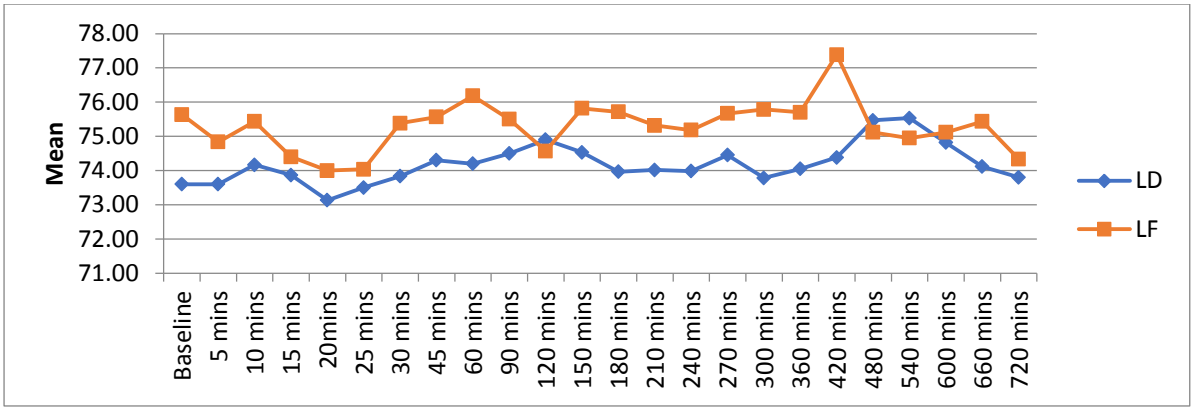
Mean time of onset and completion of the motor block was significantly lower in LD group (8.87 ± 1.53 and 21.83 ± 2.43) when compared to LF group (12.08 ± 1.80 and 26.03 ± 1.89) (p=0.001). The mean total duration of the motor block was significantly higher in the LD group (609.67 ± 38.73) when compared to the LF group (493.33 ± 33.51) (p=0.001).



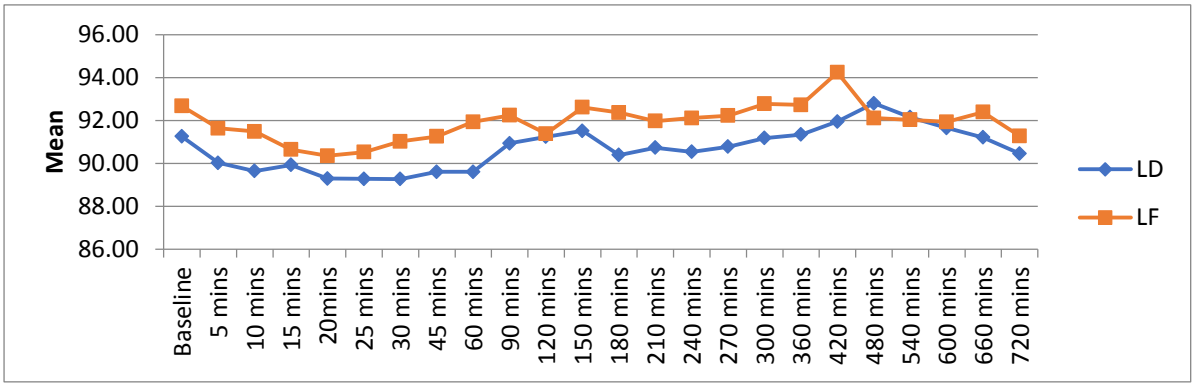
There was no significant statistical difference observed in the mean heart rate between the two groups.



There was no significant statistical difference observed in the mean systolic blood pressure between the two groups.



There was no significant statistical difference observed in the mean diastolic blood pressure between the two groups.



There was no significant statistical difference observed in the mean MAP between the two groups.

DISCUSSION

Brachial plexus block has rapid onset , complete and predictable anaesthesia for entire upper extremity particularly hand surgery. This mode of anaesthesia avoids untoward effects of general anaesthesia, is attractive and effective in terms of cost, performance, margin of safety and also provides good post operative analgesia.

