

Original Research Article

Study of Effect of Dexmedetomidine and Clonidine as Adjuvant with Bupivacaine on the onset & Duration of Analgesia and Anaesthesia in Supraclavicular Brachial Plexus Block

Dr. Harekrishna Ray¹, Dr. Kamala Kanta Pradhan², Dr. Soumyakant Sethi³, Dr. Amulya Ranjan Dash⁴

^{1,2}Asst prof, ³Senior resident, ⁴Post graduate student

Department of Anaesthesiology and critical care, SCB Medical College, Hospital, Cuttack, Odisha, India

*Corresponding author

Dr Kamala Kanta Pradhan

Email: drkitusraban@gmail.com

Abstract: Many adjuvants have been used with local anaesthetics to reduce the time of onset and prolong the duration of analgesia in brachial plexus blocks. Very few studies are there comparing dexmedetomidine versus clonidine as adjuvant. This study was done to compare the effects of dexmedetomidine and clonidine as adjuvant to local anaesthetics in supraclavicular block. In this double blinded clinical trial, 90 ASA classes I and II patients posted to undergo upper extremity surgery were divided into 3 different groups randomly. Group C patients received 35 ml of 0.25% bupivacaine and Clonidine (1 mcg/kg), Group D patients received 35 ml of 0.25% bupivacaine and Dexmedetomidine (1 mcg/kg), while group B received 35 ml of 0.25% bupivacaine only in supraclavicular brachial plexus block. Time of request for 1st rescue analgesia, onset and duration of sensory motor blocks and changes in hemodynamic parameters were studied and analyzed. Time for request for rescue analgesia was delayed in group D compared to group B and C. The mean of sensory and motor block onset time in group D was less than in group B and C, the difference between the two group being statistically significant ($p < 0.001$). In group D mean duration of sensory block was prolonged compared to group B and C, which was statistically significant ($p < 0.001$). The addition of dexmedetomidine as adjuvant to bupivacaine in brachial plexus blockade delayed the requirement of rescue analgesia with decreased onset time and prolonged duration of sensory and motor block characteristics compared to clonidine.

Keywords: supraclavicular block, dexmedetomidine, bupivacaine.

INTRODUCTION

Peripheral neural blockade is now a well accepted component of comprehensive anaesthetic care. Its role has expanded from the operating suite into post operative and chronic pain management. The recent emergence of pain management as a formal subspecialty, the advantage of regional over general anaesthesia in case of emergency surgeries and the increasing importance of outpatient (ambulatory) surgery in anaesthetic practices have further bolstered interest in peripheral nerve blocks. The main drawback of long acting drugs was delayed onset of action. To overcome this drawback various methods were tried like, addition of enzymes, buffer and carbonated solutions, opioids, vasoconstricting agents, alkalization and warming up of local anaesthetic solutions and potentiation of blockade by pain and muscular exercise [1]. There has always been a search for adjuvant to regional nerve block with drugs that prolong the duration of analgesia but with lesser side effects. The search for ideal additive continues, and led us to try the

novel α_2 adrenergic agonist dexmedetomidine and clonidine as an adjuvant to local anaesthesia in supraclavicular brachial plexus block [2].

Alpha-2 receptors are located presynaptically in sympathetic nerve endings and in noradrenergic neurons in the CNS. The receptors in the locus coeruleus area of the upper brain stem and the substantia gelatinosa mediate the sedative effects. The imidazoline group of drugs (medetomidine, dexmedetomidine, and mivazerol) has been the most thoroughly investigated as sedative, analgesic and anesthetic agents [3]. Dexmedetomidine has been used extensively in large animal veterinary practice with good success [4]. Dexmedetomidine is a very potent and specific alpha-2 adrenoreceptor agonist. It is a lipophilic compound, which is extensively distributed in the tissues, with a half-life of 6 minutes. The elimination half-life is 2 hours [5].

Dexmedetomidine, a potent α_2 adrenoceptor agonist and its α_2/α_1 selectivity is approximately eight times more selective towards the α_2 adrenoceptor than

clonidine. It has been reported to improve the quality of intrathecal and epidural anaesthesia [6]. The current study is designed to evaluate efficacy of Dexmedetomidine and clonidine when added as an adjuvant to local anaesthetic agent in supraclavicular brachial plexus block with respect to onset and duration of sensory and motor block and duration of analgesia.

