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COMPARISON OF THE EFFECTS OF FENTANYL AND DEXMEDETOMIDINE IN SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK ACHIEVED WITH ROPIVACAINE

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ABSTRACT: BACKGROUND & OBJECTIVES: Supraclavicular block of brachial plexus provides complete and reliable anaesthesia for upper limb surgeries. Ropivacaine, is an affective local anaesthetic in for brachial plexus anaesthesia. It is a potent blocker of Aδ and C fibres, rendering good sensory effect but less motor blockade. We evaluated the anaesthetic quality and length of analgesia with the addition of either fentanyl or dexmedetomidine to ropivacaine for Supraclavicular brachial plexus block. **METHODS:** In a prospective clinical trial, 90 patients were randomly allocated to either receive 30 ml ropivacaine 0.5% (Group R), 30 ml ropivacaine 0.5% with fentanyl 50 mcg (Group RF) or 30 ml ropivacaine 0.5% with dexmedetomedine 50 mcg (Group RD) in Supraclavicular brachial plexus. The characteristics for anaesthesia and analgesia were assessed for the three groups. **OBSERVATIONS:** Demographic profile was comparable in the groups. The onset of analgesia and time to complete analgesia was enhanced in Group RD and Group RF compared to Group R. Prolongation of sensory blockade and motor blockade with extended duration of postoperative analgesia was observed in Group RD and Group RF compared to Group R. There were minimum haemodynamic disturbances and side-effects in any group except for Grade 3 sedation score which was frequently noted in patients receiving dexmedetomidine as adjunct. **RESULTS:** Compared to the use of ropivacaine 0.5%, 30 ml alone for supraclavicular brachial plexus block, the addition of 50 mcg fentanyl or 50 mcg dexmedetomidine to ropivacaine 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, Ropivacaine, Fentanyl, Dexmedetomidine.

INTRODUCTION: Brachial plexus block has been proved to be a superior alternative to general anaesthesia for upper limb surgeries and also for the provision of postoperative pain relief. Reduced hospital stay, less financial burden and avoidance of complications due to general anaesthesia are the many advantages of plexus block.

Local anaesthetic, ropivacaine, an amino-amide, is similar to bupivacaine in terms of onset and duration of block[1] but, with lesser toxicity than bupivacaine when accidental intravascular injection occurs.[2] Ropivacaine given for peripheral nerve blocks blocked nerve fibres responsible for transmission of pain - Aδ and C fibres, more completely than those that control motor function – Aβ fibres.[3] 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

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motor block and VAS scores in brachial plexus blocks.[4,5] Dexmedetomedine, a centrally acting α2 receptor agonist, is widely used for anaesthesia, analgesia and monitored anaesthesia care, has also been used as an adjunct to local anaesthetics for brachial plexus block.[6,7] The purpose of this study was to examine if fentanyl or dexmedetomidine added to ropivacaine induced supraclavicular brachial plexus block improved blockade characteristics and enhanced duration of post-operative analgesia.

METHODS: This study was carried out as a prospective, randomized clinical trial on patients who underwent surgical procedures involving the distal arm and fore-arm. Following institutional ethical committee approval, 90 ASA grade I & II patients, aged between 20 and 50 years, weighing between 40 to 70 kg were included in the study. After a thorough pre-anaesthetic evaluation and minimal necessary investigation done, informed written consent was obtained from all patients selected for the study. Patients who did not consent for the procedure, with any hepatic, cardiopulmonary, renal, neurological, psychiatric or neuromuscular disease, any contra-indication to regional anaesthesia or any of the study drugs and/ or were pregnant or lactating, were excluded for the study.

Patients received Tab. Diazepam as overnight sedation and a minimum 6 hr preoperative fasting status was ensured. In the pre-operative room, an intravenous access was secured and multipara meter monitor (Philips–MP 50) was attached for monitoring heart rate, respiratory rate, oxygen saturation, non-invasive blood pressure and electrocardiography. VAS score for postoperative pain was explained to the patient. Preoperative vitals were hence noted. Intravenous ranitidine 150 mg and midazolam 0.03mg/kg was given intravenously and later shifted to the operation room.

