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A Comparative Study of Supraclavicular Brachial Plexus Blockade with Bupivacaine 0.5% Versus Bupivacaine and Clonidine in Upper Limb Surgeries

KEYWORDS: Adjuncts, Local Anaesthetics, Clonidine, Bupivacaine, Supraclavicular brachial plexus block.

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ABSTRACT *Background and Objectives: Several studies have demonstrated that certain drugs when used as adjuncts to local anaesthetics for brachial plexus block enhances the quality and duration of analgesic clonidine, an alpha-2 adrenergic agonist is such a drug known to produce antinociception and enhance the effect of local anaesthetics when given intrathecally, epidurally or in peripheral nerve blocks. This study is undertaken to assess the efficacy of clonidine when added to bupivacaine in brachia plexus block by Supraclavicular approach.*
Methods: A prospective, randomized double blinded study was carried out in Government General Hospital, Kurnool, in which 60 patients (ASA I or II) aged 18 to 60 years of either sex undergoing elective upper limb surgeries lasting more than 30 minutes were included. Patients were randomly divided into two groups of 30 each, named as B (bupivacaine) group and BC (Bupivacaine clonidine) group. Group B received 25 ml of 0.5% bupivacaine and 1 ml of normal saline and Group BC received 25 ml of 0.5% bupivacaine and clonidine 1 µg/kg. The onset time and duration of sensory and motor blockade were recorded. Haemodynamic variables (i.e. heart rate, non-invasive blood pressure, O2 saturation) and sedation scores are recorded for 24 hours post operatively.
Results: The onset of sensory and motor block was significantly faster in group BC compared to group B ($p < 0.05$). The mean time duration of sensory blockade and motor blockade was prolonged in group BC compared to group B ($p < 0.05$). Haemodynamic variables and sedation scores did not differ between two groups in the post-operative period.
Conclusion: The present study concludes that addition of clonidine 1 (µg/kg) to bupivacaine (0.5%, 25 ml) in brachial plexus block hastened onset of sensory and motor block and prolonged duration of analgesia and also motor blockade without any significant clinical side effects

INTRODUCTION

Now-a-days the emerging trend towards management of the pain perioperatively and the increasing importance of ambulatory surgery (outpatient) in anaesthetic practice led to the frequent use of regional anaesthesia when compared to general anaesthesia.

Supraclavicular brachial plexus block is the preferred regional anaesthesia for upper limb surgeries. Because by producing complete muscle relaxation, maintaining stable intra operative hemodynamics along with associated sympathetic block helps in achieving ideal operating conditions. The sympathetic block decreases post-operative pain, vasospasm, and edema.

Of Various local anaesthetics available, bupivacaine is used most frequently and it provides post-operative pain relief in many surgical procedures because of its longer duration of action by blocking signal traffic to the dorsal horn.

Certain drugs may be used as adjuncts to local anaesthesia and enhanced analgesic efficacy while reducing the incidence of adverse reactions. In brachial plexus block, tramadol and fentanyl had been successfully used previously.

Analgesic effect of clonidine (an imidazoline alpha-2 adrenergic receptor agonist) have been demonstrated in several studies when combined with bupivacaine and used in local, spinal and epidural. It produces this effect by modulating pain pathways through presynaptic alpha-2 adrenergic receptors. Clonidine also produces sedation by acting on pontine locus ceruleus where highest density of alpha-2 receptors is present. Clonidine when administrated neuraxially inhibits spinal substance P release and prevents firing of nociceptive neuron produced by noxious stimulation.

The present study is being undertaken in a randomized, double blinded manner, the aim of which is to evaluate the onset time, duration and analgesic efficacy of clonidine-bupivacaine (0.5%) for brachial plexus block by Supraclavicular approach

The study of adding clonidine (1µg/kg) to bupivacaine (0.5%) in brachial plexus block for upper limb surgeries has the following objectives:

To evaluate the, Onset of sensory and motor blockade. Duration of sensory and motor blockade. Sedation score intra and post-operatively. Haemodynamic variables (HR, BP, O2 saturation). Number of rescue analgesics in post-operative 24 hours. Compare the above effects with that of plain bupivacaine (0.5%) in brachial plexus.

Methodology:

A prospective randomized, double blinded clinical study was undertaken in Government General Hospital attached to Kurnool Medical College, Kurnool. The study was undertaken after obtaining ethical committee clearance as well as informed consent from all patients. Sixty patients aged between 18 to 60 years with ASA class I or II posted for elective upper limb orthopaedic surgeries were included in the study. The study population was randomly divided using computer generated numbers into 2 groups with 30 patients in each group.

