

Efficacy of Phenylephrine As An Adjuvant To Bupivacaine In Supraclavicular Brachial Plexus Block – A Prospective, Randomised Study.

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ABSTRACT

Background: Several adjuncts have been studied to potentiate the efficacy of local anaesthetic agents that increase the duration of analgesia, in peripheral nerve blocks, but the results have often been debated and counter debated. Phenylephrine has been studied intrathecally as an adjuvant and has been found to potentiate the effect of local anaesthetic agents. The present study was undertaken with a purpose to assess the efficacy of phenylephrine as an adjuvant to bupivacaine in supraclavicular brachial plexus block. **Methods:** A prospective, randomised, double blinded study was undertaken which included 40 ASA I or II patients, aged 18-60 years, ≥ 60 kg, scheduled for upper limb surgery under supraclavicular brachial plexus block. Patients were randomly divided into two groups of 20 each. Group S patients received 30 ml, 0.5% bupivacaine with 0.15 ml of saline and Group P patients received 30 ml, 0.5% bupivacaine with 0.15 ml (equivalent to 150 μ g) of phenylephrine. Onset and duration of sensory and motor block, haemodynamic parameters, pain score, analgesia requirement and complications, if any, were recorded. **Results:** The total duration of sensory and motor block was significantly increased in group P, as compared to group S ($p \leq 0.05$). Pain scores were significantly lower and rescue analgesia demand was also significantly low in group P, in comparison to group S ($p \leq 0.05$). Demographic variables and haemodynamic parameters were comparable in both the groups. No major complications were seen. **Conclusion:** Phenylephrine (150 μ g) when used as an adjuvant to 30 ml, 0.5% bupivacaine, in supraclavicular brachial plexus block, prolongs the duration of both the sensory and motor block thus enhances analgesia, decreases the rescue analgesic requirement and does not cause any adverse effects.

Keywords: Bupivacaine, Phenylephrine, Supraclavicular Brachial Plexus Block.

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.^[1] The supraclavicular block is performed at the level of the brachial plexus trunks where the almost entire sensory, motor and sympathetic innervation 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-operative pain, vasospasm and oedema. The amide local anaesthetic bupivacaine is the most frequently used local anaesthetic due to its long duration of action varying from three to eight hours.^[2,3] Several adjuncts have been studied to potentiate its efficacy. These include opioids, midazolam, neostigmine, bicarbonate, dexamethasone and α -2 agonists.^[4-6] The results have often been debated and counter debated but their utility remains questionable.

The use of α -2 adrenoceptor agonist for enhancement of peripheral nerve blocks has added a new dimension to their clinical application. Clonidine, when combined with a local anaesthetic, has been found to extend the duration of nerve block. However, clonidine being nonspecific for α -2, leaves unanswered the question regarding its exact mechanism. It has been postulated that this action could be due to either α -2 action or α -1 action which is seen at higher doses.^[4] The vasoconstrictive effect has also been hypothesized as a possible mechanism. Phenylephrine is more specific for α -1 adrenoceptor as compared to clonidine. The effects of

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Gehlaut et al; Phenylephrine As An Adjuvant To Bupivacaine In Supraclavicular Brachial Plexus Block

phenylephrine as an adjuvant to nerve blocks have been studied in reference to central neuraxial blockade but the effect on peripheral nerve block have not been fully elucidated.^[7] Epinephrine has been studied as an adjuvant in brachial plexus block in comparative analysis with clonidine but specific α -1 mediated blockade with phenylephrine has not been studied much in peripheral nerve blocks.^[8] The purpose of the present study is to evaluate the effects of phenylephrine on peripheral nerves during supraclavicular brachial plexus block, using 0.5% bupivacaine.

MATERIALS AND METHODS

Following approval by the board of studies, a prospective, randomised, double blinded study was undertaken. We included forty American Society of Anesthesiologists (ASA) I & II adult patients of either sex, aged 18-60 years, weighing more than 60 kg, scheduled for upper limb surgery under supraclavicular brachial plexus block.

Patients receiving clonidine, β - blockers, adrenoceptor agonist or opioids, patients with history of hypertension, myocardial infarction, peripheral neuropathy or hypersensitivity to local anaesthetic agents were excluded from the study. Detailed general physical and systemic examination of all the patients was done preoperatively and relevant investigations were obtained. A written informed consent was taken and fasting for 6 hours prior to surgery was ensured.

Patients were taken into the operating room (OR) and routine monitoring was established and base line readings of heart rate (HR), electrocardiography (ECG), pulse oximetry (SpO₂) non invasive blood pressure (NIBP) were recorded.

An i.v. access was obtained and ringer lactate started. Patient was then placed in supine position, head turned away thirty degrees to the contra lateral side and ipsilateral arm was adducted. With strict aseptic precautions the point of maximum intensity of subclavian artery was located.