Patients were then randomly assigned to one of the three groups of 30 patients each. Group R was to receive 0.5% ropivacaine 30 ml, Group RF, 0.5% ropivacaine 30 ml with 50 mcg Fentanyl and Group RD, 0.5% ropivacaine 30 ml with 50 mcg Dexmedetomidine. After aseptic preparation of the skin, supraclavicular brachial plexus block was then performed with the help of nerve stimulator – locator (TOF–Watch). A 22 guage 50mm insulated needle (Stimuplex® A 50, B Braün, Melsungen, Germany) 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 according to the randomly allocated group was injected following intermittent negative aspiration. Ringers lactate was administered as replacement and maintenance fluid.

Completion of injection was considered as time 0. Sensory and motor blockade evaluation was done every 2 min until complete sensory or motor block or till 30 min, whichever was earlier.

The sensory block was evaluated using the pin-prick method (Score 0: sharp pain; Score 1: touch sensation only; Score 2: No sensation). Onset time to sensory block was defined as the time from completion of injection (Time 0) to the time sensory block began to be detected (Score 1) in the distribution of any one of the major nerves. The time to complete sensory block was taken from time 0 to the achievement of a Score 2 in the distribution of all the major nerves. Total duration of sensory block was the duration from attaining complete block to the time score was ≤ 1. Total duration of analgesia was taken from the time of complete sensory block to the request of rescue analgesic VAS ≥ 4cm.

The motor block was evaluated using the Modified Bromage Scale (Score 1: Partial block, total forearm and partial arm flexion; Score 2: Almost complete block. Inability to flex the arm and decreased ability to flex the forearm; Score 3: Total block, inability to flex both arm and forearm).

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Onset of motor block was taken as time from the time of completion of injection of study drug to detection of a motor block of Score ≥ 1. The time from completion of drug injection to attainment of a Score of 3 was taken as the time to complete motor block. Total duration of motor block was the time between time to attain complete motor block to time to achieve a Score 0 motor blockade.

The block was judged to have failed, if anaesthesia was found inadequate in any of the major nerve distribution after 30 min of institution of drug into the sheath and such patients were then excluded from the study.

The heart rate, respiratory rate, oxygen saturation, blood pressure (Systolic, diastolic and mean arterial) were noted hence every 5 min till 30 min and then every 30 min till regression of block. Hypotension was defined to be a fall in mean arterial pressure of > 20% of baseline values and treated with bolus of 100 ml fluid and if uncorrected, injection ephedrine 6 mg bolus, intravenously.

Bradycardia was defined as pulse rate of ≤ 50/ min and treated with an intravenous bolus of injection Atropine 0.6 mg.

Injection Ondansetron were given to all patients at the end of surgery. They were hence, monitored in the postoperative period in the recovery room and then in respective wards for vitals, regression of block, VAS for pain and any other side effect – nausea, vomiting, shivering, itching, urinary retension, side effects of Supraclaviular block like respiratory distress for pneumothorax, Horner's syndrome, recurrent laryngeal nerve palsy.

Degree of sedation was monitored before institution of block and thence, at all intervals as that of vital parameter monitoring using the Ramsay Sedation Scale (1: awakened and alert; 2: sedated, but responding to verbal stimulus; 3: sedated, but responding to mild physical stimulus, 4: sedated, but responding to moderate or strong physical stimulus; 5: not arousable). At the end of the surgery, quality of anesthesia was graded as: Excellent (3): No complaint from the patient, Good (2): Minor complaint that required supplemental analgesics and Unsuccessful (1): Patient required general anesthesia.

The sample size was determined after undergoing a pilot study and the number of patients to be included was calculated from the mean and standard deviation on the assumption of a minimum difference of increase of 25% in the duration of sensory block between the groups. 28 patients were required in each group in order to have a 90% chance at the two-tailed 0.05 level of significance to detect a difference between the groups and we included 30 patients in each group in our study. Data obtained were analyzed with the Statistical software STATA version 13.1. Statistical tests for categorical data were χ^2 test. For continuous data, analysis of variance (ANOVA) and the Student's t-test were applied. The level of significance was set at P<0.05.

RESULTS: There was statistical no significant difference between the groups with respect to age, weight, sex ratio, ASA physical status, type of surgery, duration of surgery (Table 1). Inadequate or failed block necessitating administration of general anaesthesia was not required in any patient of the study.

The onset of sensory analgesia and motor blockade was quicker in patients of receiving either fentanyl or dexmedetomidine as adjuvant, the difference being statistically significant. A complete sensory block as well as complete motor block was achieved in a shorter duration in all the patients of Group RD and Group RF compared to the patients in Group R. (Table 2).

