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A comparison of dexmedetomidine and clonidine as an adjuvant to local anaesthesia in supraclavicular brachial plexus block for upper limb surgeries

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Abstract

Background: Regional anaesthesia is the recommended technique for upper and lower limb surgeries with better postoperative profile.The brachial plexus block provides a useful alternative to general anesthesia, for upper limb surgeries. Supraclavicular approach for brachial plexus block is most commonly suitable for upper limb surgeries and post operative pain relief. **Aims and objectives:** The aim of this study was designed to compare clonidine and dexmedetomidine, used as an adjunct to bupivacaine in supraclavicular brachial plexus block in terms of efficacy in onset, duration and potency of sensory and motor block, sedation score and analgesia. **Study design:** In this prospective, double blind randomized controlled clinical trial, 60 American Society of Anaesthesiologists grade 1 and 2 (ASA 1, 2) patients aged between 18 to 60 years, scheduled for upper limb surgeries under supraclavicular block were selected. **Materials and methods:** The patients were divided into two groups: Group C (n= 30) comprised of patients who received bupivacaine 0.25% (35 cc) + injection clonidine 1 mcg / kg and Group D (n= 30) who received bupivacaine 0.25% (35 cc) + inj dexmedetomidine 1 mcg / kg. Onset, duration of sensory and motor blockade, duration, efficacy and potency of postoperative analgesia, sedation score and any untoward side effects, if any were observed at scheduled intervals. **Statistics and Results:** The mean time for onset of sensory block in group D was (9.17±1.26) mins and that observed in group C was (11.07±2.14) mins. This difference was statistically significant (p = 0.001). Time to achieve complete sensory block in group D was (14.80 ± 1.37) mins and in group C was (16.40±2.09) mins. This difference was statistically insignificant (p > 0.005). Mean duration of sensory block in group D was (690 ± 87.41) mins and in group C was (470 ± 55) mins. This difference was statistically significant (p<0.05) (p = 0.001) The mean time for onset of motor block in group D was (12.63 ± 2.18) mins and (15.17±1.77) mins in group C. The difference was found to be statistically significant (p< 0.005)(p=0.0001) The mean time for complete motor block in group D was (20.40 ± 3.02) mins and (20.17±2.60) mins in group C. The difference was found to be statistically insignificant (p> 0.005) (p= 0.750). The mean duration of motor block in group D was (353.17 ± 41.24) mins and in group C was (270.51 ± 51.61) mins. This difference was statistically significant (p<0.005) (p = 0.001). The duration of analgesia was (721.33 ± 88.27) mins in group D and (516.00±45.15) mins in group C (p< 0.05) This difference was statistically as well as clinically significant. No patient in any group required intra-operative supplementation with analgesia or general anaesthesia during the surgical procedure. **Conclusion:** From our results we conclude that the onset of sensory and motor block is faster with dexmedetomidine (group D) compared to clonidine (group C), both dexmedetomidine and clonidine prolong the duration of sensory and motor block, more prolonged with dexmedetomidine. Both dexmedetomidine and clonidine have been found to have favourable effect on duration of postoperative analgesia. Significant prolongation of duration of analgesia is seen with dexmedetomidine as compared to clonidine.

Keywords: Dexmedetomidine, Clonidine, Supraclavicular brachial plexus block.

INTRODUCTION

Peripheral nerve blocks not only provide intra-operative anaesthesia but also extend analgesia in the post-operative period without any systemic side-effects [1]. The brachial plexus block is one among the most popular regional nerve blocks performed for upper limb surgeries. Supraclavicular approach for brachial plexus block is most commonly suitable for upper limb surgeries and postoperative pain relief. Local anaesthetic drugs like lignocaine, bupivacaine and levo bupivacaine are used in peripheral blocks. In addition to the use of different local anaesthetics and regional anaesthesia procedures, use of local anaesthetics with adjuvants gained widespread popularity due to the belief, that the addition of various opioids [2,3] or other components, e.g. clonidine [4] allows the reduction of the amount of local anaesthetic and thus the incidence of side effects [5,6].

