A Comparison of Dexmedetomidine with Fentanyl as an Adjuvant to Levobupivacaine in Supraclavicular Brachial Plexus Block for Upper Limb Surgery: A Prospective Randomized Single-Blind Controlled Study

Anand Kumar Yadav[1], A.P. Agrawal[2], Malti Agrawal[3], Sarafaraj Ahmad[4], Aditya Kumar Kejariwal[1], Karandeep Singh[1]

ABSTRACT

Introduction: Supraclavicular block of brachial plexus provides complete and reliable anaesthesia for upper limb surgeries. But it is of limited duration on termination of block usually general anaesthesia is required, so there is continuous demand of prolonging their effect with the adjuvants, like clonidine, dexmedetomidine and fentanyl. Therefore we evaluated the anaesthetic quality and length of analgesia with the addition of either fentanyl or dexmedetomidine to levobupivacaine for Supraclavicular brachial plexus block.

Material and methods: In a prospective clinical trial, 90 patients were randomly allocated to either receive 2mg/kg levobupivacaine 0.5% (Group LBC), 2mg/kg levobupivacaine 0.5% with fentanyl 1 mcg/kg (Group LBF) or 2mg/kg levobupivacaine 0.5% with dexmedetomedine 1 mcg/kg (Group LBD) in Supraclavicular brachial plexus. The characteristics for anaesthesia and analgesia were assessed for all the three groups. Observations - Demographic profile was comparable in all the groups. The onset of sensory and motor block and duration of analgesia and motor block was enhanced in Group LBD and Group LBF compared to Group LBC. There were minimum haemodynamic disturbances and side-effects in all the group except for sedation, bradycardia and hypotension which was frequently noted in patients receiving dexmedetomidine as adjuvant.

Results: Compared to the use of levobupivacaine 0.5%, 2 mg/kg alone for supraclavicular brachial plexus block, the addition of 1 mcg/kg fentanyl or 1 mcg/kg dexmedetomidine to levobupivacaine enhanced onset of block and also increased duration of surgical anaesthesia with prolongation of post-operative analgesia. Furthermore blockade characteristics improved better with addition of dexmedetomodine than fentanyl without increasing incidence of unwanted side-effects.

Keywords: Supraclavicular brachial plexus block, Levobupivacaine, Fentanyl, Dexmedetomidine.

INTRODUCTION

Peripheral nerve blocks are cost effective anaesthetic techniques used to provide superb anaesthesia and analgesia while avoiding airway instrumentation and the hemodynamic consequences of general and neuraxial anaesthesia and for this reason all around the world, interest in regional anaesthesia is growing rapidly.[1] The supraclavicular block is performed at the level of the brachial plexus trunks where almost entire sensory, motor and sympathetic innervations of the upper extremity is carried in just three nerve structures confined to a very small surface area. Consequently typical features of this block include rapid onset, predictability and dense anaesthesia.Satisfactory surgical conditions are obtained with complete sensory and motor blockade. Currently bupivacaine which is an amide local anaesthetic is the most frequently used local anaesthetic because of long duration.[2,3] Although local anaesthetics are generally quiet safe and effective, they may produce systemic toxic reactions affecting heart and brain.[4] However, the reported incidence of cardiovascular toxicity is much less with levobupivacaine as compared to bupivacaine though having the same pharmacological profile[5]; this led us to investigate the clinical efficacy of levobupivacaine in supraclavicular block. Adjuvants like opioids have been administered concomitantly with local anaesthetics with the possibility of providing post-operative analgesia in addition to improved quality of anaesthesia. Addition of fentanyl to local anesthetics is known to significantly improve duration of sensory and motor block in brachial plexus blocks. Dexmedetomedine, a centrally acting α_2 receptor agonist, is widely used for anaesthesia, analgesia, has also been used as an adjuvant to local anaesthetics for brachial plexus block.The purpose of this study was to examine if fentanyl or dexmedetomidine added to levobupivacaine in supraclavicular brachial plexus block improved blockade characteristics and enhanced duration of post-operative analgesia.

MATERIALS AND METHOD

This prospective randomized single blind controlled study was carried out in 90 patients selected on base on previous similar studies, divided in to three groups, each comprising 30 patients. The study was conducted after obtaining the requisite approval from ethical committee of the institute. The purpose and entire anaesthetic procedure was explained in detail to them and written informed consent was taken from all the patients.