MATERIAL AND METHOD

The study was conducted in SCB Medical College & Hospital between November, 2015 and October, 2016. Written informed consent was obtained from all patients and the study was approved by the Institutional Ethics Committee. Ninety patients aged 18 to 60 years, scheduled for elective Orthopaedic surgery operations in the upper limb, under supraclavicular brachial plexus block, were included in this study. Patients with severe cardiopulmonary disease, thyroid disorders, diabetes mellitus, central or peripheral neuropathies, pregnant woman, bleeding disorders history of allergy to local anaesthetics, or other contraindications to regional anaesthesia were excluded from the study.

Participants were allocated to three equal groups of 30 each using a computer generated random number list. Group C patients received 35 ml of 0.25% bupivacaine and Clonidine (1 mcg/kg), Group D patients received 35 ml of 0.25% bupivacaine and Dexmedetomidine (1 mcg/kg), while group B received 35 ml of 0.25% bupivacaine through a supraclavicular approach for brachial plexus block. All observations (hemodynamic variables, oxygen saturation, level of sedation, time required to achieve surgical block in the operation theater and the time to rescue analgesic in the postanesthesia care unit) were also recorded in a blinded manner. Once a patient was brought into the operation theatre, standard monitoring was set up, including non-invasive arterial blood pressure, heart rate, and pulse oximetry. An 18-gauge IV cannula was inserted in the nonoperated forearm and an infusion started with lactated Ringer's solution. Hemodynamic variables were measured 10 min before block placement and every 5 min thereafter till the end of surgery. The entire patients received brachial plexus block through the supraclavicular approach by an anaesthesiologist different from the one assessing the patient intra-operatively and post-operatively. Both were blinded to the treatment groups. Neural localization was achieved by using a nerve locator connected to a 22G, 50mm long stimulating needle. The location end point was a distal motor response with an output lower than 0.5mA in the median nerve region.

Following negative aspiration, 35ml of a solution containing local anaesthetic combined with clonidine or dexmedetomidine or local anaesthetic alone was injected.

Sensory block was assessed by the pinprick method. Assessment of sensory block was done at each min after completion of drug injection in the dermatomal areas corresponding to median nerve, radial nerve, ulnar nerve & musculocutaneous nerve till complete nerve blockade. Sensory onset was considered when there was a dull sensation to pin prick along the distribution of any of the above-mentioned nerves. Complete sensory block was considered when there was loss of sensation to pinprick. Sensory block was graded as-

Grade-0: Sharp pin felt.

Grade-1: Analgesia, dull sensation felt.

Grade 2: Anaesthesia, no sensation felt [7].

Assessment of motor block was carried out by the same observer at each minute till complete motor blockade after drug injection. Onset of motor blockade was considered when there was Grade 1 motor blockade. Peak motor blockade was considered when there was Grade 2 motor blockade. Motor blockade was determined according to a modified Bromage scale for upper extremities on a 3-point scale.

Grade 0: Normal motor function with full flexion and extension of elbow, wrist and finger.

Grade 1: Decreased motor strength with ability to move the fingers only.

Grade 2: Complete motor block with inability to move the fingers [8].

The block was considered incomplete if any of the segments supplied by median; radial, ulnar and musculocutaneous nerve did not have analgesia even after 30min of drug injection. These patients were supplemented with intravenous fentanyl (1mcg/kg) and midazolam (0.02mg/kg). When more than one nerve unaffected, it was considered a failed block. In this case, general anaesthesia was given intra-operatively. Patients were monitored for haemodynamic variables such as heart rate, blood pressure, and oxygen saturation every 5min after the block intra-operatively and every 60min post-operatively. Clinically relevant bradycardia (heart rate <50bpm) spells were treated with atropine (0.6mgIV).

