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A Comparative Evaluation Of Dexamethasone As An Adjunct To Bupivacaine And Levobupivacaine For Supraclavicular Brachial Plexus Block Using Peripheral Nerve Stimulator.

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ABSTRACT

Background: Dexamethasone appears to be effective in prolonging the duration of analgesia from supraclavicular brachial block using levobupivacaine or Bupivacaine. Long acting local anaesthetic, Bupivacaine is associated with cardiac and central nervous system toxicity which prompted the researchers to develop new local anaesthetic agent with a profile similar to bupivacaine but avoiding the toxic effects. Therefore, the aim of the present study is to test the hypothesis that adding dexamethasone significantly prolongs the duration of analgesia for levobupivacaine and bupivacaine and the magnitude of the effect differs among the two local anaesthetics. **Methods:** A prospective, randomized study was undertaken at JN Medical College. 120 patients posted for upper limb surgeries under Supraclavicular Brachial Plexus Block were assigned into four groups, each containing 30 patients. Group I received 25 ml Bupivacaine 0.5% and 2ml NS. Group II received 25 ml of Bupivacaine 0.5% and 2ml dexamethasone(8mg) .Group III received 25 ml of Levobupivacaine 0.5% and 2ml NS. Group IV received 25 ml of Levobupivacaine 0.5% and2ml dexamethasone (8mg). **Results:** Dexamethasone significantly prolonged the duration of analgesia of both levobupivacaine and bupivacaine. **Conclusion:** Dexamethasone prolongs analgesia in supraclavicular blocks using either levobupivacaine or bupivacaine. Considering the less cardiotoxic profile of levo-bupivacaine it should be preferred over bupivacaine.

Keywords: Bupivacaine, Dexamethasone, Levobupivacaine.

INTRODUCTION

The supraclavicular approach to the brachial plexus characteristically is associated with a rapid onset of anesthesia and a high success rate. This technique is favoured by many as it produces a more extensive area of blockade and has many advantages over other approaches to brachial plexus block.[1-3] It is easiest and most effective approach for upper limb anaesthesia.[4] The plexus are more superficial by supraclavicular approach and the narrowest part of the plexus may be encountered by this technique. It can be performed with the patient's arm in any position to provide excellent anaesthesia for elbow, forearm and hand surgery.[5]

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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, predictable and dense anaesthesia. Satisfactory surgical conditions are obtained with complete sensory and motor blockade. Concurrent sympathetic blockade reduces post-op pain, vasospasm and oedema.[6,7]

Bupivacaine an amide local anaesthetic is one of the most popular and frequently used due to its higher potency and prolonged duration of action. However, the drawbacks are its cardiotoxicity especially when injected directly into subclavian artery. The cardiotoxicity may be life threatening as the dysrrhythmia produced are resistant to all routinely used antiarrhythmic. Hence there is a need for a drug which can have all the advantages of bupivacaine without its cardiotoxicity.[8]

Levobupivacaine a new amino-amide local anaesthetic is the S-enantiomer of bupivacaine associated with less vasodilation compared to bupivacaine. Preclinical animal and volunteer studies showed less cardiac toxicity than bupivacaine alone.[9]

The efficacy of local anaesthetic can be increased by adding adjuncts to brachial plexus block. The goal of which is to prolong analgesic effect without the disadvantage of systemic side effects or prolonged motor block. It may also allow for a reduction in the total dose of local anaesthetic used. The various adjuncts added to local anaesthetics till date include opioids (as morphine, pethidine, fentanyl, butorphanol, buprenorphine), clonidine, verapamil, dexmeditomedine, neostigmine, and tramadol but the results are either inconclusive or associated with side effects.[10-12]

The steroid have also been added to local anaesthetic to provide long term pain relieve in persistent painful condition. Till date use of long acting steroid is the most important adjuvant mixed with local anaesthetics in the pain clinic. They reduce inflammation and blocking transmission of nociceptive C-fibres by suppressing ectopic neural discharge and might bring about this effect by altering the function of potassium channels in the excitable cells.[13] Steroids decreases local anaesthetics absorption by causing vasoconstriction, thus prolonging action. The most studied drug among steroids is the dexamethasone. The various studies performed without an additive in the past shows insignificant differences among the group with regard to onset time and the duration of sensory blockade for lower abdominal surgery and epidural blockade.[14,15] Whether the effect differs among these commonly used drugs after addition of additive is a matter of discussion.

