A COMPARITIVE EVALUATION OF 0.75% ROPIVACAINE WITH CLONIDINE AND 0.75% ROPIVACAINE WITH DEXMEDETOMIDINE IN SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK- A PROSPECTIVE RANDOMISED DOUBLE-BLIND STUDY

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ABSTRACT

BACKGROUND

Brachial plexus blockade is considered as cornerstone of regional anaesthesia practice. Ropivacaine is a new amide, long acting, pure S (-) enantiomer and local anaesthetic. This study was done to compare clonidine and dexmedetomidine as an adjuvant to 0.75% ropivacaine in supraclavicular brachial plexus block.

MATERIALS AND METHODS

A prospective randomised double-blind study was done in 80 patients of American Society of Anesthesiologist (ASA) grade I and II undergoing elective upper limb surgeries under supraclavicular block. Patients were randomised into 2 groups. Group 1 (n=40) received 30 mL of 0.75% ropivacaine with clonidine 1 mcg/kg and group 2 (n=40) received 30 mL of 0.75% ropivacaine with dexmedetomidine 1 mcg/kg. Onset and recovery time of sensory and motor block, duration of analgesia and quality of block, haemodynamic variables and level of sedation were studied in two groups.

RESULTS

Sensory and motor block onset times were shorter in group 2 (onset of sensory block was 4.9 ± 1.08 minutes and onset of motor block was 8.9 ± 1.41 minutes) than in group 1 (onset of sensory block was 10.7 ± 4.05 minutes and onset of motor block took 12.1 ± 4.11 minutes) (p value <0.0001). Sensory and motor block durations and duration of analgesia were longer in group 2 than in group 1 (p<0.0001). Blood pressure and heart rate were lower in group 2 as compared to group 1 (p value <0.0001). The number of patients achieving grade 4 quality of block was higher in group 2 as compared to group 1.

CONCLUSION

Dexmedetomidine (1 mcg/kg) hastens the onset of sensory and motor block, prolongs the duration of sensory and motor block, enhances the quality of block and sedation and also prolongs duration of analgesia as compared with clonidine (1 mcg/kg) when used as an adjuvant to 0.75% ropivacaine in supraclavicular block.

KEYWORDS

Clonidine, Dexmedetomidine, Ropivacaine, Supraclavicular Brachial Plexus Block.

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BACKGROUND

Brachial plexus block is well-accepted technique to provide anaesthesia and analgesia for upper limb orthopaedic surgeries. Peripheral nerve blocks provide intraoperative anaesthesia and also extend analgesia in the postoperative period without any systemic side effects.[1] Success rate of the block can be further enhanced by using electric nerve stimulator to identify the nerves and depositing the drug perineurally.[2]

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Variety of local anaesthetics can be used to perform ideal and complete block. Among them, ropivacaine is a propyl analogue of bupivacaine, which combines the anaesthetic potency and longer duration of action of bupivacaine with low toxicity profile.[3] The concurrent injection of alpha-2 adrenergic agonist drugs improve the nerve block characteristics of local anaesthetics through either local vasoconstriction[4] and facilitation of C-fibre blockade[5] or spinal action caused by retrograde axonal transport or simple diffusion along the nerve.[6]

Clonidine, selective alpha-2 agonist, has been used as an antihypertensive agent. Various studies have shown that clonidine can be used as an adjunct to local anaesthetics in peripheral blocks.[7]

Dexmedetomidine was introduced two decades ago as a sedative and supplementation to sedation in the intensive care unit for intubated patients. Studies have shown that dexmedetomidine is more specific for alpha-2

adrenoreceptors than clonidine (ratio of alpha 2:alpha 1 activity, 1620:1 for dexmedetomidine, 220:1 for clonidine).[8]

The aim of our study was to assess and compare the characteristics of supraclavicular brachial plexus block using 0.75% ropivacaine with clonidine and dexmedetomidine as an adjuvants in terms of onset and duration of sensory and motor block, postoperative analgesia, side effects and complications.