Sedation of patients was assessed by using the University of Michigan Sedation Scale (UMSS) of 0 to 4 [0 = awake and alert; 1 = minimally sedated/sleepy, appropriate response to conversation and/or sound; 2 = moderately sedated, somnolent/sleepy, easily aroused with tactile stimulation and/or simple verbal command; 3 = deeply sedated/deep sleep, aroused only with significant stimulation and 4 = could not be aroused] [9]. At the end of the procedure, quality of the operative condition was assessed according to the following numeric scale:

Grade 4: (Excellent) No complaint from patient

Grade 3: (Good) Minor complaint from patient with no need for the supplemental analgesics.

Grade 2: Moderate) Complaint that required supplemental analgesics.

Grade 1 : (Unsuccessful) Patient given General anaesthesia [9].

Assessment of the blood loss was done and fluid was administered as per the loss. Duration of surgery was noted.

The intra-operative and post-operative assessment was done by an anaesthesiologist who was unaware of the drug used. Patients were assessed for postoperative pain as per a numeric rating scale of 0 to 10. The numeric rating scale was recorded post-operatively every 60min till the score of 5. The rescue analgesia was given in the form of inj. Tramadol 100mg intravenously at the Numeric Rating Scale of 5. All patients were observed for any side-effect like nausea, vomiting, dryness of mouth and complications like pneumothorax, haematoma, local anaesthetic toxicity and post-block neuropathy in the intra-operative and post-operative periods.

The duration sensory block was defined as the time interval between the end of local anaesthetic administration and the complete resolution of

anaesthesia on all nerves. The duration motor block was defined as the time interval between the end of local anaesthetic administration and the recovery of complete motor function of the hand and forearm.

Statistical Analysis:

The statistical software namely SPSS (Statistical Package for Social Sciences) software version 21, were used for the analysis of the data and Microsoft Word and Excel have been used to generate graphs, tables etc. Continuous data are presented as mean ± SD one way ANOVA test were used for parametric data analysis. P<0.05 was considered statistically significant

RESULT

The minimum age of the patient was 18 years and the maximum age was 60years. The mean age of the patients in group B, group C and group D were 38.07±10.11, 33.13±10.88 and 33.43±10.86 year respectively. Age incidences between three groups were comparable. The mean weight of the patients in group B, group C and group D were 57.17±5.95, 55.57±5.84 and 57.27±6.05 kg respectively. Weight and gender in three groups were comparable.

Table 1: Age, sex and weight distribution of Study groups

Parameters	B	C	D	P-value	Significance
No of pts	30	30	30		
Age in yrs (Mean± SD)	38.07±10.11	33.13±10.88	33.43±10.86	>0.05	NS
Weight(kg) (Mean± SD)	57.17±5.95	55.57±5.84	57.27±6.05	>0.05	NS
Gender(M/F)	18:12	20:10	17:13	>0.05	NS