The effectiveness of combination of dexamethasone as an adjunct to the plain Bupivacaine and Levobupivacaine for prolonging the duration and extent of analgesia for supraclavicular brachial plexus block is still contentious.[16,17]

Therefore, the aim of the present study is to test the hypothesis that adding dexamethasone significantly prolongs the duration of levobupivacaine and bupivacaine and that the magnitude of the effect differs among the two local anaesthetics.

MATERIALS AND METHODS

After ethical committee approval and informed consent, 120 ASA I & II adult patients of either sex, age ranging between 18 to 70 years, weighing 40 to 80 kg, undergoing elective or emergency upper limb surgery were selected and randomly divided into four groups of 30 patients each depending on the drug administered. Patients receiving anticoagulants, β-blockers or opioids, those with a history of hypertension, myocardial infarction, peripheral neuropathy, neurological deficit, cardiac, respiratory, hepatic and/or renal failure and contra lateral phrenic nerve palsy or hypersensitivity to local anaesthetic agents were excluded from the study.

Patients were randomly allocated to one of the four groups using a standard randomization code. Group I received 25 ml Bupivacaine 0.5% and 2ml NS, Group II received 25 ml of Bupivacaine 0.5% and 2ml Dexamethasone(8mg) Group III received 25 ml of Levobupivacaine 0.5% and 2ml NS and Group IV: 25 ml of Levobupivacaine 0.5% and 2ml Dexamethasone(8mg). A specially designed proforma was used to collect the data which includes patient's particulars, the anaesthetic details, intra-operative and post-operative monitoring and observation for side effects for a prospective, randomized study. The study formulations was prepared by a collaborator not involved in data recording and an appropriate code number was assigned, the same collaborator administers drugs while a blind observer collected the data.

Patients were not premedicated before the block. After insertion of a 20-gauge IV cannula in the non-operated arm, a 5 ml/kg/h infusion of ringer lactate solution was started. After standard anesthesia monitoring, baseline measurements of heart rate (HR), noninvasive arterial blood pressure, peripheral oxygen saturation (SpO2), and respiratory rate were recorded before the block was performed. Patient was pre-medicated with Inj. Midazolam 0.04 mg/kg and positioned supine with the head to the opposite side. After strict aseptic and antiseptic precautions, midclavicular point, external jugular vein and subclavian artery pulsations were identified as landmark. A point 2 cm above the midclavicular point and just lateral to the subclavian artery pulsation a 22 gauge 2-inch (Stimuplex insulated needle; B. Braun Medical) needle was introduced and connected to a nerve stimulator (Stimuplex-DIG Stim-300, B. Braun) at an initial current intensity of 1 mA and advanced caudal and medially until it elicited a desired motor responses in the distribution of the axillary, musculocutaneous, ulnar, radial, or median nerves. The current was gradually decreased to a range of 0.4 to 0.5 mA, with a persistent acceptable motor response. The total 27 mL of local anaesthetic mixture was injected in 5-mL aliquots, with frequent aspirations to assess and prevent intravascular needle migration.

A blinded observer recorded the time to find the onset time of sensory and motor blocks. The degree of sensory block was assessed by pinprick in the relevant dermatome of the musculocutaneous nerve (forearm), radial nerve (dorsal 1st and 2nd intermetacarpal area), median nerve (palmar side of the tip of 3rd finger), and ulnar nerve (palmar side of the tip of the 5thfinger) and was graded according to a three -grade scale 0 = no block(complete sensation), 1 = partial block(partial sensation) , 2= complete loss of pinprick sensation (complete loss

of sensation). The degree of motor block was measured by assessing the following motor functions: elbow flexion for the musculocutaneous nerve; extension/supination of arm and finger for the radial nerve; flexion/pronation of wrist and 2-3rd finger for the median nerve; 4-5th finger flexion/thumb adduction for the ulnar nerve. When a patient achieved surgical anaesthesia the time was noted and the patient was assumed to be "ready for surgery".

Onset time of sensory blockade: was defined as the time interval between the end of total local anesthetic administration and complete sensory block. Sensory block was evaluated by pin prick method with a 23 gauge needle and compared with the same stimulation on the opposite hand. The time when complete sensory blockade achieved was noted.

Duration of sensory block: was assessed by asking the patient to record the time of first pain sensation.