Alpha-2 adrenergic receptor agonists have been the focus of interest for their sedative, analgesic, peri operative sympatholytic and cardiovascular stabilizing effects with reduced anaesthetic requirements. There has always been a search for adjuvants to the regional nerve block with drugs that prolong the

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duration of analgesia but with lesser adverse effects. The search for the ideal additive continues, and led us to try the α2 adrenergic agent, dexmedetomidine and clonidine.

Dexmedetomidine, an α2-receptor agonist, with α2/α1 selectivity 8 times than that of clonidine has also been reported to improve the quality of intrathecal and epidural anesthesia [3,4] when used along with LA as adjuvant.

Clonidine is a selective alpha 2 adrenergic agonist with some α1 agonist property. In addition to its antihypertensive effect, in recent studies, clonidine has been demonstrated to be an effective sedative and analgesic which reduces the amount of anaesthetic agents required when used as part of anaesthetic technique.

The aim of this prospective, double blind randomized controlled clinical study was to compare clonidine and dexmedetomidine, used as an adjunct to bupivacaine in supraclavicular brachial plexus block for upper limb surgeries, in terms of efficacy in onset, duration, potency of sensory and motor block, sedation score and analgesia.

MATERIALS AND METHODS

With Ethical Committee approval and written informed consent , a prospective, randomized, double blind and comparative study was planned among 60 American Society of Anesthesiologist (ASA) Grade I and II patients in the age group of 18-60 years, posted for elective upper limb orthopedic surgeries under brachial plexus block using supraclavicular approach. Patients with known hypersensitivity to clonidine, dexmedetomidine and LAs, severe diabetes, peripheral neuropathy, coagulopathy, infection at the site of block, pregnancy, cardiovascular disorders , patients on beta blockers and psychological disorders were excluded from the study. Patients who fulfilled the inclusion and exclusion criteria and satisfied the requirement of preoperative evaluation were selected for the study. Visual analogue scale was explained to the patient. Bupivacaine sensitivity test was done. Patients were randomly allocated to two groups C and D, of thirty patients each as per computerized random table.

Investigator; i.e. the one who checked the vital parameters and sensory and motor block, as well as the anesthesiologist who performed the block were blinded to the patient groups. Drug solution was prepared by a senior qualified anaesthesiologist who was not a part of the study team and block was given by a senior qualified anaesthetist in all cases. 2 solutions were prepared.

Group C Bupivacaine 0.25% (35 cc) + inj clonidine 1 mcg / kg.

Group D Bupivacaine 0.25% (35 cc) + inj dexmedetomidine 1 mcg / kg

Code numbers were put on the patient's record sheets. . Decoding was done at the end of the study for statistical analysis.

Adequate starvation and consent taken, IV access with 18 G cannula and RL started on the nonoperative hand prior to performing supraclavicular brachial plexus block.

Electrocardiogram, SpO_2 and non invasive blood pressure monitoring done Baseline parameters were recorded i.e. pulse rate, Systolic (SBP) and diastolic (DBP) blood pressure and SpO_2 on room air. Patients were kept in the supine position with the arm by side of the trunk and extended along the side towards.

the ipsilateral knee as far as possible, and the head slightly turned to the opposite side. The supraclavicular brachial plexus block was performed using subclavian perivascular technique described by Kulenkampff, modified by Winnie and Collins [7]. After eliciting paraesthesia and following negative aspiration, 35 mL of a solution containing local anaesthetic combined with clonidine or dexmedetomidine as mentioned above was injected followed by a 3 mins massage to facilitate an even drug distribution.

The onset and duration of sensory and motor blockade, duration of postoperative analgesia and untoward side effects, if any were observed.