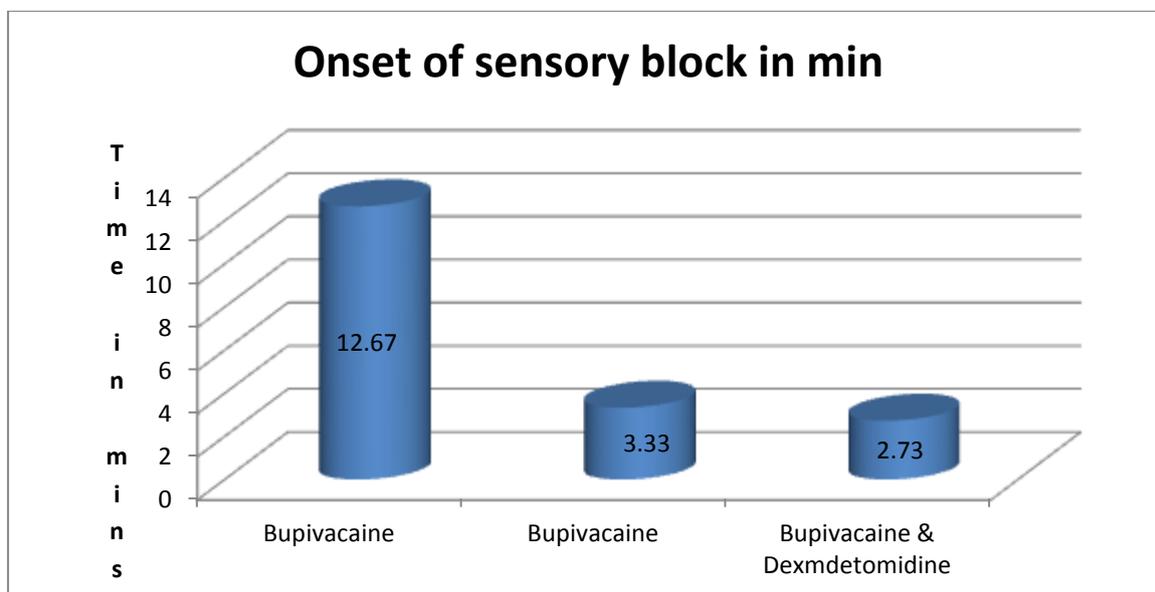


Fig-1: Onset of sensory block in min

The mean time for onset of sensory block in group B, group C and group D were 12.67±1.02, 3.33±1.02 and 2.73±0.94 min respectively. The time for onset of sensory block in group C and group D were

significantly faster than group B. Onset of sensory block was also faster in group D when compared to group C but not significant (P> 0.05).

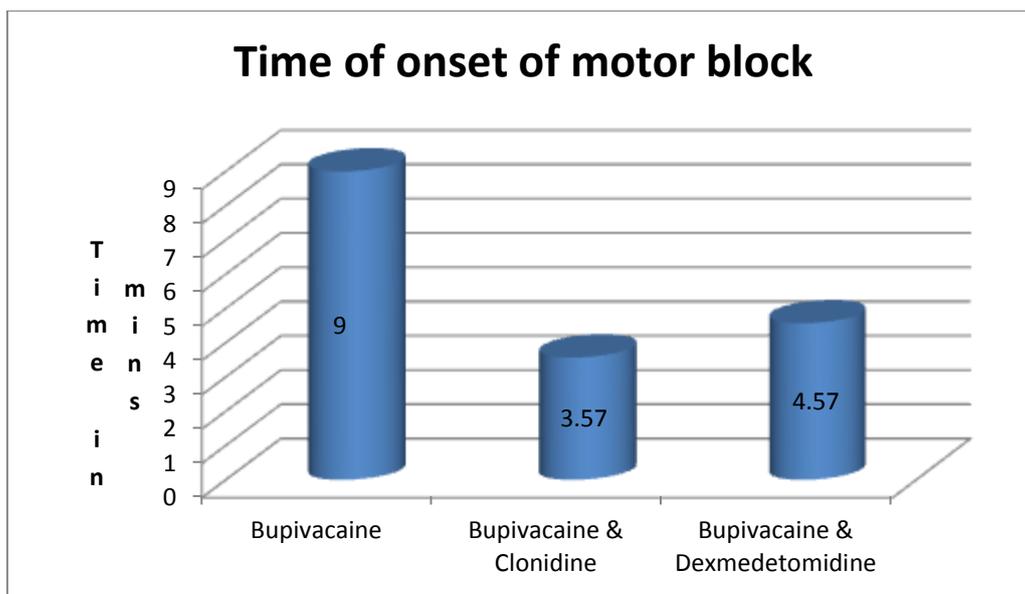


Fig-2: Time of onset of motor block

The mean time for onset of motor block in group B, group C and Group D was 9.00 ± 0.78 min, 3.57 ± 1.61 min and 4.57 ± 2.17 min respectively. The time for onset of motor block was significantly faster in

group C and D when compared to group B ($P < 0.001$). Onset of motor block was faster in Clonidine group than Dexmedetomidine group but not statistically significant.