The duration of motor block: was assessed postoperatively on hourly basis by asking the patients to move their fingers and to see whether they were able to raise the hand or not. The duration of motor block was defined as the time interval between the local anaesthetic administration and complete recovery of motor function in all nerve distributions.

Duration of analgesia: appearance of pain requiring rescue analgesia was noted according to 0-10 visual analogue score (VAS) for pain at every half an hour for first 10 hours and then hourly till 24 hours. When the patients began to experience worst pain (VAS =8-10), it was considered that analgesic action of the drugs was over and terminated, then rescue analgesic in the form of diclofenac sodium 1.5mg/kg IM or Inj paracetamol 1gm I.V was given.

Post operative analgesic requirement: the number of boluses of analgesic required was also noted, up to twenty four hours, from the time of block.

Adverse events comprised: seizures, circumoral numbness, vertigo, slurred speech, sudden hypotension or cardiac arrest (accidental intravascular injection of bupivacaine) bradycardia, arrhythmias, headache, chest pain, anxiety and allergic reactions (due to either of the drug), nerve injury, vascular injury, neuropathy and pneumothorax if occurred within 24 hrs were recorded and appropriate intervention was done. The failure of the procedure was also noted. In the circumstance of inadequate or patchy action of the block, the block was supplemented with sedatives/ analgesics. In case of unduly prolonged surgery, and the effect of the block was wore off, then rescue analgesia with IV Ketamine was given. If there was complete failure, general anaesthesia was given and patient was excluded from study.

Results obtained were analyzed statistically. The statistical analysis was performed after completion of the observation. All results were expressed in mean ± standard deviation (SD) or percentage as applicable. Statistical analyses were carried out using Statistical Package for Social Science (SPSS) for Windows Version 17.0, if required modification was made accordingly. The level for all analysis was set to $p<0.05$ and $P < 0.05$ which was considered statistically significant.

For quantitative variables, the data were presented in term of range (minimum, maximum) or mean and standard deviation. Qualitative variables were summarized as frequency (%). The statistical significance of quantitative variables in the four groups was determined by one way ANOVA with post hoc test. The statistical significance for qualitative variables was detected by chi square/fisher exact test to compare the frequency among groups. A p value of <0.05 was considered statistically significant. The collected data were analyzed using Windows Microsoft excel 2007 version and SPSS for Windows(version 17.0) statistical package (SPSS.Inc.,Chicago,IL).

RESULTS

The patient in the four groups were comparable ($p<0.05$) with respect to age, sex and weight thereby chances of biasing of result due to demographic profile of patient were minimized.[Table 1]

Onset of sensory and motor block:

The mean onset time of sensory block was 12.7± 2.12 min, 9.4±2 min, 11.56±1.82 min and 8.32±2.52 min in group I, II, II and IV respectively [Table 2]. The mean onset time of motor blockade was 15.87 ±1.634 min, 12.47±1.592 min, 14.77±1.135 min and 11.4±2.328 min in group I, II, III, and IV respectively [Table 2]. On statistical analysis the present study found that the sensory and motor block was achieved statistically faster ($p<0.0001$) in groups were dexamethasone was used as an adjuvant.

Duration of sensory and motor block:

The mean duration of sensory blockade was 698.6 ± 94.63 min , 906.5 ± 97.64 min, 657.5 ± 53.9 min and 843 ± 109 min for Group I,II,III, and IV respectively [Table 2].

The mean duration of motor block for group I was 606.9 ± 94.63 min, for group II was 796 ± 101 min, for group III it was 571.9±53.9 min and for group IV it was 758±87 min. The mean duration of sensory and motor was significantly longer in dexamethasone added groups ($p<0.0001$) [Table2].

Duration of Analgesia

The duration of analgesia was 757.3 ± 116.8 min, 974 ± 116 min, 698.6±78.75 min and 902±114.3 min for group I,II,III and IV respectively. The duration of analgesia was increased statistically significantly ($p<0.0001$) in groups were dexamethasone was used as an adjuvant (group II and IV) [Table 2].

Table 1: Patient characteristics.

Variables	Group B	Group BD	Group L	Group LD	P value
Age(years)	33.3±15.4	37.3 ± 14.5	36.9±15	35.2±13	> 0.05
Sex M/F	21/9	21/9	14/16	19/16	> 0.05
Weight (Kg)	56±9.3	57±7.5	55.4±8.68	59±7.9	>0.05
BMI	22.7±3.1	24.3±4.5	23.8±3.6	22.2±3.9	>0.05

Value expressed as Mean ± SD

Table 2: Block Characteristics.