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Group BC (n = 30) received 25 ml of 0. 5% Bupivacaine and 1µg/kg clonidine

Group B (n = 30) received 25 ml of 0.5% Bupivacaine

Inclusion criteria:
Normal adult patients of either sex, aged between 18 to 60 years belonging to ASA class I or II, without any co-morbid disease, admitted for elective upper limb orthopaedic surgeries.

Exclusion criteria:
1. Patients with known hypersensitivity or contraindications to study drugs.
2. Skin infection at the site of block.
3. Patients with known coagulopathy or patients on anticoagulants.
4. Patients with severe renal, hepatic, respiratory or cardiac disease.
5. Morbidly obese patients.
6. Pregnant women.
7. Patients with neurological, psychiatric or neurovascular disorders.
8. Patients with alcohol abuse.
9. Patients with injury to any of the nerves of the upper limb.

A thorough preanaesthetic assessment was done . Solid foods were restricted for 6 hours, milk for 4-5 hours and clear fluids for 2-3hours prior to surgery.

All patients included in the study were premedicated with tablet alprazolam 0.25mg and ranitidine 150mg orally at night before surgery and they were kept nil orally 10pm onwards.

On arrival of patients in the operating room, an 18 gauge intravenous cannula was inserted under local anaesthetic infiltration on the non-operating hand and an infusion of normal saline was started. The patients were connected to DASH 3000, multichannel monitor which records heart rate (HR), non-invasive measurements of systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP), continuous electrocardiogram (ECG) monitoring and haemoglobin oxygen saturation (SPO2). The baseline blood pressure and heart rate were recorded. The heart rate and rhythm were also monitored from a continuous visual display of electrocardiogram from lead II.

One of the anaesthesiologist not involved in the care or monitoring of the patient prepared the local anaesthetic study solutions. The patients and the observing anaesthesiologist were blinded to the study drug used.

All patients were premedicated with i.v. 1mg midazolam. The patients were placed in the dorsal recumbent-position with the head turned away from the site of injection. Under aseptic precautions, skin infiltration done with lignocaine 2% at the site of block prior to block placement. All supraclavicular subclavian perivascular brachial plexus blocks were performed as described by Winnie using 22G 50mm insulated blunt needle [Stimuplex (B Braun) needles with extension tubing] and B Braun nerve stimulator. The interscalene groove was indentified at the level of cricoid cartilage and traced downwards till the clavicle. Subclavian artery pulsations were felt in the groove just above the clavicle. The needle entry point was just above the finger palpating the subclavian artery in the interscalene groove. The positive electrode of the nerve stimulator was connected to an ECG electrode placed on the skin of the patient at site of surgery. The negative electrode is connected to the needle. The intensity of stimulating current was initially set to deliver 1mA with impulse duration of 0.1ms. The needle was introduced parallel to midline and to the table. A motor response was sought distal to elbow in fingers/hands. The current was gradually decreased to <0.5 mA after the proper motor response. After an appropriate response was localized with a current 0.4mA, 25 ml of the study drug was injected in 3ml increments, after a negative aspiration test, with repeat aspirations every 3ml. An intercostobrachial nerve block was then performed separately using 5ml of lignocaine with adrenaline 1% to provide anaesthesia for the possible placement of the tourniquet.

Immediately after block placement, patients were evaluated every 1 minute, for the assessment of onset of sensory and motor blockade, quality of motor blockade, overall quality of the block, duration of sensory and motor blockade and haemodynamic variables. Assessments were carried out every 1 minute till the achievement of motor and sensory blocks until 30 minutes. After 30 minutes if the block was considered to be adequate, surgeons were allowed to apply the tourniquet and start the surgery.

During the surgery tourniquet time, haemodynamic variables like HR, SBP, DBP, MAP, SPO2, ECG were monitored 1st, 5th and 15th minute and then every 10 minutes till the completion of the surgery, later every 30 minutes till 5 hrs post block, every 60 minutes until complete recovery. Patients were monitored for any signs of cardiovascular or central nervous system toxicity (changes in HR/BP/rhythm/signs of CNS stimulation) throughout the study. Any hypersensitivity reaction for the drugs, evidence of pneumothorax, and other adverse events were also monitored. Dermatomes located in the surgical field could not be tested during the operative procedure. Because all patients were applied plaster of Paris cast after the procedure, individual dermatomes could not be assessed, instead to evaluate sensation, patients were asked to document the time when incisional discomfort began and the time when full power returned to the shoulder. In the post-operative period, when the patient complained of pain at the operative site, inj. ketorolac 30mg was given and study was concluded. Data were obtained after 24 hrs of block placement.