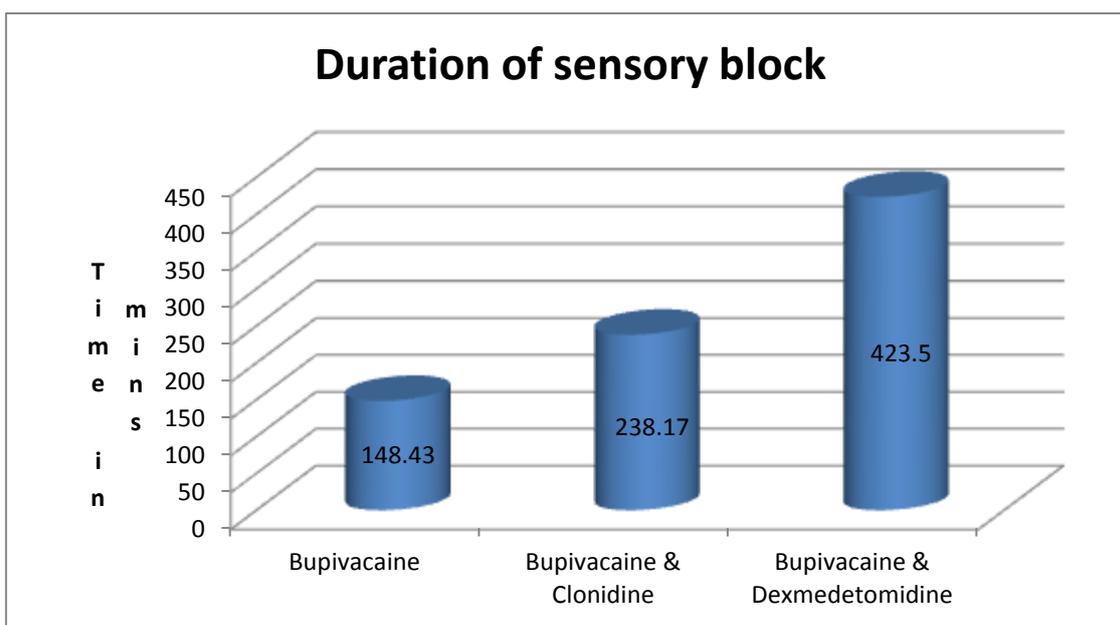


Fig-3: Duration of sensory block

The mean duration of sensory block in group B, group C and group D were 148.43 ± 17.18 min, 238.17 ± 26.25 min and 423.50 ± 45.09 min respectively. The time for duration sensory block were significantly

longer in group C and D when compared to group B ($P < 0.001$). In group D duration of sensory block was significantly longer than the group C ($P < 0.001$)

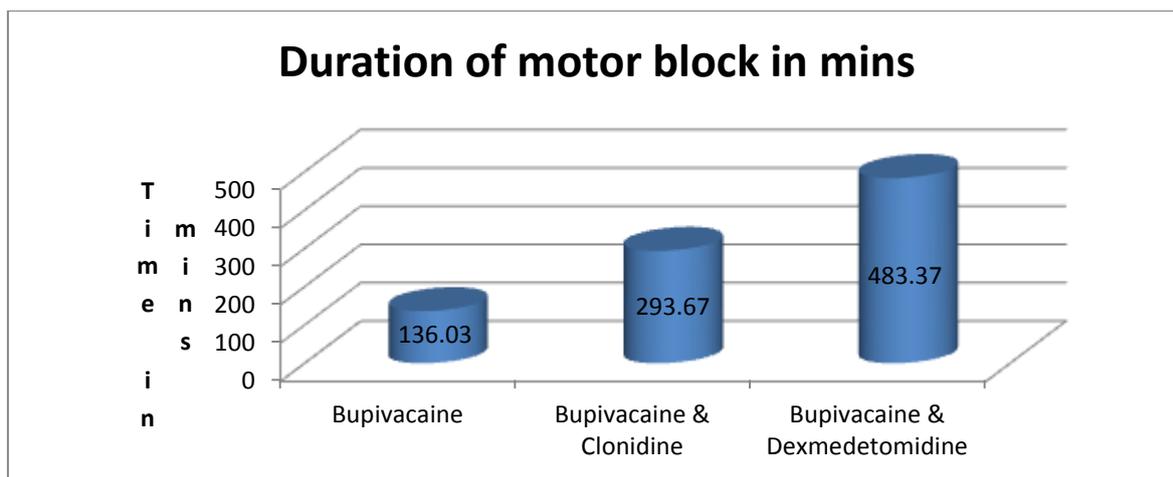


Fig-4: Duration of motor block in mins

The mean duration of motor block in group B, group C and group D were 136.03±16.34 min, 293.67±31.20 min and 483.37±62.78 min respectively. The time for duration motor block were significantly

longer in group C and D when compared to group B (P<0.001). In group D duration of motor block were significantly longer than the group C(P<0.001)