[1]JR 3, Department of Anaesthesia), [2]Associate Professor, Department of Orthopedics, [3]Professor and Head of the Department, Department of Anaesthesia, [4]Senior Resident, Department of Anaesthesia, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh, India

Corresponding author: Ashish Royal Park, Phase 3, Flat no. 46, Bareilly, 243006, India

How to cite this article: Anand Kumar Yadav, A.P. Agrawal, Malti Agrawal, Sarafaraj Ahmad, Aditya Kumar Kejariwal, Karandeep Singh. A comparison of dexmedetomidine with fentanyl as an adjuvant to levobupivacaine in supraclavicular brachial plexus block for upper limb surgery: a prospective randomized single-blind controlled study. International Journal of Contemporary Medical Research 2016;3(3):785-789.

This study was conducted in the adults between 18-60 years of age and ASA grade I and II patients.Patients were divided into 3 groups;

Group LBC -Were scheduled to receive supraclavicular brachial plexus block with 0.5% (2mg/kg) levobupivacaine only.

Group LBF - Were scheduled to receive supraclavicular brachial plexus block 0.5% (2mg/kg) levobupivacaine with 1µg/kg fentanyl as an adjuvant.

Group LBD - Were scheduled to receive supraclavicular brachial plexus block 0.5% (2mg/kg) levobupivacaine with 1µg/kg dexmedetomidine as an adjuvant.

Exclusion Criteria were: Patient refusal for procedure, any bleeding disorder or patient on anticoagulants, impaired coagulation profile, neurological deficits involving brachial plexus, patients with allergy to local anaesthetics, local infection at the injection site, body mass index >35, any other condition that precludes the administration of supraclavicular brachial plexus block.

Patients were advised to remain nil orally for 8 hrs for solid and 3 hrs for clear liquid before surgery.Patients were pre medicated with tablet alprazolam 0.25mg and tablet ranitidine 150mg in the night before surgery, informed.

Before shifting the patient to the operation theatre, an intravenous access was obtained and RL started inj. Ondansetron 4 mg intravenous was given. Patient was made to lie supine on the OT table and routine monitoring leads were applied. Baseline values of pulse rate, blood pressure, arterial saturation of oxygen(SpO_2), ECG and respiratory rate were recorded. A sand bag was kept posteriorly under the respective the scapula. The head was turned away to the opposite side by 30˚. After aseptic preparation of the skin, supraclavicular brachial plexus block was then performed with the help of nerve stimulator – locator. A 22 guage 50mm insulated needle (Stimuplex® A, B Braün) was attached to the locator and inserted at an initial current output of 1.5mA and 2 Hz frequency. Once desired contractions i.e. flexion with supination of the forearm was appreciated, the current was decreased to 0.5mA and on persistence of contractions, the drug was injected following intermittent negative aspiration. Pulse and blood pressure was recorded preoperatively and immediately after giving the block. Thereafter pulse and blood pressure was recorded every at 5, 10, 15, 30, 45, 60, 90, 120, 180, 240, 360, 480 and 720 minutes after the block.

	Group LBC	Group LBF	Group LBD
Age (years)	38.73 ± 11.20	31.73 ± 11.11	37.4 ± 10.45
Sex (M/F)	11/19	19/11	25/5
Duration of surgery(Min)	104.3	104.83	107.83
BMI	21.87 ± 3.00	20.57 ± 2.70	21.53 ± 3.29

Table-1: Demographic Data between Three Groups

Onset of sensory blockade and onset of motor blockade was observed every 2 minutes and compared with the corresponding areas of the other arm.

The motor block was assessed by using modified Bromage scale.

0 = can lift extended arm, 1 =inability to raise extended arm, can bend elbow, 2 = inability to bend elbow, can flex wrist and fingers, 3 = No movement

Inj tramadol 100 mg in 100 ml normal saline (infused) was given for rescue analgesia and number of doses of rescue analgesia given were noted.

The regression of block was similarly observed till complete recovery. Side effects and complication during injection, during operation and postoperatively were properly recorded and treated accordingly.

Pain scores were recorded at thirty minutes, two hours, four hours, six hours, eight hours and at twelve hours from the time of block. Assessment of pain in intraoperative and post anesthesia care unit (PACU) was done using numerical pain scale between 0 – 10.

0 = No pain

10 = The most severe pain

STATISTICAL ANALYSIS

Statistical analysis of the data was done using the statistical package for the social science (SPSS 17.0) using Chi-square and One way Anova test and Tukey post hoc test $P< 0.05$ was considerd statistically significant. The data was compiled using Microsoft excel sheet (windows 2007).