Variables	Group B	Group BD	GROUP L	GROUP LD	P value
Onset sensory block	12.7±2.12	9.4±2.0	11.56±1.82	8.321±2.52	< 0.0001
Onset motor block	15.87 ±1.63	12.47±1.592	14.77±1.135	11.4±2.328	< 0.0001
Duration sensory block	698.6±94.63	906.5±97.64	657.5±53.9	843±109	<0.0001
Duration motor block	606.99±94.63	796±101	571.9±53.9	758±87	<0.0001
Duration analgesia	757.3±116.8	974±116	698.6±78.75	902±114.3	<.0.0001

Value expressed as Mean ± SD minutes.

Analgesic requirement

At 12 hours, the difference in pain score was statistically significant ($p<0.05$) between group I and group II and between group III and IV. Pain score were less in groups in which dexamethasone was used as an adjuvant [Figure 1]. Less rescue analgesic dose was required in group in which dexamethasone was used as adjuvant. The percentage of patients who required rescue analgesia in Group I were 36.6%, 60%, 3.33% who needed 3, 2, 1 dose of analgesics in 24 hr respectively, whereas in Group B 6%, 26.6%,66.6% needed 3,2,1 dose of rescue analgesics respectively. The percentage of patients who required rescue analgesia in Group III were 36.6%, 53.3%, 10% who needed 3, 2, 1 dose of analgesics in 24 hr respectively, whereas in Group IV 3.33, 26.6%,70% needed 3,2,1 dose of rescue analgesics in 24 hr respectively.

The mean value of boluses of analgesic required up to 24 hr post operatively in group I was 2.3±0.59 as compared to 1.4±0.621 in Group II, the difference being statistically significant (p value <0.05). Also there was statistically significant difference between mean value of analgesic requirement between group III and IV. All our patients were operated successfully under nerve stimulator guided brachial plexus block without any supplementation or failure. The effect of the procedure on the hemodynamic was also studied in all the groups in this study. Pulse rate and mean arterial blood pressure were recorded and compared at specified intervals i.e. pre-operative, at five minutes, thirty minutes, sixty minutes and ninety minutes. The mean pulse rate and mean MAP in all groups were comparable with no statistically significant difference. Intraoperative hemodynamic parameters like BP/ECG/SPO2/HR were within normal limits in all the groups.

Adverse events

The incidence of complication including hematoma, pneumothorax, accidental intravascular injection, post block nausea/vomiting/convulsions/neuralgia were nil in all four groups. No patient required any intervention.

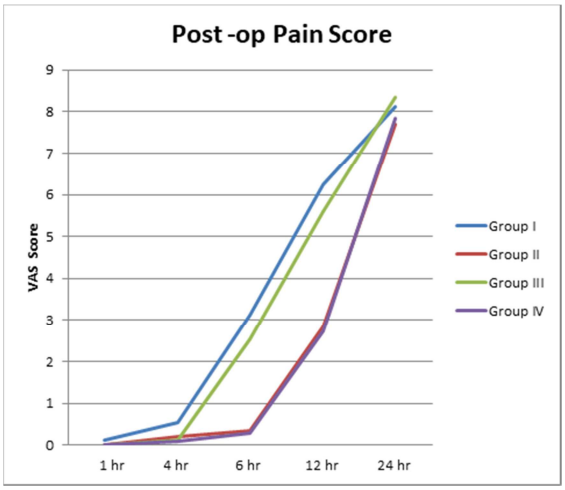

Figure 1: Comparison of Pain Score (VAS score)

DISCUSSION

In present study we found that onset of sensory and motor block was significantly faster in patients who received dexamethasone as adjuvant and block characteristics of bupivacaine was found similar to that of levobupivacaine. Birader et al.[18] reported that dexamethasone as an adjuvant resulted in earlier onset of sensory block as compared to 1.5% lidocaine with adrenaline (13.4±2.8 vs. 16.0±2.7 min). In one study by Shrestha et al.[19] onset of action was 18.15±4.25 min in plain local anaesthetic group and 14.5±2.10 min in local anaesthetic plus steroid group. In another study by Shrestha et al.[19] comparing effect of tramadol and dexamethasone on bupivacaine found earlier onset time of sensory block in dexamethasone group(16.67±2.34 min) compared to tramadol group(18.47±2.03 mins).