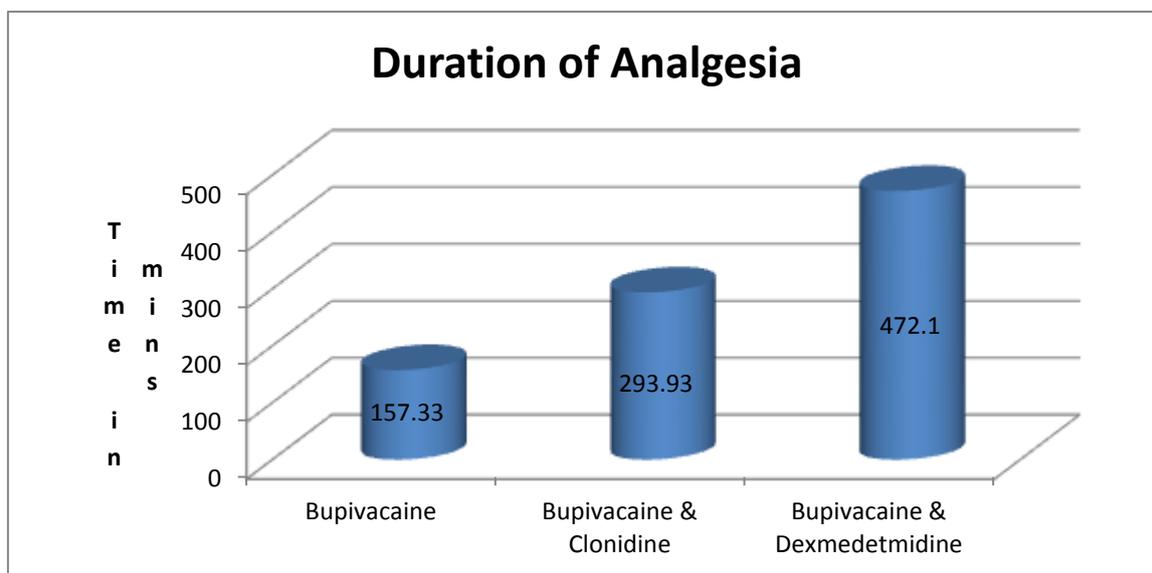


Fig-5: Duration of Analgesia

The mean duration of analgesia in group B, group C and group D were 157.33±16.58 min, 293.93±33.56 min and 472.10±60.77 min respectively. The time for duration analgesia were significantly

longer in group C and D when compared to group B (P<0.001). In group D duration of analgesia was significantly longer than the group C (P<0.001)

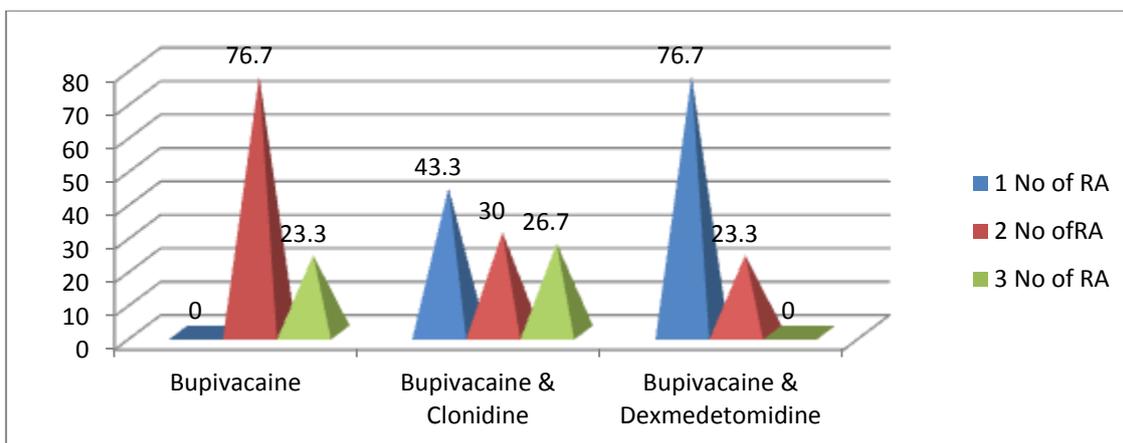


Fig-6: No of rescue analgesia

In group D, 76.7% patients required only 1 rescue analgesia dose and 23.3% of patients required 2 rescue analgesic dose in post operative 24hrs, in group C 43.3% of the patients required 1 rescue analgesia, 30% patients required 2 rescue analgesia and 26.7% patients required 3 rescue analgesia dosage and in group