RESULTS

The group were comparable with respect to age, weight, sex ratio, duration of surgery (Table 1).

The mean onset time of sensory and motor blockade was (14.26 ± 3.64) and (20.70 ± 3.96) minutes in Group LBC, (11.50 ± 3.10) and(16.60 ± 4.43) minutes in Group LBF and (5.78 ± 2.05) and (10.03 ±2.17) minutes in Group LBD. The difference between the three groups was statistically highly significant with ($p = 0.000$) at 95% confidence interval.

The mean duration of analgesia (sensory) for Group LBC was (624.83 ± 152.89) minutes, for Group LBF it was (789.33 ± 134.88) minutes and for Group LBD it was (1078.33 ± 195.42). The mean duration of motor blockade was [(552.50 ± 155.11), (642.0 ± 127.83) and (912.17 ± 190.32)] minutes for Group LBC, Group LBF and Group LBD respectively (Table 2). The difference in the duration of analgesia and motor blockade was statistically highly significant ($p< 0.0001$).

The mean pulse rate and mean of MAP in Group LBC, Group LBF and Group LBD were comparable preoperatively, intra operative and post operatively (Graph 1and2). The mean pulse rate and MAP were slightly lower in Group LBD than

	Group LBC	Group LBF	Group LBD	
Onset time of sensory block	14.26 ± 3.64	11.50 ± 3.10	5.78 ± 2.05	p =0.000
Onset time of motor block	20.70 ± 3.96	16.60 ± 4.43	10.03 ± 2.17	p =0.000
Duration of analgesia (sensory)	624.83 ± 152.89	789.33 ± 134.88	1078.33 ± 195.42	p =0.000
Duration of motor block	552.50 ± 155.11	642.0 ± 127.83	912.17 ± 190.32	p =0.000

Table-2: Sensory and Motor block onset time, Duration of Motor and Analgesia

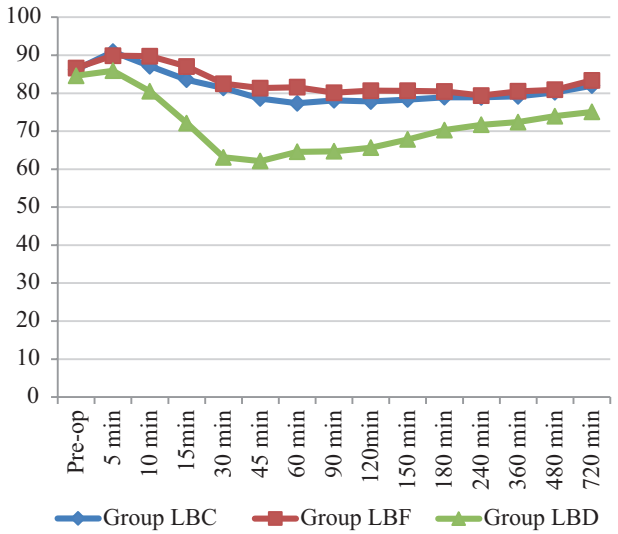

Figure-1: Comparison of Mean Pulse Rate / (Min) in Group LBC, Group LBF and Group LBD

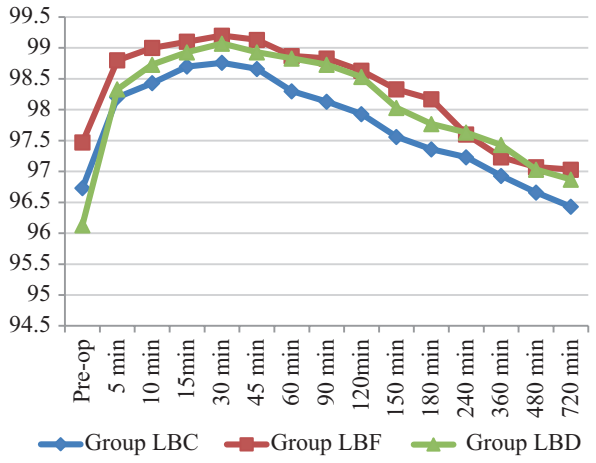

Figure-2: Comparison of Mean Arterial Pressure (Mm of Hg) In Group LBC, Group LBF and Group LBD

Group LBC and Group LBF. The difference was statistically significant as the p value was <0.005.