The sensory block was evaluated by pinprick on skin dermatomes C4 to T2 with 22G hypodermic needle. Motor block was evaluated by thumb movements i.e abduction (radial nerve), adduction (ulnar nerve), opposition (Median nerve) Musculocutaneous nerve block assessed by flexion of elbow and supination-pronation of forearm. Hollmen scale was used to assess both sensory (Sensory Block: 1=normal sensation of pinprick, 2=pin prick felt as sharp point, but weaker compared with same area in the other upper limb, 3=pin prick recognised as touch with blunt object, 4=no perception of pin prick) and motor blockade (Motor block: 1=normal muscle function, 2=slight weakness, 3=very weak muscular action, 4=complete loss of muscle action).

Evaluation was carried out for every 2 mins for the first 10 mins after completion of the injection and after that every 15 mins intraoperatively till the end of surgery. Time to onset of sensory and motor block was considered as the interval between completion of local anaesthetic injection and grade 2 in Hollmen scale. Time to complete sensory block was considered as interval between completion of local anaesthetic injection and grade 3 in Hollmen scale.Time to complete motor block was considered as interval between completion of local anaesthetic injection and Grade-3 motor blockade in hollmen scale. The duration of sensory blockade, defined as the time between onset of action and return of pinprick response in at least 3 major nerve distributions. Duration of motor blockade was considered as the time interval between onset of action and the ability of the patient to move his fingers. Duration of analgesia was considered as the time interval between the completion of local anaesthetic injection and the onset of pain in the postoperative period (VAS >3).

If supplementation with IV analgesics or general anaesthesia was required due to inadequate/ partial block, the case was not included in study. All patients received oxygen (O_2) through Hudson's mask at the rate 5-6 litres/min throughout the procedure and postoperatively in PACU.

All patients were monitored with continuous pulse rate, systolic blood pressure, diastolic blood pressure, ECG, SPO2, respiratory rate every 15 mins intraoperatively till the end of surgery. Intraoperative sedation was noted as per Ramsay sedation score (1- Anxious or restless or both, 2- Cooperative, oriented and tranquil, 3- Responding to commands, 4- Brisk response to stimulus, 5-Sluggish response to stimulus, 6- No response to stimulus).

Any adverse events such as hypotension (20% decrease in relation to the baseline value), bradycardia (HR <60 bpm), hypoxemia (SpO_2 90%) nausea, vomiting, pneumothorax, horners syndrome, haematoma were recorded. Postoperatively, patients were shifted to PACU and monitored for 24 hrs to assess total duration of sensory and motor blockade and VAS pain score Continuous SpO_2, 1hrly pulse and BP were recorded. Rescue analgesia was provided by injection diclofenac IM 1mg/kg on demand when VAS>3. Inj Ondansetron 0.05 to 0.15mg/kg IV was given for nausea and vomiting.

Statistical Analysis

Qualitative data was represented in form of frequency and percentage Association between qualitative variables was assessed by Chi-Square test with Continuity Correction for all 2 X 2 tables and Fisher's exact

test for all 2 X 2 tables where p-value of Chi-Square test was not valid due to small counts.Adjacent row data of more than 2X2 tables was pooled and Chi-Square test reapplied in case more than 20.0% cells having expected count less than 5 Quantitative data was represented using mean ± sd and Median & IQR (Interquartile range). Analysis of quantitative data between the two groups was done using unpaired t-test if data passes 'Normality test' and by Mann-Whitney Test if data fails 'Normality test'. Analysis of quantitative data measured over more than 2 times was done using repeated measures ANOVA if data passed 'Normality test' and by Friedman's repeated measures ANOVA on Ranks test if data failed 'Normality test', with application of appropriate Post Hoc test if P-value of ANOVA came statistically significant. (p> 0.05 Not Significant). Results were graphically represented. SPSS (Statistical package for social sciences) Version 17 was used for most analysis.