Golwala et al. [20] has added dexamethasone to lignocaine for supraclavicular brachial plexus block and showed that it shortens the onset time of both sensory and motor block. Parrington et al.[21] reported no significant difference between the onset of motor and sensory blockade in control and dexamethasone group.

In our study we also find no statistically significant difference between onset of sensory and motor block between plain bupivacaine and plain levobupivacaine groups. Duma et al.[22] also found no difference between levobupivacaine and bupivacaine in onset of axillary plexus block. In the study of Liisanatti et al.[23] used 3 local anaesthetics either 0.5% levobupivacaine, or 0.5% ropivacaine or 0.5% racemic bupivacaine, with total volume of 45 ml had observed that the latency of sensorial block was similar in three groups. Cox et al.[24] also did not observed statistically significant differences in the latency of the sensorial blockade between the groups using 0.4 mg/kg of 0.25% and0.5% levobupivacaine, and 0.5% racemic bupivacaine.

The mean duration of motor block was longer in dexamethasone group than either bupivacaine or levobupivacaine. [Table 2] Statistically significant prolongation associated with dexamethasone was reported by Shrestha et al.[25] Tandov et al.[26] and Vieira et al.[27]

The duration of analgesia was increased in patients using dexamethasone as an adjuvant to bupivacaine or levobupivacaine in present study [Table 2]. Addition of dexamethasone to local anaesthetic in brachial blocks significantly prolonged the duration of sensory (analgesia) blockade in our study as well as the studies done previously by others.

Shrestha et al.[25] reported adjuvant dexamethasone increases duration of analgesia four times as compared to the control group. Cummings et al.[28], Desmet et al.[29], Parrington et al.[21], Biradar et al.[18] and Movafegh et al.[30] also reported prolonged duration of analgesia in groups receiving dexamethasone as compared to control group.

We have found similarity in block quality with supraclavicular approach of both levobupivacaine and bupivacaine. Duma et al.[22] also found no difference in duration of axillary plexus block. Liisanantti et al.[23] showed with 45 ml of 5mg/ml of either racemic bupivacaine, levobupivacaine,or ropivacaine that duration of block was similar in levobupivacaine and bupivacaine performed group. However Cacciaputi et al.[31] found duration of sensory block longer with levobupivacaine than bupivacaine.

The mechanism by which dexamethasone prolongs analgesia is not fully understood, but is likely to be multifactorial. One theory says dexamethasone reduces local anaesthetic absorption by causing vasoconstriction. Other better explanation seems that dexamethasone increases the activity of inhibitory potassium channels on nociceptive C fibre (via glucocorticoid receptors), thus decreasing their activity.

The result in this study showed that sensory block tended to last longer as compared to motor block which agrees with the observation by De Jong et al.[32] These authors explained that large fibres require a higher concentration of local anaesthetic than small fibres. The minimal effective concentration of local anaesthetic for large (motor) fibres is greater than for small (sensory) fibres. Thus, motor function return before pain perception and duration of motor block is shorter than the sensory block.[32]

At 12 hours, the difference in pain score was statistically significant ($p<0.05$) between Group I and Group II and between Group III and IV. Pain score were less in Groups in which dexamethasone was used as adjuvant [Figure 3]. Less rescue analgesic dose was required in group in which dexamethasone was used as adjuvant. Parrington et al. [24] found a significant reduction in PACU fentanyl requirement in adjuvant dexamethasone group. Vierra et al,[30] also found significant reduction in post-op day 1 opiate requirement with adjuvant dexamethasone. Yadav et al.[33] found significantly less rescue analgesic requirement at 12 hours in dexamethasone group.

CONCLUSION

After going through various aspects of adding dexamethasone as an adjuvant to bupivacaine and levobupivacaine for PNS guided supraclavicular brachial plexus block, we concluded that Dexamethasone significantly shortens the onset time of sensory & motor block. Total duration of analgesia & motor blockade was prolonged, when dexamethasone was added to bupivacaine and levobupivacaine. Therefore, the requirement for analgesic drugs in the postoperative period can be decreased with the use of dexamethasone as an adjuvant to local anaesthetic. Levobupivacaine can be used as an alternative to bupivacaine for brachial plexus block considering it's less cardiotoxic and neurotoxic profile with consistent and prolong analgesia. However, further studies, more validation and research are required to strengthen the findings of this study.

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