The mean pain score were recorded and compared at specified intervals i.e at thirty minutes, two hours, four hours, six hours, eight hours, and at twelve hours. The mean pain score was slightly lower in Group LBD and group LBF than Group LBC at eight and twelve hours. The difference between three groups was statistically significant (p value of <0.0001 at 95% confidence interval). However, pain scores were significantly lower in patients who received the addition of dexmedetomidine to levobupivacaine, when compared to the addition of fentanyl.

The number of boluses of rescue analgesic needed in post operative period for 24 hr. were as: 6.7 % of patients in group LBC and 13.3 % of patients in group LBF and 76.7 % of patients in group LBD needed only one dose of analgesic. Where as 46.7 % of patients in group LBC and 66.7 % of patients in group LBF and 20% of patients in group LBD needed 2 dose of analgesics in 24 hr of post operative period. 46.7 % of patients in group LBC and 20 % of patients in group LBFand 3.3 % of patients in group LBD, needed 3 dose of rescue analgesics in 24 hr of post operative period. The difference in the requirement of rescue analgesics between the three groups is statistically significant with a p value (< 0.05) with 95% confidence interval.

Side effects such as nausea and vomiting were not a major problem in Groups LBC, Group LBF and Group LBD. Hypotension, bradycardia and sedation were observed in some patients in Group LBD for which no treatment was required.

DISCUSSION

In the present study, we found that addition of Inj. Fentanyl 1mcg/kg or Inj. Dexmedetomidine 1mcg/kg to 2mg/kg 0.5% levobupivacaine led to earlier onset and duration of analgesia and motor block when compared to 0.5% levobupivacaine alone. However,the addition of Dexmedetomidine to levobupivacaine led to a significant improvement in the onset and duration of sensory and motor blockade and prolonged analgesia compared to the addition of fentanyl.

In the present study, readiness to surgery with a faster onset and establishment of block was observed in Group LBD and Group LBF compared to Group LBC. An earlier onset and completion of motor and sensory block in patients of Group LBF compared to Group LBC may be related to the peripheral effects of opioids. The lipid solubility of fentanyl may have a perineural effect and fentanyl is also reported to have a local anesthetic action that has probably led to the quicker onset of action and establishment of complete block.[6] Similarly, a quicker onset in Group LBD compared to Group LBC could be attributed to the addition of dexmedetomidine. Though the Several mechanisms of action have been suggested to explain the analgesic effect of dexmedetomidine, some of these include vasoconstriction around the injection site[7], direct suppression of impulse propagation through neurons as a result of a complex interaction with axonal ion channels or receptors[8], local release of enkephalin-like substances[9], a decrease in localized proinflammatory mediators[10] and an increase in anti-inflammatory cytokines through an α_2-adrenoceptormediated mechanism.[11]

Sandhya Agarwal *et al.*[12] studied fifty patient posted for upper limb surgeries showed that onset time of sensory and motor block was shorter in SD group (P < 0.001).

Kenan Kaygusuz *et al.*[13] also studied 64 patients randomly divided into 2 groups and showed onset time of sensory and motor block was shorter in group D than group L (P < 0.01).

P. Manohar *et al.*[14] in a prospective clinical trial of 90 patients were randomly allocated to either receive 30 ml bupivacine 0.5 % (group B), 30 ml bupivacaine 0.5 % with fentanyl 50 µg (group BF) or 30ml bupivacine 0.5% with dexmedetomidine 50 µg (group BD) in supraclavicular brachial plexus were studied and they found that onset of sensory and motor blockade was quicker in patients of receiving either fentanyl or dexmedetomidine as adjuvant, the difference being statistically significant.

C Piangatelli *et al.*[15] compared the effects of 30 mL of 0.5 % levobupivacaine and 30 mL of ropivacaine 0.5 % in infraclvicular brachial plexus block and reported that the sensory onset time was (13.46±1.06) min, motor onset time (19.33±2.58) min, respectively in levobupivacaine group,

our results are comparable to the mentioned study.