RESULTS AND OBSERVATIONS

All 60 patients enrolled in the study, completed the study according to the protocol and were included in the analysis. The two groups, Group D (n=30) received supraclavicular brachial plexus block with a mixture of 0.25% bupivacaine 35ml with dexmedetomidine (1 mcg/kg) and Group C (n=30) received supraclavicular brachial plexus block with a mixture of 0.25% bupivacaine 35ml with Clonidine (1 mcg/kg)

The demographic criteria like age, sex, weight, ASA status and duration of surgery were comparable in both groups and there was no statistically significant difference between two groups (p > 0.05) (Table 1)

Table 1: Demographic data, ASA status, Characteristic of sensory and motor block, duration of surgery and analgesia (* N = Number of patients)

	Group	N	Mean	Std. Deviation	P value
Age(yrs)	Dexmedetomidine	30	35.40	11.385	0.675
	Clonidine	30	36.53	9.372	
Weight(kgs)	Dexmedetomidine	30	56.47	2.129	0.525
	Clonidine	30	56.87	2.688	
ASA	Dexmedetomidine	30	1.33	.479	1.000
	Clonidine	30	1.33	.479	
Sensory block onset (minutes)	Dexmedetomidine	30	9.17	1.262	0.001
	Clonidine	30	11.07	2.149	
Motor block onset (minutes)	Dexmedetomidine	30	12.63	2.189	.0001
	Clonidine	30	15.17	1.763	
Duration of motor block (minutes)	Dexmedetomidine	30	353.17	41.241	.0001
	Clonidine	30	270.67	31.616	
Duration of sensory block (minutes)	Dexmedetomidine	30	690.00	87.415	.0001
	Clonidine	30	470.33	55.677	
Sensory block complete	Dexmedetomidine	30	14.80	1.375	0.001
	Clonidine	30	16.40	2.094	
Motor block complete	Dexmedetomidine	30	20.40	3.024	0.750
	Clonidine	30	20.17	2.601	
Duration of surgery (minutes)	Dexmedetomidine	30	95.13	3.702	0.203
	Clonidine	30	93.70	4.851	
VAS>3 (minutes)	Dexmedetomidine	30	721.33	88.268	0.0001
	Clonidine	30	516.00	45.151	

As shown in table 1, onset of sensory block in group D was (9.17±1.26) mins and that observed in group C was (11.07±2.15) mins. This difference was statistically significant (p<0.05 is significant) (figure 1) and onset of motor block in group D was (12.63±) mins and in group C was (15.17±) mins(figure 2) This difference was statistically significant (p<0.05 is significant)

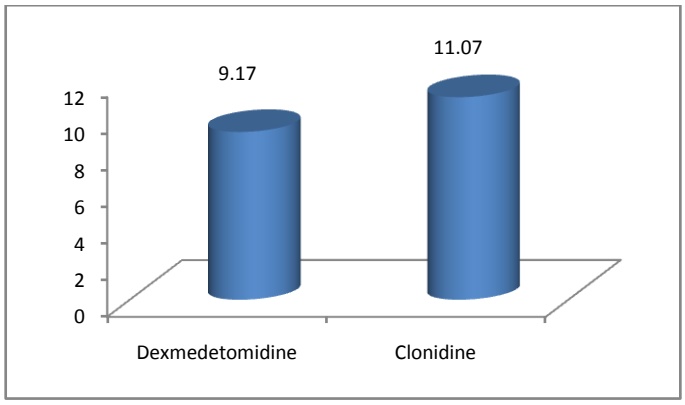

Figure 1: Onset of sensory block (min)

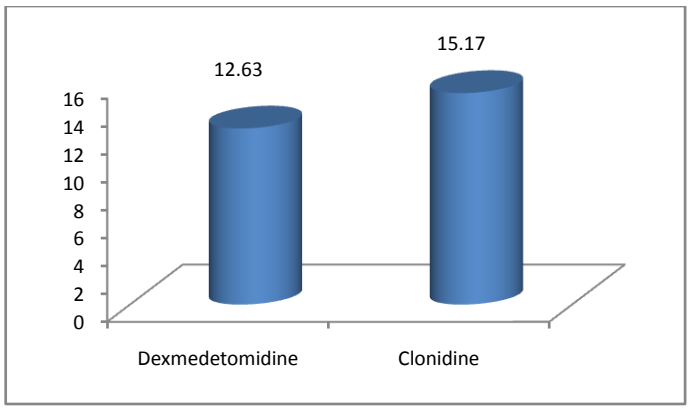

Figure 2: Onset of Motor block (min)

The onset of duration of analgesia in group D was (721.33±88.26) mins and that observed in group C was (516±45.15) mins. This difference was statistically significant (p<0.05 is significant).