MATERIALS AND METHODS

This prospective randomised double-blind study was done from January 2016 to December 2016 in which 80 patients of American Society of Anaesthesiologist grade 1 and 2 in the age group of 18 and 60 years of either sex scheduled to undergo forearm and hand surgeries under supraclavicular brachial plexus block were included after taking approval from the institutional ethical and scientific committee. Patients with significant neurological, psychiatric, neuromuscular, cardiovascular, pulmonary, renal and hepatic diseases, allergy to study drugs, pregnant or lactating woman, morbid obesity and coagulation disorders were excluded from the study. A written informed consent was taken from all patients included in the study.

A detailed preanaesthetic check-up of the patients was carried out a day before surgery. General physical examination and systemic examination was done. Routine investigations were reviewed. The interpretation of the Visual Analogue Scale (VAS) was explained to the patients to determine the level of analgesia in the intra and postoperative period. This was carried out with a 10 centimetres line. The first end marked "0" means "no pain" and the end marked "10" means "severe pain."

All patients were given Tab. Alprazolam 0.5 milligrams orally a night prior to surgery. Patients were randomly recruited into two groups of 40 each using a computer generated random number list.

- Group 1 (n=40) received 30 mL of 0.75% ropivacaine plus 1 mcg/kg clonidine.
- Group 2 (n=40) received 30 mL of 0.75% ropivacaine plus 1 mcg/kg dexmedetomidine.

The sample size was estimated from data of previous studies using an alpha level of 0.05 to establish a desired power of 0.80.

On arrival to the operation room, adequate fasting status was confirmed. Patients' baseline pulse rate, electrocardiogram and non-invasive blood pressure was recorded and a wide bore intravenous line was established on unaffected limb and an infusion started with lactated ringer solution. Haemodynamic variables were measured every 5 minutes until the end of surgery.

The patients were administered brachial plexus block by supraclavicular approach under strict aseptic precautions. The injection site was infiltrated with 1 mL of lidocaine 2% subcutaneously. A nerve stimulator (Braun) was used to locate the brachial plexus. A 21G, 50 mm insulated, short-bevelled needle is directed in caudal and posterior direction until required. Motor response is elicited using nerve stimulator with a current of 0.5 mA for 0.1 milliseconds at 2 Hz. When hand twitches were elicited at a current of 0.5 mA, it was taken as endpoint and the study drug was given in 5 mL increment doses after aspiration before each dose to avoid intravascular injection. A 3-minute massage was performed to facilitate an even drug distribution.

Patients in group 1 received 30 mL of 0.75% ropivacaine hydrochloride plus clonidine (1 mcg/kg) diluted to 1 mL and patients in group 2 received 30 mL of 0.75% ropivacaine hydrochloride plus dexmedetomidine (1 mcg/kg). The study drugs were prepared by separate anaesthesiologist in an identical syringes and the volume of the drug was also kept constant to avoid bias. The anaesthesiologist performing the block was unaware of the drug used.

Same anaesthesiologist also monitored all the variables throughout the study.

Oxygen was routinely administered via oxygen mask at 6 L/minute after performing the block. Patients were monitored for block characteristics, haemodynamic parameters and side effects and complications. All durations were calculated considering the time of administering the block as time 0.

Sensory Block- Sensory block was assessed by the pinprick method. Assessment of sensory block was done using a 3-point score at every 2 minutes for the first 20 minutes and then every 5 minutes till 30 minutes. Score 0 was taken as a sharp pain felt, 1 as dull sensation felt (analgesia), 2 as no sensation felt (anaesthesia). Time to onset of motor block (Bromage 2), time to complete motor block (Bromage 0) and total duration of motor block (regression to Bromage 3) was noted.

Motor Block- Patients were assessed for motor block every 5 minutes interval for 30 minutes. The motor block was assessed using the modified Bromage scale as- 0 - No movement, 1 - Finger movement only, 2 - Flexion of the wrist against gravity, 3 - Extension of the elbow against gravity. Time to onset of motor block (Bromage 2), time to complete motor block (Bromage 0) and total duration of motor block (regression to Bromage 3) was noted.