The total duration of sensory block was significantly prolonged by almost 1½ hr in Group RD compared to Group R. Prolongation was also observed in Group RF, however, less than that observed

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in Group RD. Motor block also took a significantly longer time to regress in Group RD compared to both Group RF and Group R. The total duration of analgesia was significantly increased in Group RD (by 2½ hr) compared to Group RF and (by 1 hr) Group R. The three groups had an average VAS Score below 3 cm at all measured intervals except at the time of reception of Inj. Diclofenac, when highest Scores were observed.

Quality of anaesthesia was Excellent in all patients of Group RD and most patients except for – in Group RF and Group R where 9 and 11 patients respectively required supplemental analgesia in the form of Inj. fentanyl 50 mcg.

No episode of respiratory depression or hypoxaemia was observed in any patient of the study intra-operatively and 24 hrs postoperatively. The trends in mean heart rate depict that they remained lower than mean baseline values in all the groups, however, this difference in mean heart rates compared to respective preoperative mean baseline values was found to be statistically significant ($p < 0.01$) in group RD. A mean MAP lower than mean baseline MAP was observed in Group RD, which was statistically significant from interval of 30 min onwards. However, a fall of < 25 % of MAP was not observed in any patient of Group RD. Fluctuation in mean MAP was however, insignificant in Group R and RF (Figure 1 & 2). Both, mean heart rate and MAP returned to preoperative mean values with the regression of sensory level.

A sedation Score of 3 was most often noted in patients of Group RD (17 patients) compared to Group RF and R, a statistically significant observation. Bradycardia was observed in 2 patients in Group RD and Hypotension in 1 patient of Group RF. Itching was seen in 2 patients receiving fentanyl as adjuvant. Technical complication of supraclavicular brachial plexus block placement like haematoma formation, pneumothorax was not noted in patient of the study. (Table 3)

Table 1: Characteristics of patients in the study			
	Group R	**Group RF**	**Group RD**
Age (in years) Mean ± SD	34.23 ± 12.02	37.33 ± 10.94	34.13 ± 9.73
Weight (in kg) Mean ± SD	54.86 ± 6.56	56.73 ± 6.93	53.26 ± 10.49
Height (in cm) Mean ± SD	164.4 ± 3.83	164.46 ± 3.84	164.12 ± 3.77
Male : Female ratio	17 : 13	20 : 10	17 : 13
ASA Grade I / II	28 / 2	26 / 4	24 / 6
Type of surgery Lower arm / elbow / fore-arm / hand	5 / 2 / 21 / 3	3 / 3 / 18 / 6	6 / 3 / 20 / 1
Duration of surgery (in min) Mean ± SD	85.66 ± 30.5	92 ± 25	92.16 ± 22.5
* ʃ - p < 0.05 **/ʃʃ - p < 0.001			

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Table 2: Characteristics of blockade in patients

	Group R	Group RF	Group RD
Onset of sensory block (in min)	5.16 ± 0.8	2.06 ± 0.25^	2.13 ± 0.34*
Onset of motor block (in min)	7.16 ± 0.69	3.06 ± 0.25^	3.26 ± 0.45*
Time to complete sensory block (in min)	28. 45 ± 4.8	21 ± 5.03^	21.83 ± 4.45*
Time to complete motor block (in min)	36.33 ± 3.14	27.83 ± 2.84^	28.5 ± 3.25*
Total duration of sensory block (in min)	415 ± 19.56	458.15 ± 20.62^^	511.33 ± 30.45**
Total duration of motor block (in min)	409.4 ± 62.42	442 ± 23.54^^	508 ± 25.37**
Total duration of analgesia (in min)	503 ± 24.51	569 ± 36.04^^	648 ± 25.37**
Quality of Anaesthesia Excellent / Good / Unsatisfactory	19 / 11 / 0	21 / 9 / 0	30 / 0 / 0

* / ^ – p < 0.05   ** / ^^ – p < 0.001

Table 3: Incidence of side effects

	Group R	Group RF	Group RD
Hypotension	-	1	-
Bradycardia	-	-	2
Sedation (grade 3)	-	-	17**
Respiratory depression	-	-	-
Nausea vomiting	2	2	2
Pruritis	-	2	-
Pneumothorax	-	-	-
Horner's syndrome	-	-	-
Recurrent laryngeal nerve palsy	-	-	-