The duration of motor block in group D was (353.17±41.24) mins and that observed in group C was (270.67±31.61) mins (figure 3) This difference was statistically significant (p<0.05 is significant) and duration of sensory block in group D was (690±87.45) mins and that observed in group C was (470.33±55.67) mins(figure 4) This difference was statistically significant (p<0.05 is significant).

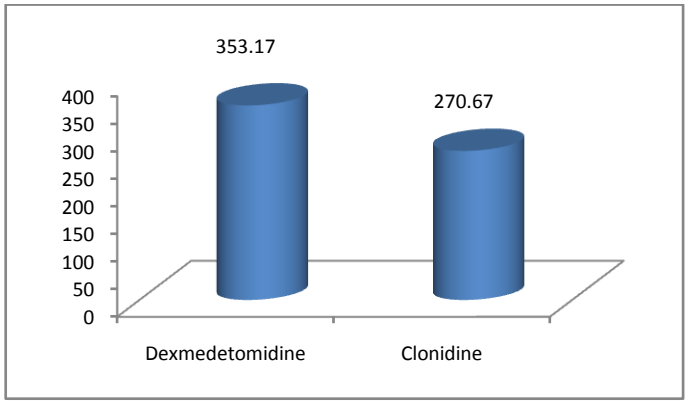

Figure 3: Duration of motor block (min)

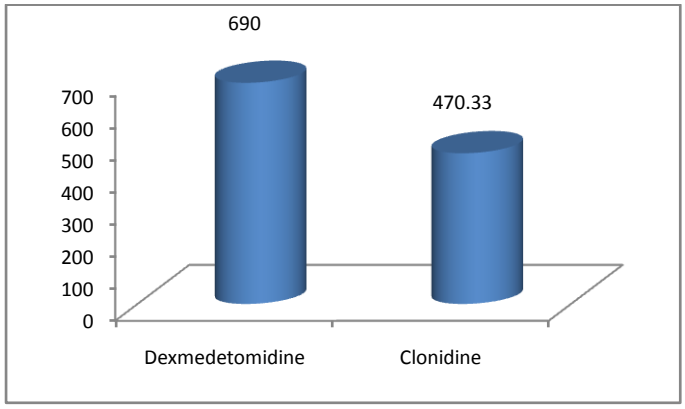

Figure 4: Duration of Sensory block (min)

Haemodynamically, we observed a statistically significant difference in pulse rate between two groups from 10 mins to 120 mins intraoperatively and postoperatively from 2 hrs to 12 hrs but this was not clinically significant. There was statistically significant difference in mean systolic blood pressure between two groups from 10 mins to 40 mins and at 90 mins intraoperatively and immediate postoperative, 1, 2 and 4 hrs after that but this was not clinically significant. The baseline diastolic blood pressure in two groups was comparable (79.73±3.63mmHg and 79.40±3.87mmHg in group D and group C respectively) Both the groups were comparable for RR and SpO2 at each interval, and the results were statistically insignificant. Both group patients achieved sedation score of 2 (cooperative, oriented and tranquil).

Patients in both groups suffered nausea and vomiting (5 patients in group D and 2 patients in Group C, dryness of mouth was observed in 1 patient in group B and blurring of vision was observed in 1 patient in group C (figure 5) With regard to complications this difference was not statistically significant between two groups (p>0.05).