A skin wheal was raised with local anaesthetic and a 22 gauge, 4 cm, nerve locator needle (Stimuplex® A, B Braun) was directed just above and posterior to the subclavian pulse, directed caudally, at a very flat angle against skin. The needle was advanced, until distinct muscle contractions of forearm were seen. Once the desired twitch was obtained, the needle was carefully manipulated, whilst reducing the current until the muscle contractions occurred at lower current levels.

Persistence of contraction with stimulator voltage decrease to 0.5 mA was taken as the confirmation of brachial plexus. Negative aspiration for blood was confirmed and study drugs were injected, after negative aspiration every two to three ml.

Patients were randomised using random number of tables into two groups (n=20 each) and were given

either 0.15 ml normal saline (group S) or 0.15ml (equivalent to 150 μ g) of phenylephrine (group P), (using an insulin syringe to draw the study drug) along with 30 ml of 0.5% bupivacaine. The nature of drug given or group of the patient was not known to the one performing the block and recording the observations. If rib or blood was encountered the needle was withdrawn and the landmarks were re-evaluated. Inj. midazolam 0.02-0.05mg/kg i.v. was given to the patient once complete block had been confirmed.

We defined the successful block as one that allows the surgery to proceed within a 30 minute time period, without discomfort to the patient or need for any supplemental techniques.

Hemodynamic parameters like heart rate, non-invasive blood pressure and oxygen saturation were measured immediately after the block. Thereafter, the measurements for above parameters were recorded every five minutes, for the first half an hour and thereafter, at intervals of fifteen minutes, till the end of the surgery. Post operative, the observations were recorded at thirty minutes, two, eight, twelve and twenty four hours after the surgery.

Onset of sensory block was defined as time between drug injection and complete loss of cold perception of hand. The assessment was done every minute starting from time of injection till the patient had no cold perception, using spirit soaked cotton swabs.

Onset of motor block was defined as time between injection of the drug till complete motor block occurred. The assessment was made every two minutes starting from time of injection till establishment of complete block.

Duration of sensory block was defined as time from injection of drug to appearance of pain, requiring analgesia. Pain was assessed on a numeric rating scale, zero representing no pain and 100 meaning worst possible pain. Injection tramadol 2mg/kg i.v. infusion was given as rescue analgesic when the pain score was found to be more than 40. The no. of boluses and total amount of analgesic required was also noted, up to twenty four hours, from the time of block.

Duration of motor block was defined as time from injection of drug till complete return of motor power. Any complications or side effects occurring up to 24 hours were recorded and appropriate intervention was done. Specifically looked for were nerve injury, pneumothorax hypertension, bradycardia (due to phenylephrine).

Statistics

Sample size of 17 patients per group was calculated, assuming 90% statistical power in another study.^[9] So, total 40 patients were enrolled, divided into two groups of 20 each. The information was collected on a pre-designed Performa. The collected data was analyzed using software SPSS for Windows (version 17.0) statistical package (SPSS Inc., Chicago, IL).

Data was presented as mean±SD. Independent and paired sample t-test were used as per the type of data. Chi-square test was used to compare rescue analgesia requirement in both the groups. The difference was considered significant at a p value of less than 0.05.

RESULTS

In both the groups mean age, weight and sex distribution were comparable. The onset of sensory blockade occurred within 6-15 minutes in both the groups. In 100% of patients in group S and 95% in group P the onset of sensory blockade occurred within 15 minutes of the injection of the drugs. Overall failure rate of brachial plexus block in this study was 2.5%.

In group S, onset of sensory blockade was 8.40 ± 1.90 minutes and in group P it was 9.74 ± 1.88 minutes, the difference was statistically significant with p = 0.03 (<0.05). Onset of motor blockade in group S was 18.40 ± 2.21 minutes and in group P it was 19.22 ± 2.48 minutes. The difference was statistically insignificant.

The mean duration of analgesia for group S was 483.50 ± 87.37 minutes, less than that for group P, 748.42 ± 133.219 minutes. As group P showed wide variations in the range of duration, mode was also calculated. Mode for group S is 480 minutes and for group P it is 780 min. Total duration of motor blockade was also less in S, 373.50 ± 66.43 minutes

as compared to group P, 594.21 ± 104.47 minutes. The differences were statistically significant with p < 0.05).

Mean±SD of heart rate and mean arterial blood pressure were compared in both groups, S and P and were found statistically insignificant at all intervals, till 24 hours post operatively.

The pain scores of the patients in group P were lower than those in group S, in the post-operative period, with a p value of < 0.05. In group S, 45% patients and only 5.2% patients in group P required rescue analgesic drug, even at 12 hours postoperatively. At 24 hours duration, in group S, all the patients had taken rescue analgesic at least once and only 42.10 % patients needed it in group P.