The effects of the anaesthetic agents on the following parameters were observed:

The **onset time of sensory blockade**, defined as time between injection and total abolition of temperature sensation, was evaluated in 4 nerve areas (median, ulnar, radial and musculocutaneous) at every 5 minutes until 30 minutes after the injection. The block was judged to have failed if anaesthesia was not present in 2 or more peripheral nerve distributions and such patients were excluded from the study.

The **onset time of motor blockade** was determined according to a modified Lovett rating scale[15,26] ranging from 6 (usual muscular force) to 0 (complete paralysis), as follows: thumb abduction for the radial nerve, thumb-adduction for the ulnar nerve, thumb opposition for the median nerve and flexion of elbow for the musculocutaneous nerve.

The **duration of sensory blockade**, defined as the time between onset of action and return of pinprick response, was assessed every 30 minutes in at least 3 major nerve

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distributions.

The **duration of analgesia** defined as the time between onset of action and onset of pain, was the time when patients received the first dose of analgesic. Supplemental analgesia was given when visual analogue scale score was more than 4.

The **duration of motor block** was assessed every 30 minutes till the return of complete muscle power in three major nerve distributions.

During surgery pulse, arterial blood pressure and peripheral oxygen saturation were monitored. Symptoms such as nausea, vomiting, drowsiness and other adverse effects / complications were also monitored.

DISCUSSION

When a long acting LA such as bupivacaine is used alone in brachial plexus block; post-operative analgesia provided by it is usually of short duration. The peripheral administration of appropriate drugs named adjuncts which acts on variety of receptors mediating antinociception on peripheral sensory axons may have extended analgesic benefits. Various adjuncts such as opioids, verapamil, midazolam, neostigmine, hyaluronidase have been administrated concomitantly with LA into brachial plexus sheath in an attempt to improve perioperative analgesia. But they were found to be either less effective or had a tendency to produce high incidence of adverse effects which were unacceptable. Clonidine when used in combination with LA and administrated intrathecally and epidurally is known to produce antinociception and enhances the effect of local anaesthetic by its action an alpha-2 adrenergic receptors found in peripheral nerves.

Our study carried out at Government general hospital, Kurnool was a prospective, randomized, double blinded study in which an attempt has been made to assess the efficacy of clonidine as an adjunct to bupivacaine (0.5%) in brachial plexus block by supraclavicular approach in terms of onset time, duration of block, analgesic and haemodynamic variables and requirement of rescue analgesics in first 24 hours was also observed.

60 patients (ASA Grade I and II) within age group of 18-60 undergoing elective upper limb surgery lasting more than 30 minutes were included in the study. Patients were divided into two groups of 30 each (labelled as Group BC and Group C).

Group B – received 25 ml of Bupivacaine (0.5%) with 1 ml of normal saline

Group BC – received 25ml of mixture of Bupivacaine (0.5%) and clonidine (1µg/kg)

mean age of Group B (receiving only Bupivacaine) was 35.9 + 13.06 and mean age of group BC (receiving B and C) was 35.6 + 13.74. Hence both groups were comparable in regard to age. Male to female ratio was almost same in both groups.

Onset of sensory block

In our study we observed that the onset of sensory block was earlier in group BC who received a combination of clonidine and bupivacaine when compared to group B who received bupivacaine alone.

Onset of sensory block in group BC is 9.56 + 1.194 min and in group B is 15.2 + 1.845 min and when compared is statistically highly significant (P =< 0.001).

This is attributed to local direct action of clonidine and its synergistic action with local anaesthetics.

The observation in our study regarding onset time of sensory block matches well with the study of susmitha chakraborthy32. Onset of sensory block was 6.2 + 0.78 minutes and 8.7 + 1.01 minutes in clonidine group and control group respectively. Similar observation was made by Gabriella, Iohom43, where the onset time of sensory block was much faster in clonidine group (21.3 + 7.2 min) compared to that of placebo (24.7 + 5.5 min).

Our observation matches well with a meta-analysis- conducted in various studies by Daniel, M.Popping31 using clonidine doses ranging from 90 to 150 µg in brachial plexus blocks. Onset of sensory block time with clonidine was 12.8 minutes where as in control was 15 minutes.

Onset of motor block

In our study, the onset of motor block was early in group BC with a mean value of 11.3 + 1.465 min compared to the control group B with a mean value of 19.0 + 1.575 min which is statistically significant (p =< 0.001).