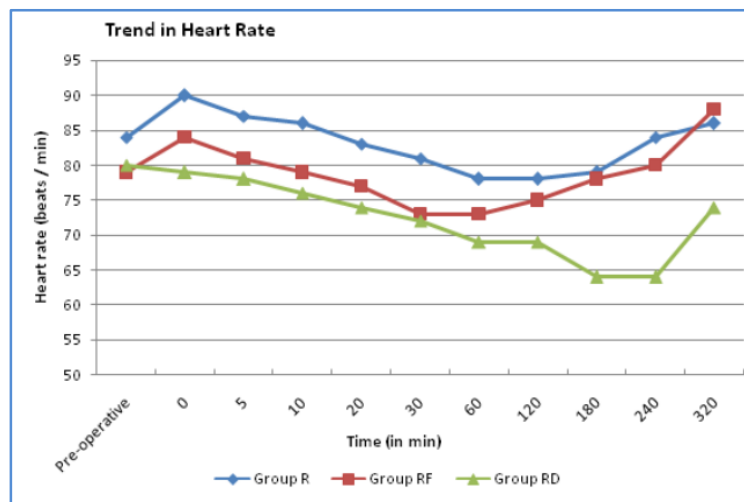* / ^ – p < 0.05   ** / ^^ – p < 0.001

Diagram 1: Trend in Heart Rate
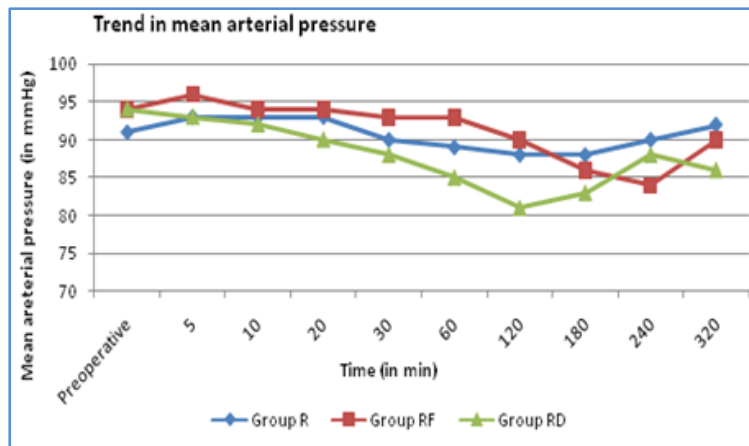
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Diagram 2: Trend in Mean Arterial Pressure

DISCUSSION: In the present study, we found that addition of Inj. Fentanyl 1mcg/kg or Inj. Dexmedetomidine 1mcg/kg to 30 ml 0.5% ropivacaine led to earlier onset and duration of sensory and motor of block as well as increased duration of analgesia when compared to 0.5% ropivacaine alone. However, except for the onset and establishment of block, the addition of Dexmedetomidine to ropivacaine led to a significant improvement in the 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 RD and Group RF compared to Group R. An earlier onset and completion of motor and sensory block in patients of Group RF compared to Group R 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.[8] Similarly, a quicker onset in Group RD compared to Group R could be attributed to the addition of dexmedetomidine. Though the exact mechanism of action of dexmedetomidine has not been completely elucidated, the action of dexmedetomidine on peripheral α2 receptors could be a probable reason.[9]

Kardas K et al[10] stated that 75 mcg fentanyl did not produce any change in blockade characteristics in 1.5% mepivacaine induced supraclavicular brachial block. In axillary block, no difference in onset was observed when100mcg fentanyl was added to 0.25% bupivacaine as quoted by Karakaya D et al.[11] In contrast, however, Nishikawa K et al[5] and Chavan SG et al[12] mentioned that onset time of analgesia was prolonged in every nerve trunk by adding fentanyl to axillary brachial plexus block, probably due to changes in pH on addition of 100 mcg.

These conflicting results are probably caused by differences in local anesthetics or techniques for nerve blockade. It is well known that the injection site of the local anaesthetic attribute varying clinical effects in addition to the concentration and the approach to the brachial plexus.[13]

Kathuria S et al[14] and Esmaoglu et al[15] mentioned of a highly significant acceleration on the onset of block with 50 mcg dexmedetomidine to 0.5% ropivacaine in congruence to our findings. Ammar AS et al,[6] Kaygusuz K et al[16] found an earlier onset in sensory block only with no difference in onset of motor block. Gandhi S et al[17] in their study found that motor block onset was hastened by the use of dexmedetomidine adjuvant in brachial plexus block with bupivacaine whereas Das A et al[18] did not note any difference in onset times with the use of dexmedetomidine with ropivacaine.