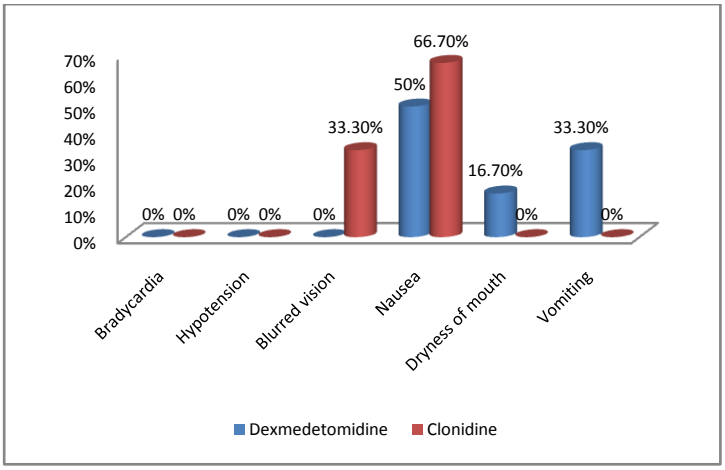

Figure 5: Comparison of side effects between dexmedetomidine and clonidine

DISCUSSION

In this prospective, randomized, double blind, comparative study to assess and compare the safety and efficacy of α_2 agonists, Clonidine (1 mcg/kg) and Dexmedetomidine (1 mcg/kg) added to local anesthetic (Bupivacaine 0.25%) as adjuvants in supraclavicular brachial plexus block for patients undergoing upper limb surgeries, the onset, duration of sensory and motor block along with post operative analgesia were compared.

Peripheral nerve blocks with local anaesthetics provide excellent operating conditions with good muscle relaxation but the duration of analgesia is rarely maintained for more than 4 – 6 hours even with the longest acting local anaesthetics (Bupivacaine, Ropivacaine and levo-bupivacaine).

Continuous infusion of local anaesthetics into brachial plexus sheath requires an infusion pump and has potential for cumulative toxicity and unpredictable variability in absorption. So there had been search for a method, which can provide longer duration of analgesia without the above side effects and inconvenience to the patient.

Various studies have shown that addition of several adjuvants like neostigmine [8] opioids [9,13] dexamethasone [10] hyaluronidase [11] tramadol [12] midazolam [12,13] and α_2 agonist like clonidine [14] dexmedetomidine [14] in local anaesthetic solution in peripheral nerve blocks prolonged the duration of analgesia, but the results have been inconclusive because of associated side effects or doubtful efficacy.

Perineural injection of α_2 agonists is reported to influence post op analgesia [15] Since the 1980s clonidine has been used as an adjuvant to local anaesthetics in various regional techniques to extend the duration of block.

Gaumann *et al* [16] studied admixture of clonidine (150mcg) or epinephrine (200mcg) to lidocaine for brachial plexus block with regard to duration of block, postoperative analgesia, and plasma concentrations of lidocaine. They concluded that clonidine may be a useful adjunct to local anesthetics in those patients in whom the administration of epinephrine is contraindicated.

Ahmed N *et al* [17] compared the quality of anaesthesia and duration of analgesia with clonidine (150mcg)-bupivacaine or fentanyl (100mcg)-bupivacaine in supraclavicular brachial plexus block(total volume 40ml). They concluded clonidine and bupivacaine combination is a better alternative to fentanyl and bupivacaine in respect to quality of anaesthesia and duration of analgesia.

Trivedi V *et al* [18] conducted a randomised clinical study in 60 ASA I-II patients undergoing elective upper limb orthopaedic surgeries (duration of surgery < or =120 minutes). They gave injection bupivacaine 0.5% plain 20 ml and injection lignocaine 2% plain 10 ml in supraclavicular brachial plexus block. Patients were divided into two groups (n=30 each), group C (clonidine) and group M (midazolam) In group C patients, injection clonidine 150 mcg and in group M, injection midazolam preservative free 5 mg were administered along with local anaesthetics. They concluded injection clonidine provides better postoperative analgesia and more sedation than midazolam.