Addition of fentanyl or dexmedetomidine to local anaesthetic in brachial blocks significantly prolonged the duration of sensory (analgesia) and motor blockade. The extended anaesthetic and analgesic effect as observed in fentanyl Group could be attributed to fentanyl directly acting on the peripheral nervous system. The existence of endogenous and exogenous opioid receptors in the peripheral nervous system and the initiation of anti-nociceptive action by the activation of such receptors offer the possibility of extended analgesic action. It may also diffuse from the brachial plexus sheath to extradural and subarachnoid spaces and then bind with opioid receptor in the dorsal horn to exert its action. Another cause could be ascribed to the action of fentanyl in the substantia gelatinosa after its centripetal axonal transport after perineural injection.[16] However, the addition of dexmedetomidine to levobupivacaine led to a significant prolongation of the duration of sensory (analgesia) and motor blockade compared to the addition of fentanyl in our study as well as the studies done previously by others. The mechanism by which α_2 adrenergic receptor agonists produce analgesia and sedation is not fullyunderstood, but is likely to be multifactorial. Peripherally, α_2 agonists produce analgesia by reducing release of nor epinephrine and causing α_2 receptor-independent inhibitory effects on nerve fibre action potentials. Centrally α_2 agonists produce analgesia and sedation by inhibition of substance P release in the nociceptive pathway at the level of the dorsal root neuron and by activation of α_2 adrenoceptors in the locus ceruleus.[17,18]

Aliye Esmaoglu *et al.*[19] studied a comparison between dexmedetomidine added to levobupivacaine in axillary brachial plexus block in 60 patients scheduled for elective forearm and hand surgery were divided into two groups in group L 40 ml (200mg) of 0.5 % levobupivacaine plus 1ml saline and in group LD 40ml (200mg) of 0.5 % of levobupivacaine plus 1ml dexmedetomidine and concluded that the duration of analgesia and motor block in group LD was 1008.69 ± 164.04 minutes and 773.00 ± 67.62 minutes and in group L was 887.14 ± 260.82 minutes and 575.00 ± 65.00 minutes, showing that duration of analgesia and motor block in dexmedetomidine was prolonged.

Soma C Cham *et al.*[20] in a prospective random clinical trial of 90 patients, either receive 30 ml ropivacine 0.5 % (group R), 30 ml ropivacaine 0.5 % with fentanyl 50 µg (group RF) or 30ml ropivacine 0.5% with dexmedetomidine 50 µg (group RD) in supraclavicular brachial plexus, and they found that duration of analgesia and motor block was prolonged in patients receiving either fentanyl or dexmedetomidine as adjuvant, the difference being statistically significant. Duration of analgesia and Motor block was significantly increased in group RD compared to both groups RF and R.

The mean pulse rate and MAP were slightly lower in Group LBD than Group LBC and Group LBF. The fall in PR and MAP can be attributed to the effect of fentanyl and dexmedetomidine. Bradycardia and hypotension were seen in group LBD as compared to group LBC and group LBF.

Aliye Esmaoglu *et al.*[19] did a randomized double blind fashioned study comparing dexmedetomidine added to levobupivacaine, they found that heart rate level in dexmedetomidine group were significantly lower than levobupivacaine except basal measurement ($P < 0.05$).

Soma C. Cham *et al.*[20] did a prospective clinical study comparing hemodynamic effect of fentanyl and dexmedetomidine in supraclavicular brachial plexus block achieved with ropivacaine and reported bradycardia in patients belonging to dexmedetomidine group.

The mean pain score were recorded and compared at specified intervals i.e at thirty minutes, two hours, four hours, six hours, eight hours and twelve hours. The mean pain score was slightly lower in Group LBD and group LBF than Group LBC at eight and twelve hours. However, pain scores were significantly lower in patients who received the addition of dexmedetomidine to levobupivacaine, when compared to the addition of fentanyl. Inj.Tramadol 2mg/kg was given to patients when pain scores were found to be more than 4, on a scale of zero to ten.

The number of boluses of rescue analgesic needed in post operative period for 24 hr. was lower in Group LBD and Group LBF than Group LBC. However, rescue analgesic needed in dexmedetomidine group was less as compared to the fentanyl group.

Anjan Das *et al.*[21] did a prospective clinical study comparing effect of dexmedetomidine as adjuvant in ropivacaine induced supraclavicular block and they found that patients of dexmedetomidine group required significantly less number of diclofenac sodium injection in first 24 hours of post operative period than the patient ropivacaine group ($P < 0.01$).

CONCLUSION

From the results of the present study it can be concluded that the local anesthetic levobupivacaine is a suitable drug for supraclavicular brachial plexus block, it provides a long duration of pain free period and with minimum disturbances in hemodynamic variables and toxicity. The addition of 1 mcg/kg of fentanyl or 1 mcg/kg dexmedetomidine as an adjuvant to levobupivacaine prolongs the duration of sensory and motor block and at the same time shortening the latency (onset) period, however dexmedetomidine prolongs the duration of motor block and postoperative analgesia much more as compaired to fentanyl without any significant side effect.