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Differences in local anaesthetics, varying doses of dexmedetomidine, approach to brachial plexus and assessment method of blockade characteristics could have led to these diverging observations.

A faster onset of action could be achieved by increasing the concentration of ropivacaine to 0.75% but was kept to 0.5% in the present study since increasing the concentration of ropivacaine failed to improve blockade characteristics and that the risk of increasing the total milligram dose of local anaesthetic may not be warranted.[19]

In our study, a prolongation of sensory and motor as well as duration of analgesia was observed both in Group RF and Group RD, however, maximally observed in Group RD compared to Group RF and Group R. Addition of fentanyl prolonged both surgical anaesthesia and time to request for first analgesia by 30 min whereas dexmedetomidine as an adjunct prolonged anaesthetic duration by an hour and total analgesic duration by two hours compared to the patient receiving only ropivacaine for achievement of block.

Addition of fentanyl enhances postoperative analgesia, but the duration of this effect is too brief to be clinically useful which was stated Kardas K et al[10] and in congruence with our observation in patients receiving fentanyl as adjunct. Karakaya D et al[11] observed that 100 mcg/kg fentanyl added in axillary brachial plexus produced no difference in block characteristics of bupivacaine 0.25% but doubled postoperative analgesia. Supportive observation in increase in duration of sensory and motor block with postoperative analgesia has also been observed in studies by Geze et al,[20] Madhusudan et al,[4] Sindjelic et al[21] and Chavan SG et al.[12]

The extended anaesthetic and analgesic effect as observed in Group RF 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.[22]

A significant prolongation in surgical anaesthetic and analgesic duration in patients receiving adjuvant - dexmedetomidine as observed in our study lend support to various studies by Ammar A et al,[6] Esmaoglu et al,[15] Gandhi et al,[17] Kathuria et al[14] with the use of dexmedetomidine in dose ranging from 50–100 mcg.

The action of dexmedetomidine on the α2 receptors in the locus coerulus and dorsal horn of spinal cord reduces central sympatholytic output, resulting in increased firing of inhibitory neurons and hence producing analgesia is a known feature. Peripheral α2 receptors may also provide anti-nociception. The inhibitory action of α2 receptor agonist is expressed by hyperpolarization of cell membrane and decreased firing of excitable cells of the CNS. Reduction of calcium conductance into cells, thus inhibiting neurotransmitter release is other prominent physiologic action ascribed to α2 adrenoceptors. The nerve is prevented from firing and it also prevents propagation of signals to the neighbours, providing analgesia in two different ways.[16,18,23]

Marhofer et al reported a profound prolongation of ulnar nerve block (UNB) of 60% with perineural dexmedetomidine when added to 0.75% ropivacaine whereas, systemic administration of 20 mcg dexmedetomidine resulted in a prolongation of only 10% during UNB with 0.75% ropivacaine.[24]

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It is unlikely that perineural administration of drug would produce significant systemic side effects, but a central effect that results from the systemic absorption of the drug cannot be excluded.

Haemodynamic parameters were similar in all groups. No respiratory depression, fall in SpO_2 was observed in any patient of the study. Hypotension was noted in one patient in Group RF, bradycardia in 2 patients of Group RD. Incidence of nausea and vomiting were similar in all groups and insignificant in the study. Itching was observed in 2 patients receiving fentanyl as adjuvant. Abdallah et al in the metaanalysis of perineural application of dexmedetomidine as a local anaesthetic adjuvant stated that dexmedetomidine produced reversible bradycardia in 7% of brachial plexus lock patients with no incidence of hypotension.[25]

Quality of anaesthesia was excellent in Group RD and was excellent to good in Groups RF and Group R with no incidence of block failure necessitating induction of general anaesthesia. Sedation of score 3 was most frequently observed in patients receiving dexmedetomidine and resolved with recession of block. Achievement of score 3 sedation with the lack of haemodynamic or any other side effect, can make 50 mcg dexmedetomidine an attractive choice for supraclavicular brachial plexus block.

To conclude, we would like to state that both dexmedetomidine and fentanyl improves readiness for surgery but dexmedetomidine prolongs the duration of sensory and motor block and postoperative analgesia as compared with fentanyl when used as an adjuvant to ropivacaine in supraclavicular brachial plexus block without any significant side effect.

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