A score of 2 for sensory block and score of 0 for motor block was taken as successful block. Surgery was allowed to begin once full surgical anaesthesia was established. Patients were monitored for pain using VAS score. VAS was recorded just before block, immediately after the block and then every 30 minutes during surgery. If patients experienced pain during surgery, that is, VAS >3, then supplementary analgesia was given as injection ketamine 0.5 mg/kg body weight, and if needed, it was repeated at an interval of 10 minutes twice, after which the patient was given general anaesthesia and was excluded from the study.

Perioperatively, patients were monitored for respiratory rate, pulse rate, systolic and diastolic blood pressure, ECG, oxygen saturation and sedation every 5 minutes interval for first 30 minutes, then every 10 minutes interval for 60 minutes and then every 15 minutes till 180 minutes of giving

the block. Bradycardia of heart rate less than 60/minute was treated with Inj. Atropine 0.3 mg IV, hypotension of systolic blood pressure <100 mmHg or 30% fall from baseline was treated with additional ringer lactate solution and Inj. Ephedrine hydrochloride 5 mg IV titrated according to blood pressure.

Sedation was monitored by using four-point scales. Score 1 - Awake; Score 2 - Drowsy, but responsive to verbal command; Score 3 - Very drowsy, but responsive to the painful stimulus; Score 4 - Unresponsive.

Patients were monitored for postoperative pain every half hourly for first 1 hour, then 1 hourly till 12 hours and then 3 hourly till 24 hours postoperatively using VAS score. Rescue analgesia in the form of injection diclofenac sodium 75 mg IM was given when VAS score >3. Time to request for the first dose of rescue analgesia and total doses of rescue analgesia were recorded. The patients were monitored for any side effects and complications throughout intraoperative and postoperative period for 24 hours such as pneumothorax, haematoma, tinnitus, circumoral numbness, dizziness, nausea and vomiting, respiratory depression, bradycardia, hypotension and seizures.

Duration of sensory blockade- It is the time from the onset of sensory blockade to onset of pain at the surgical site. Duration of motor blockade- It is the time from the onset of motor blockade to the complete recovery. Duration of analgesia- Time from onset of sensory block to VAS score more than 4 in 24 hours, postoperatively.

The quality of the nerve blockade was evaluated prior to surgical incision using 4-point scale. 1 = Complete failure (converted to general anaesthesia), 2 = Insufficient block (inadequate analgesia, inadequate relaxation or patient requiring supplemental analgesia), 3 = Satisfactory block (minimal complaint - no need of analgesia), 4= Excellent block - no complaints. Sedation during block was assessed using Ramsay sedation score.

Successful block of brachial plexus block was defined as presence of adequate motor block and absent sensation to pinprick sensation within 30 minutes of injection. Failed block is defined as "absence of surgical anaesthesia at 30 minutes in at least one of the tests or need to convert to general anaesthesia for completion of surgery."

Statistical Analysis- Duration of analgesia was taken as the outcome measure of interest for the purpose of sample size calculation. The calculated sample size n=40 with failures of 2 in each group requiring general anaesthesia. Hence, a total number of 38 patients in each group with inclusion and exclusion criteria were selected for study. Power of the study was 80% with 5% probability of type 1 error. The data from the present study was systematically collected, compiled and analysed using Standard Statistical Software SPSS 19.0 version (SPSS Inc., Chicago, IL, USA). Data was summarised as mean ± standard deviation or as number and percentages. Numerical variables were normally distributed and were compared using Chi-square test for nonparametric data and Student's t-test for parametric data. The P value was determined to finally evaluate the level of significance. P <0.05 was considered as significant at 5% significance level, P <0.01 as significant at 1% significance level and P <0.001 was considered as highly significant.

OBSERVATION AND RESULTS

In the present study, both groups were comparable with respect to the demographic profile (P>0.05) as shown in Table 1. The onset of sensory block was 10.7 ± 4.05 minutes in group 1 and 4.9 ± 1.08 minutes in group 2. It was found to be statistically significant when we compared group 1 and group 2 (P<0.0001) (Table 2).

The onset of motor block took 12.1 ± 4.11 minutes in group 1 and 8.9 ± 1.41 minutes in group 2. It was statistically significant when we compared groups 1 and 2 (P <0.0001) (Table 2).