In our study, we demonstrated that the addition of dexmedetomidine to levobupivacaine can significantly shorten the sensory and motor block onset time and prolong the duration of postoperative analgesia in comparison to fentanyl added to levobupivacaine. Local anaesthetic agent selection, dose, concentration, volume, and physical modifications can affect onset, spread, quality, and duration of anaesthesia. Levobupivacaine, the S-enantiomer of bupivacaine, which has less cardiac and neural toxicity than bupivacaine, is currently the closest to the ideal agent for neural blockade.

However there are minimal studies comparing levobupivacaine along with dexmedetomidine and fentanyl in supraclavicular brachial plexus block for upper limb surgery. Hence this study was undertaken to evaluate the efficacy of it. A prospective, randomized, double-blinded study was conducted on 120 patients aged 16-60 years of ASA PS I and II. The baseline demographic data such as age, gender, weight, height were comparable between the 2 groups.

Sensory block

The mean time of onset and of sensory block in our study was 6.57minutes ± 1.36 in the levobupivacaine -dexmedetomidine group and 9.62minutes ± 1.69 in the levobupivacaine-fentanyl group (p = 0.001) which was statistically significant.

The mean time of completion of sensory block was 19.43 minutes ± 1.52 and 23.15 minutes ± 1.08 (p = 0.001) respectively in the levobupivacaine-dexmedetomidine and levobupivacaine-fentanyl group which was statistically significant.

The total duration of sensory block was 625.92 minutes ± 36.19 and 509.00 minutes ± 33.13 (p=0.001) respectively in the levobupivacaine-dexmedetomidine and levobupivacaine-fentanyl group which was again statistically significant. The result of our study corroborated with the study conducted by Swami et al which concluded that dexmedetomidine (1mcg/kg) compared to clonidine (1mcg/kg) when added to 35ml of 0.25% bupivacaine in supraclavicular brachial plexus block enhanced the duration of sensory and motor block and also the duration of analgesia (4). However, the duration of sensory blockade in the bupivacaine - dexmedetomidine group in this study was 413.97± 87.13 when compared to our study which was 625.92 ± 36.19. The extended duration of sensory blockade in our study could be attributed to levobupivacaine which was used instead of bupivacaine in the study conducted by Swami et al.

Motor block

The mean time of onset of motor block in our study was 8.87 minutes ±1.53 in the levobupivacaine-dexmedetomidine group and 12.08 minutes ± 1.80 in the levobupivacaine-fentanyl group (p = 0.001) which was statistically significant. The mean time of completion of motor block was 21.83 minutes ± 2.43 and 26.03 minutes ± 1.89 (p = 0.001) respectively in the levobupivacaine-dexmedetomidine and levobupivacaine-fentanyl group which was statistically significant. The total duration of motor block was 609.67 minutes ± 38.73 and 493 minutes ± 33.51 (p=0.001) respectively in the levobupivacaine-dexmedetomidine and

lebupivacaine-fentanyl group which was again statistically significant. The results of our study corroborated with the study conducted by Singh AP et al where in 100mcg of Dexmedetomidine was added to 30 ml of 0.5 % Levobupivacaine and compared with 1ml of NS added to 30ml of 0.5% Levobupivacaine for supraclavicular brachial plexus block and the onset of motor and duration of motor blockade in the Dexmedetomidine- Levobupivacaine was when 2.83 ± 1.19 and 1051.2 ± 125.4 compared to 8.87 ±1.53 and 609.67 ± 38.73 in our study. The onset and duration of motor blockade in the NS-Levobupivacaine group was 12.21 ± 2.52 and 550.8 ± 102. This concludes that Dexmedetomidine added as an adjuvant to Levobupivacaine prolongs the duration of motor blockade when compared to Levobupivacaine alone (5).