This observation matches well with study of susmitha chakraborthy32 who had earlier onset of motor blockade in clonidine group (10.6 + 1.36 min) compared to control group (18.1 + 1.35 min).

Duration of sensory block

In our study, duration of sensory blockade was 349.4 + 26.11 min in group BC compared to 310.2 + 23.32 min for group B which is statistically significant (p =< 0.001).

Our observations matched well with the results obtained from Gabriella, Iohom43 study, in which the duration of sensory block was longer in clonidine group (275 + 75 min) when compared to placebo (163 + 57 min).

In another study conducted by Henri Iskandar24 the-median sensory block duration was 235 min (195-250 min) in the clonidine group, compared to 150 min (135 – 160 min) in the control group. And these observations were similar to the observations in our study.

In another study conducted by Giovanni Cucchiaro27 on children using 0.25% Bupivacaine found prolongation of duration of sensory block with clonidine group (1140 min) compared to control group(840 min) which was clinically significant.

Duration of Motor Block

In our study, the duration of motor blockade was found to be 818.2 + 75.72 min in Group BC compared to 487.6 + 33.533 min in group B and this difference was statistically significant (p < 0.0001)

These observations matched well with the study by susmitha chakraborthy32 in which the duration of motor block in clonidine group was 5.54 + 0.53 hours compared to control group (2.41 + 0.40 hours). These results are comparable with our study.

The average duration of motor blockade in the meta-analysis conducted by Daniel M.Popping31 was 405 min in

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control group compared to 546 min in clonidine group.

In study conducted by Wolfgane Erlacher et al44, the duration of blockade in bupivacaine group was 728 min and in comparison it was 972 min in clonidine group.

Duration of analgesia
Total duration of analgesia is taken as the mean time from onset of block to request of /requirement of rescue analgesics. In Group BC, it was 527.67 + 81.80 min compared to 340 + 58.07 min in group B, which is statistically significant (p =< 0.0001).

Murphy et al20 concluded in their study that clonidine provided an analgesic effect that lasted almost twice the duration of placebo (492 min and 260 min) respectively.

According to Bernard et al19 clonidine reduced the use of supplementary intravenous anaesthetic agents for surgery by producing dose dependent prolongation of analgesia. A mean of 770 min (range 190 to 1440 min) was reached further for the largest dose 300 µg, which matches well with our study.

In a study by Daniel M.Popping31 the duration of post-operative analgesia for clonidine group was 584 min when compared to 461 min in control group.

In a study conducted by Eldejam et al7 by using 150 µg clonidine and 40 ml of bupivacaine of 0.25% in supraclavicular block, the duration of analgesia was longer with clonidine (994.2 + 34.2) compared to epinephrine (control group) 728.3 + 35.8 min.

Our observation matched well with the studies conducted by Susmitha Chakraborthy et al32 where the duration of analgesia with clonidine was 6.9 + 0.63 hours compared to control group where it was 3.23 + 0.48 hours.

The prolonged analgesia could be due to the action of clonidine by inhibiting action potential of A and C fibres in peripheral nerves as demonstrated by Gaumann et al8.

Masuki et al45 suggested clonidine may produce local vasoconstriction resulting in a delayed absorption of local anaesthetic and enhance prolongation.

Butterworth et al46 found clonidine to produce tonic and phasic block of nerve conduction in rat sciatic nerve fibres by directly binding to alpha-2 adrenergic receptors on presynaptic peripheral nerves to modify neuronal excitability.

A mild decrease in systolic, diastolic as well as mean arterial treasure was noticed during our study. But none of the patients had hypotension (decrease in blood pressure by 20% of baseline), bradycardia (decrease in pulse rate by 20% of basal pulse rate) and haemodynamic parameters were well within normal range. These results are similar to the study conducted by Eisenach A.G et al6 and culebras X et al22.

Sedation:
No undue sedation was noticed in either groups and Ramsay sedation score was 2 in both the groups.

CONCLUSION
the present study we conclude that the addition of clonidine (1 µg/kg) as an adjuvant to bupivacaine (0.5%) has following effects Faster onset of sensory block. Faster onset of motor block. Longer duration of sensory block. Longer duration of motor block. Longer duration of analgesia i.e. less number of rescue analgesics were given in post-operative 24 hours. No significant difference in haemodynamic variables i.e. pulse rate, systolic blood pressure, diastolic blood pressure and oxygen saturation. Comfortable sedation intra operatively without any need for airway assistance.

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