Duration of analgesia was 713.25 ± 30.24 minutes in group 1 and 1014.25 ± 68.00 in group 2. It was statistically significant when we compared group 1 and 2 (p <0.0001) (Table 2).

Duration of motor block was 626.25 ± 33.42 minutes in group 1 and 769.25 ± 42.75 in group 2. It was statistically significant when we compared group 1 and 2 (p<0.0001) (Table 2).

Duration of sensory block was 675 ± 26.89 minutes in group 1 and 844 ± 40.56 minutes in group 2. It was statistically significant when we compared group 1 and 2 (p<0.0001) (Table 2).

In group 1, (27/40) were awake and alert and 13 patient are drowsy. In group 2, (18/40) were awake and alert and 22 patients were drowsy (Table 3). There was no significant difference between the groups regarding the incidence of adverse effects.

Variables	Group 1 (n=40)	Group 2 (n=40)	p-value
Age (years), mean ± SD	31.9 ± 12.9	25.8 ± 7.5	1.0
Body weight (kg), mean ± SD	51.5 ± 7.7	56.4 ± 3.0	0.9
Duration of surgery (minute), mean ± SD	71.2 ± 12.5	72.2 ± 16.7	2.0
ASA I/II	21/19	24/16	1.8
Gender (M/F)	26/14	29/11	0.7

Table 1. Demographic Profile

Parameters	Group 1	Group 2	p-value
Onset of sensory block in minutes (mean ± SD)	10.7 ± 4.0	4.9 ± 1.0	<0.0001
Onset of motor block in minutes (mean ± SD)	12.1 ± 4.1	8.9 ± 1.4	<0.0001
Duration of analgesia in minutes (mean ± SD)	713.2 ± 30.2	1014.2 ± 68.0	<0.0001
Duration of motor block in minutes (mean ± SD)	626.2 ± 33.4	769.2 ± 42.7	<0.0001

Duration of sensory block in minutes (mean ± SD)	675 ± 26.8	844 ± 40.5	<0.0001

Table 2. Onset of Sensory and Motor Block, Total Duration of Sensory and Motor Block, Total Duration of Analgesia

Score	Degree of Sedation	Group 1	Group 2
1	Awake and alert	27	18
2	Drowsy, but responsive to command	13	22
3	Very drowsy, responsive to pain	0	0
4	Unresponsive	0	

Table 3. Degree of Sedation

Sl. No.	Adverse Effects	Group 1	Group 2
1.	Hypotension	0	1
2.	Bradycardia	0	2
3.	Nausea/vomiting	0	0
4.	Headache	0	0
5.	Dryness of mouth	0	0

Table 4. Adverse Effects

During surgery, supplementary analgesia was given as injection ketamine IV, if VAS >3. Two patients (6.7%) in group 1 and 2 patients (6.7%) in group 2 required supplementary analgesia and the difference among the 2 groups was statistically not significant (P=1.00).

During postoperative period, patients were monitored for pain using VAS score at various time intervals. VAS scores were comparable in the two groups for first 8 hours of the study. At 10, 12 and 15 hours, VAS score was on the higher side in group 1 as compared to group 2 and the difference was highly significant. Later on, at 24th hour, VAS was at higher side in group 1 when compared to group 2. Rescue analgesia was given when patient had a VAS of 3.

Baseline haemodynamic parameters were comparable. Haemodynamic parameters remained stable and comparable in two groups at all measured intervals. Patients were monitored for side effects and complications for 24 hours.

DISCUSSION

Supraclavicular brachial block is preferred for its rapid onset, reliable anaesthesia and as a safe technique for any surgery in the upper extremity that does not involve the shoulder.[9] This is because the block is performed at the level of nerve trunks, where almost the entire innervations of the upper extremity are confined to very small surface area.[10] Using nerve stimulator to identify nerves, further improves the success rate of block as the drug is deposited close to the nerve sheath and chances of vascular and neurological injuries are also less.[2]