B 76.7% patients required 2 rescue analgesia dose and 23.3% patients required 3 rescue analgesia dose. The numbers of rescue analgesia used were much less in group C and D when compared to group B. Dexmedetomidine group required less numbers of rescue analgesia than Clonidine group.

Table-2: Side Effects

Side effects	Bupivacaine	Bupivacaine + Clonidine	Bupivacaine + Dexmedetomidine	Significance
Nausea	1	1	0	p>0.05
Vomiting	1	1	1	p>0.05
Dryness of mouth	0	1	0	p>0.05

During our study we monitored for any side effect, we found out in Group B one patient complained for nausea and one patient for vomiting, in Group C one patient complained for nausea, one patient for vomiting and one patient for dryness of mouth and in Group D only one patient complained for vomiting. There was no complication found in three groups.

DISCUSSION

Singelyn *et al.*; in 1996 Reported that a minimum dose of Clonidine (0.5µg/kg) added to mepivacaine prolongs the duration of anaesthesia and analgesia after brachial plexus block. No added benefits were found with dose exceeding 1.5µg/kg. This enhancing effect of small dose of Clonidine on lignocaine may be because of the evoked inhibition of C-fiber action potential. Therefore in present study we have used Clonidine at a dose of 1µg/kg which was same as the dose used by Swami S.S *et al.*; in 2012. Dexmedetomidine has a α₂/α₁ selectivity ratio that is eight-times higher than that of Clonidine. The dose selection was based on previous studies where the Dexmedetomidine 1µg/kg and Clonidine 1µg/kg were used in Bier’s block as an adjuvant to the Lignocaine. After literature review, we found that Dexmedetomidine and Clonidine had peripheral action, which may be useful in using a lesser concentration of local anaesthetic (0.25%) to prolong the block with adequate

anaesthesia. This in turn may be beneficial in high-risk patients.

A total of 90 patients within the age group of 18-60 years were included in the study, 30 in each group. Out of which the mean age of group B (Bupivacaine) was 38.07±10.11 years, the mean age of group C (Bupivacaine with Clonidine) 33.13±10.88 and Group D (Bupivacaine with Dexmedetomidine) was 33.43±10.86 years. Hence all the groups were comparable in respect to age. Male was higher in number to female. The mean weight in Group B, Group C and Group D were 57.17±5.95, 55.57±5.84 and 57.27±6.05 kg respectively were comparable to each other.

Esmaoglu *et al.*; in 2010 [10] added dexmedetomidine to levobupivacaine for axillary brachial plexus block and showed that it shorten the onset time of both sensory and motor block, prolongs the duration of block and the duration of post-operative analgesia. This may be because peripheral α₂ agonist produces analgesia by reducing the release of norepinephrine, leading to α₂ receptor-independent inhibitory effects on nerve fiber action potentials. However in our study we found that onset of sensory block was a little faster with group D (2.73±0.94 min) as compared to group C (3.33±1.02 min), but was

statistically insignificant. Both the group C and Group D significantly faster than the plain bupivacaine group (12.67 ± 1.02 min). The onset of motor block was a little longer in Group D (4.57 ± 2.17 min) than Group C (3.57 ± 1.61 min) but not significant statistically. However both Group C and Group D significantly shorter onset of motor block than Group B (9.00 ± 0.78).