Duration of analgesia

The mean total duration of analgesia in our study was higher in the Levobupivacaine-Dexmedetomidine group (507.63 minutes ± 21.36) when compared to the Levobupivacaine-Fentanyl group (425.75 minutes ± 20.05), the p value being 0.001 which was statistically significant.These results were comparable to the study conducted by Manbir Kaur et al (6). conducted in 2011 comprising of 120 patients in the age group of 30–55 years with physical status American Society of Anaesthesiologists (ASA) Classes I and II undergoing elective upper limb surgeries under ultrasound-guided supraclavicular brachial plexus block were randomly divided into three groups of 40 each. Group A received 25ml of 0.5% levobupivacaine with 5ml normal saline (NS), Group B received 25ml of 0.5% levobupivacaine with 1μg/kg dexmedetomidine diluted to the volume of 5ml NS, and Group C received 25ml of 0.5% levobupivacaine with 1 μg/kg fentanyl diluted to the volume of 5ml NS. The mean total duration of analgesia in the Levobupivacaine-NS group was 590.54 ± 45.2, Levobupivacaine-Dexmedetomidine group was 802.32 ± 33.4 and Levobupivacaine-Fentanyl group was 648.42 ± 33.68. These values were comparable to our study and it could be concluded that Levobupivacaine-Dexmedetomidine provided longer duration of analgesia when compared to Levobupivacaine-Fentanyl.

Hemodynamic parameters

Hemodynamic parameters were comparable between the two groups in our study ($p>0.05$) which was identical to the study conducted by Manbir Kaur et al 2011 comprising of 120 patients in the age group of 30–55 years, randomly divided into 2 groups of 40 patients each. Group A received 25ml of 0.5% levobupivacaine with 5ml normal saline (NS), Group B

received 25ml of 0.5% levobupivacaine with 1 μg/kg dexmedetomidine diluted to the volume of 5ml NS, and Group C received 25ml of 0.5% levobupivacaine with 1μg/kg fentanyl diluted to the volume of 5ml NS. The study also concluded that hemodynamic parameters were comparable between the two groups.

Adverse events

There are various techniques described for supraclavicular brachial plexus block. In our study, we used the USG technique so as to reduce the incidence of pneumothorax and other mechanical complications. Winnie et al. in 1964 described the subclavian perivascular technique and found that out of 100 cases, 98 had complete anaesthesia; there was no incidence of pneumothorax and nerve damage while one case reported phrenic nerve paralysis (7). Although symptomatic pneumothorax occurred in 6.1% of patients reported by Brand and Papper, we observed no such complication.Pham-Dang C et al. in 1997 used the inter sternocleidomastoid technique for supraclavicular approach. Ipsilateral phrenic paralysis was observed in 60% of the patients without any intraoperative desaturation. They inferred the chest X-ray performed 30 min after injection of local anaesthetics may have underestimated frequency of the paralysis. TransientHorner's syndrome in 10%, and transient recurrent laryngeal nerve block in 2 patients were observed (8). Sah MK et al. in a case study observed total spinal anaesthesia with interscalene brachial plexus block by Winnie approach (9). In this case there could be a possibility of intrathecal injection of anaesthetic agent. Ultrasound guided techniques has allowed for additional refinements and improved block consistency with reduced local anaesthetic volume. Hypotension and bradycardia are the most common side effect observed with $\alpha 2$ agonists. In a study that Esmaglu and his colleagues had done, adding 100mcg of dexmedetomidine to levobupivacaine had caused bradycardia in 7 of the 30 patients (10).

In Kwon's study, heart rate and mean arterial pressure in the dexmedetomidine group had decreased significantly (11). However, in some studies, the use of dexmedetomidine was not associated with hypotension and bradycardia, whereas in our study, this decrease occurred in mean arterial pressure and mean heart rate, and it was not statistically significant. In our study, there was one patient from Levobupivacaine-Dexmedetomidine group who experienced nausea, which was treated with Inj. Ondensetron 4mg IV. One patient in the Levobupivacaine-Fentanyl group experienced hoarseness of voice possibly due to blockade of recurrent laryngeal nerve, which was treated with Inj. Dexamethasone 8mg IV. In the

Levobupivacaine-Dexmedetomidine group two patients experienced sedation but the patients were easily arousable. This can be explained on the basis that some amount of systemic absorption of drug could be present. There were no significant adverse events in any of the two groups which was comparable to the previous study conducted by Manbir kaur et al in 2011. Three patients were removed from the study, one in Levobupivacaine-Fentanyl group and two in Levobupivacaine-Dexmedetomidine due to inadequate block effect. In these patients mode of anaesthesia was converted to general anaesthesia. All the above studies correlated with our study findings, none of the patients in either of the groups exhibited significant side effects or hemodynamic variability during the perioperative period as well as no incidence of complications such as pneumothorax (12) and arterial puncture were noted due to the use of ultrasound guidance for the administration of the block.

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