REFERENCES

1. Peripheral nerve blocks: Principles and Practice by Admir Hadzic, Jerry Vloka, New York School of Regional Anesthesia. 2004;4:340.
2. Lund PC, Cwik JC, Vallesteros F: Bupivacaine- a new long-acting local anesthetic agent. A preliminary clinical and laboratory report. Anesth Analg. l970;49:103-14.
3. Dejong RH. Axillary block of brachial plexus. Anesthesiology. 1961;22:215-25.
4. Moore DC, Bridenbaugh PO, Thompson GE, Balfour RI, Horton WG. Bupivacaine: A Review of 11,080 Cases. Anesth Analg. 1978;57:42-53.
5. Morrison SG, Dominguez JJ, Erascarolo P, Reiz S: A comparison of the electrocardiographic cardiotoxic effects racemic bupivacaine, and ropivacaine in anaesthetized swine, Anesth Analg. 2000;90:1308-14.
6. Gissen AJ, Gugino LD, Datta S, Miller J, Covino BG. Effects of fentanyl and sufentanil on peripheral mam-

malian nerves. AnesthAnalg. 1987;66:1272-6.
7. Yoshitomi T, Kohjitani A, Maeda S, Higuchi H, Shimada M, Miyawaki T. Dexmedetomidine enhances the local anesthetic action of lidocaine via an alpha-2A adrenoceptor. AnesthAnalg. 2008;107:96-101.
8. Kosugi T, Mizuta K, Fujita T, Nakashima M, Kumamoto E. High concentrations of dexmedetomidine inhibit compound action potentials in frog sciatic nerves without alpha(2) adrenoceptor activation. Br J Pharmacol. 2010;160:1662-76.
9. Fürst S. Transmitters involved in antinociception in the spinal cord. Brain Res Bull. 1999;48:129-41.
10. Kawasaki T, Kawasaki C, Ueki M, Hamada K, Habe K, Sata T. Dexmedetomidine suppresses proinflammatory mediator production in human whole blood in vitro. J Trauma Acute Care Surg 2
11. Xu L, Bao H, Si Y, Wang X. Effects of dexmedetomidine on early and late cytokines during polymicrobial sepsis in mice. Inflamm Res. 2013;62:507-14.
12. SandhyaAgarwal, RituAggarwal, Praveen Gupta. Dexmededetomidine prolongs the effect of bupivacaine in supraclavicular block. J AnaesthesiolClin Pharmacol. 2014;30:36-40.
13. Kaygusuz K, Kol IO, Duger C, Gursoy S, Ozturk H, Kayacan U et al. The effect of Adding Dexmedetomidine to Levobupivacaine in Axillary Brachial Plexus. CurrTher Res ClinExp. 2012;73:103–11.
14. P. Manohar, M.Prakash. Comparision of the effect of fentanyl and dexmedetomidine in supraclavicular brachial plexus block.J Med Scie and Clin Res. 2015;03:7131-7138.
15. C. Piangatelli, C.De Angelis, Pecora, F.Recanatini, P. Cerchiara, D. Testasecca; Levobupivacaine and ropivacaine in the infraclavicular brachial plexus block. Minerva anestesiol 2006;72:217-21.
16. Viel EJ, Eledjam J, De La Coussaye JE, D'Athis F. Brachial plexus block with opioids for postoperative pain relief; a comparison between morphine and buprenorphine. Regional Anaesthesia. 1989;14:274-8.
17. Eisenach JC, De Kock M, Klimscha W: Alpha(2)-adrenergic agonists for regional anesthesia. A clinical review of clonidine(1984 – 1995). Anesthesiology. 1996;85:655–74.
18. Guo TZ, Jiang JY, Buttermann AE, Maze M: Dexmedetomidine injection into the locus ceruleus produces antinociception. Anesthesiology. 1996; 84:873–81.
19. Esmaoglu A, Yegenoglu F, Akin A, Turk CY. Dexmedetomidine added to Levobupivacaine prolongs Axillary Brachial Plexus Block. Anesth Analg. 2010; 111:1548-51.
20. Soma C. Cham, Medha A. Sangawarz, Umesh L. Ramtani, Bhupendra S. Chavan et al. Effects of fentanyl and dexmedetomidine in supraclavicular brachial plexus block achieved with ropivacaine. 2015;54:9427-9436.
21. Anjan Das, SaikatMajumdar, SusantaHalder, Surajit-Chattopadhyay. Saudi J Anaesthesia. 2014;8:72-77.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 27-01-2016; **Published online**: 17-02-2016