Sarita S. Swami *et al* [19] studied sixty ASA I and II patients scheduled for elective upper limb surgeries under supraclavicular brachial plexus block, divided into two equal groups in a randomized, double-blinded fashion. Group C received clonidine 1 µg/kg and Group D received dexmedetomidine 1 µg/kg added to bupivacaine 0.25% (35 cc). Onset and recovery time of sensory and motor block, duration of analgesia and quality of block were studied in both the groups. Study confirmed that duration of sensory block and motor block was 227.00±48.36 and 292.67±59.13 mins, respectively, in group C, while it was 413.97±87.13 and 472.24±90.06 mins, respectively, in group D. There was no statistically significant difference in onset of sensory and motor block between the two groups.

A study by Brumett *et al*. showed that dexmedetomidine enhances duration of bupivacaine anaesthesia and analgesia of sciatic nerve block in rats without any damage to the nerve [20,21]. The efficacy of peripheral perineural dexmedetomidine added to bupivacaine and ropivacaine for sciatic nerve blocks in rats has been established [20,21].

The increase in duration of analgesia is dose dependent and the effect is peripheral (i.e., not caused by centrally mediated or systemic analgesia) [21]. However all studies carried out so far to prove the peripheral action of α2 agonists were in animal studies. There are very few human studies, i.e. greater palatine and axillary brachial plexus nerve blocks which have subsequently demonstrated that increased duration of sensory blockade can be achieved by adding dexmedetomidine to bupivacaine and levobupivacaine, respectively [22,23]. Study of effect of dexmedetomidine as an adjuvant to levobupivacaine in supraclavicular brachial plexus block done by Haramritpal Kaur, Gurpreet Singh, *et al* [24] showed decrease in onset time of motor and sensory block , better patient comfort and lower VAS pain scores. Keeping these facts in mind, we decided to compare the action of two α2 agonists, clonidine and dexmedetomidine with bupivacaine in lesser concentration (0.25%), in peripheral nerve blocks so that by increasing the duration of analgesia with a single shot block we can achieve a longer duration of post-operative analgesia without significant clinical side-effects and hence, avoid large dosages of local anaesthetics as in continuous regional block techniques.

Our study showed that the onset of sensory and motor block is faster with dexmedetomidine compared to clonidine, both dexmedetomidine and clonidine prolong the duration of sensory and motor block, more prolongation seen with dexmedetomidine. None of the patients in any group required intraoperative supplementation with analgesia or general anaesthesia during the surgical procedure. Thus both dexmedetomidine and clonidine have been found to have favourable effect on duration of postoperative analgesia. Significant prolongation of duration of analgesia is seen with dexmedetomidine as compared to clonidine.

Both dexmedetomidine and clonidine when used in the doses mentioned above did not produce haemodynamic instability and respiratory depression.

None of the patients in study group developed bradycardia (pulse rate<50/min), hypotension (fall in SBP> 20% baseline) or respiratory depression (RR< 8/min and SpO2 < 90%).

No serious side-effects (pneumothorax, hematoma, Horner's syndrome, prolonged nerve palsy) were reported in both groups. Of those observed sedation, nausea (3 patients in group B and 2 in group C), vomiting (2 patients in group B and none in Group C), dryness of mouth (1 patient in group D and none in Group C) blurring of vision (1 patient in group C) Sedation score was achieved in both groups but all patients were arousable and none of the patient developed respiratory complications.

CONCLUSION

From our study, of the use of α-2 agonists, Dexmedetomidine (1 mcg/kg) and Clonidine (1 mcg/kg) as adjuvants to local anaesthetic solution (0.25% bupivacaine) in supraclavicular brachial plexus block for upper limb surgeries, we conclude that faster onset of sensory and motor block is seen with dexmedetomidine as compared to clonidine. Duration of sensory and motor block and duration of postoperative analgesia is significantly prolonged with dexmedetomidine as compared to clonidine and haemodynamic parameters, side effects and sedation scores are comparable between the two drugs.

[There has always been a search for adjuvants to the regional nerve block with drugs that prolong the duration of analgesia but with lesser adverse effects. The search for the ideal additive continues, and led us to try the α-2 adrenergic agent, dexmedetomidine and clonidine and compare their efficacy, effects and potency].

Conflicts of interests

No external funding or competing interests declared

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