Local anaesthetic used alone in peripheral nerve blocks are effective in providing good operative conditions, but with shorter duration of analgesia in the postoperative period. To improve the block characteristics and to enhance the postoperative analgesia, various adjuvants are added to LAs like opioids, vasoconstrictors, alpha 2 agonists, etc. Clonidine, an α_2 adrenergic agonist was initially used as an antihypertensive, but with the discovery of α_2 receptors in the central nervous system and dorsal horn of spinal cord. The role of this drug in centrally-mediated sedation and analgesia has been widely explored.[11]

Dexmedetomidine, the pharmacologically active D-isomer of medetomidine is a highly specific and selective α2 adrenoceptor agonist with α2:α1 binding selectivity ratio of 1620:1 as compared to 220:1 for clonidine, thus decreasing the unwanted side effects of α1 receptors.[12,13]

Previously, bupivacaine and ropivacaine alone were compared for sensory and motor block characteristics in BPB and it was found that ropivacaine provides faster onset of sensory and motor block and the duration of sensory and motor block was comparable.[14]

Ropivacaine is a pure S (-) enantiomer, structurally related to bupivacaine, developed for the purpose of reducing potential toxicity and improving relative sensory and motor block profiles.[15] The efficacy of ropivacaine is similar to that of bupivacaine and levobupivacaine for peripheral nerve block. Ropivacaine with its efficacy, lower propensity for motor block and reduced potential for cardiotoxicity and central nervous system toxicity appears to be an important option for regional anaesthesia and management of postoperative pain.[16,17]

Casati[18] evaluated the effects of clonidine 1 mcg/kg added to ropivacaine and found longer onset of time to establish block in clonidine group. Erlacher et al[19] compared the effect of adding clonidine to different LAs like mepivacaine, bupivacaine and ropivacaine and found that clonidine has a different impact on each of the LAs in terms of onset and block prolonging action.

Aliya Esmoglu et al[20] have reported that 100 mcg dose of dexmedetomidine when used as an adjuvant for ropivacaine in axillary lock shortens the onset of sensory and motor block and prolongs duration of blockade without significant change in the heart rate, blood pressure and sedation.

Swami et al[21] compared the effects of clonidine (2 mcg/kg) and dexmedetomidine (1 mcg/kg) added to 35 cc of 0.5% bupivacaine in supraclavicular brachial plexus block and found that dexmedetomidine enhanced the duration of sensory and motor block and also the duration of analgesia. In our study, we observed that both clonidine and dexmedetomidine have enhanced the duration of sensory and motor block and duration of analgesia.

In another study, Kenan Kayqusuz et al[22] observed a 3.5 hour prolongation of analgesia when dexmedetomidine 100 mcg was added to levobupivacaine. In our study, we have found significant prolongation of analgesia (5 hours) with dexmedetomidine compared to clonidine. This shows that the dose of dexmedetomidine 1 mcg/kg is appropriate for brachial plexus block and in fact superior to higher dose of clonidine (2 mcg/kg).

In our study in group 1, no significant change in heart rate was seen in the intraoperative as well as postoperative period. In group 2, statistically significant reduction in heart rate were observed. These results are consistent with the

studies done by Adnan et al[23] and Swami et al who found no change in heart rate with clonidine in axillary and supraclavicular brachial plexus block, respectively.

Aliya Esmaoglu et al[20,21] and Swami et al who described significant bradycardia with dexmedetomidine.

Blood pressure (systolic and diastolic) showed no difference in group 1. In group 2, it showed significant reduction both intraoperatively and postoperatively as compared to baseline values, but no active clinical intervention is required. These findings are in line with the works of El Saied et al[24] who found no significant changes in blood pressure when 150 mcg of clonidine was added to ropivacaine.

Aliya Esmaoglu et al[20] and Swami et al[21] have observed a decrease in the blood pressure and heart rate when dexmedetomidine was added to local anaesthetic in brachial plexus block.

CONCLUSION

The upper limb surgeries performed under supraclavicular brachial plexus nerve block with 0.75% ropivacaine and dexmedetomidine 1 mcg/kg as an adjuvant result in early onset of sensory and motor blockade, prolongation of the duration of sensory and motor blockade and postoperative analgesia with better quality of block as compared to clonidine 1 mcg/kg.

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