In the present study the mean duration of sensory block in group B, group C and group D were 148.43 ± 17.18 min, 238.17 ± 26.25 min and 423.50 ± 45.09 min respectively. The time for duration sensory block were significantly longer in group C and D when compared to group B ($P < 0.001$). In group D duration of sensory block were significantly longer than the group C ($P < 0.001$). The mean duration of motor block in group B, group C and group D were 136.03 ± 16.34 min, 293.67 ± 31.20 min and 483.37 ± 62.78 min respectively. The time for duration motor block were significantly longer in group C and D when compared to group B ($P < 0.001$). In group D the duration of motor block were significantly longer than the group C ($P < 0.001$). The mean duration of analgesia in Group D (472.10 ± 60.77 min) were longer than in Group C (293.93 ± 33.56 min) and it was statistically significant. Both the Group D and Group C were longer duration of analgesia than Group B (157.33 ± 16.58 min) which was statistically significant. All the above findings relating to onset and duration of sensory and motor block and duration of analgesia were similar to the study conducted by Swami S.S *et al.*; in 2012. Memis *et al.*; in 2004 [11] in their study showed that addition of dexmedetomidine to lignocaine for intravenous anaesthesia improves both the quality of anaesthesia as well as intraoperative and post-operative analgesia. In our study, the quality of block in 80% of the patients in Group D were grade IV (i.e excellent block without any supplementary sedation or analgesia) while 40% in Group C achieved grade IV quality, which was similar to the study conducted by Swami S.S *et al.*; in 2012. This improved quality of block might be the result of various mechanisms of nerve conduction block such as hyperpolarisation, decreased CAP and inhibition of voltage gate of sodium pump as per the study conducted by Popping DM *et al.*; in 2009 And Kosugi T *et al.*; in 2010 [12]. In our study group D, 76.7% patients required only 1 rescue analgesia dosage and 23.3% of patients required 2 rescue analgesic dosage in post operative 24hrs, in group C 43.3% of the patients required 1, 30% patients required 2 rescue analgesia and 26.7% patients required 3 rescue analgesia dosage and in group B 76.7% patients required 2 analgesia dosage and 23.3% patients required 3 analgesia dosage. The number of rescue analgesia used were significantly less in group C and D when compared to group B. The prolonged analgesia in Group D could be due to the action of Dexmedetomidine by inhibiting action potential of A & C fibers in peripheral nerves as demonstrated by Gaumann *et al.*;

In our study in group B all patients were awake and alert and had sedation score of 1. In group C and group D sedation corresponding to score 2 was observed in some patients at 15 min and 60 min from time of injection. The sedation can be explained on the basis of that some amount of systemic absorption of drugs could be present. As α_2 agonists produce sedation by central action, they produce inhibition of substance P release in the nociceptive pathway at the level of dorsal root neuron and by activation of α_2 adrenoceptors in the locus ceruleus as per the study conducted by Abosedira MA *et al.*; in 2008 [13]. In our study pulse rate, systolic BP, diastolic BP, O₂ saturation was recorded at 0 min, 5 min, 15 min, 30 min, 60 min, 2 hour, 6 hour, 12 hour, 24 hour. There were no significant difference in pulse rate between the three groups ($P > 0.05$) except at 30min and 60min group D showed significant decreased pulse rate in comparison to group C and group B ($P < 0.05$). There were no significant difference in systolic blood pressure between the three group ($P > 0.05$) except at 60min and 2hrs group D showed significant decrease in systolic blood pressure ($P < 0.05$). There were no significant difference in diastolic blood pressure between the three group ($P > 0.05$) except between 60mins to 2hrs group D showed significant decrease in diastolic blood pressure ($P < 0.05$). There were no significant difference in O₂ saturation between the three groups ($P > 0.05$). All the above findings in relation to heart rate, systolic blood pressure, diastolic blood pressure, O₂ saturation were similar to the findings of the study conducted by Swami S.S. *et al.*; in 2012 [14].

CONCLUSION

Dexmedetomidine $1 \mu\text{g}/\text{kg}$ when added to 35ml of Bupivacaine 0.25% for supraclavicular brachial plexus block speeds the onset of sensory and motor blocks, prolongs the duration of sensory and motor block. The combination produces improved analgesia resulting in a prolonged effect and reduces the requirement of rescue analgesia as compared to Clonidine. The above findings suggest that the Dexmedetomidine combination with Bupivacaine much superior to the Clonidine combination with Bupivacaine and Plain Bupivacaine group.

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