No major complications were observed in any patient. Only 1 patient in group S had complaints of nausea in post-operative period and 1 patient in group P had failure of block and general anaesthesia had to be administered.

Table 1: Demographic Variables.

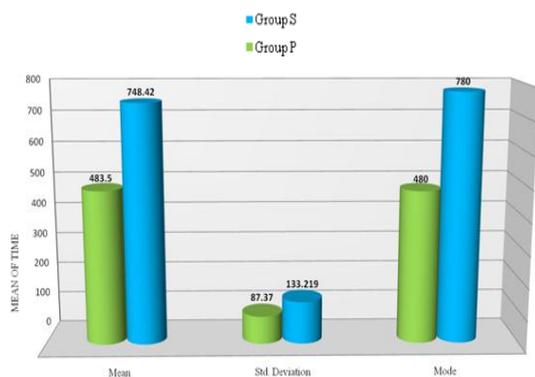
S. No.	Variable	Group S	Group P
1.	Age of patients (years)	35 ± 10.90	34.0 ± 9.87
2.	Gender (M:F)	13:7	14:6
3.	Body weight (kg)	66.25 ± 3.985	64.8 ± 2.745

Group S- received bupivacaine (30ml, 0.5%) with 0.15 ml normal saline
Group P- received bupivacaine (30ml, 0.5%) with 0.15 ml (150 µg) phenylephrine

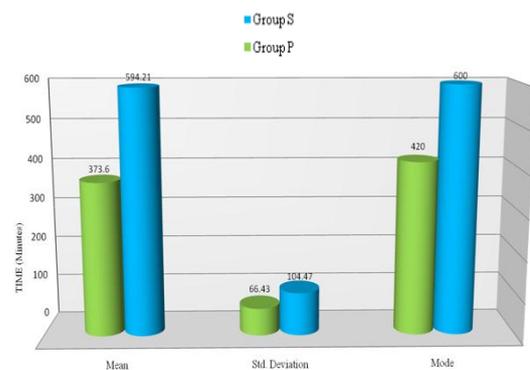
Table 2: Block characteristics.

Variables		Sensory block		p value	Motor block		p value
		Group S	Group P		Group S	Group P	
Onset time (min)	Mean ± SD	8.40 ± 1.90	9.74 ± 1.88	0.03	18.40 ± 2.21	19.22 ± 2.48	0.28
Total duration (min)	Mean ± SD	483.50 ± 87.37	748.42 ± 133.219	0.00	373.50 ± 66.43	594.21 ± 104.47	0.00
	Mode (min)	480	780		420	600	

Group S, n=20 and group P n=19 as in one patient failure of block was observed. p value ≤ 0.05 considered as statistically significant.



Graph: 1 Comparison of mean duration of sensory block (in minutes)

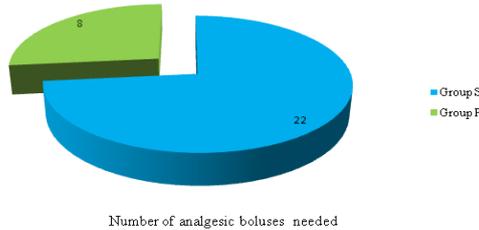


Graph: 2 Comparison of mean duration of motor block (in minutes)

Table 3: Pain scores in patients (Mean ± SD).

Time (post operative)	Group S (n = 20)	Group P (n = 19)
at 30 minutes	0.00±0.00	0.00±0.00
at 2 hours	1.50±6.70	0.00±0.00
at 8 hours	34.75±18.02	4.74±11.72
at 12 hours	53.00±17.50	18.05±12.00
at 24 hours	63.50±14.05	48.20±16.70

Pain scores at a numeric rating scale of 0-100, 0= no pain and 100= worst possible pain



Graph: 3 Rescue analgesia requirement

DISCUSSION & CONCLUSION

Supraclavicular brachial plexus block provides superb surgical anaesthesia and analgesia, though the total duration of analgesia is short, when only bupivacaine is used. Hence, a lot of adjuvant drugs have been tried along with injection bupivacaine to enhance its effect. Each of these adjuvant has their own limitations in form of various side effects or failure to enhance the duration of analgesia significantly.^[4-6] So, the present study was undertaken to assess the effect of phenylephrine on the block characteristics, using bupivacaine as local anaesthetic.

In our study sensory blockade onset occurred faster than motor blockade in both groups. Sensory blockade was first observed in the proximal part of the limb and later in the distal part this may be because the sensory fibres to the distal part are located centrally in the cord of the plexus so the drug takes a longer time to penetrate the nerve bundle to the core.

According to Moore et al, time of onset and establishment of maximum operative anaesthesia vary markedly, depending on 3 factors: concentration of local anaesthetic, volume and type of block performed. They reported 5.6 minutes as the onset of sensory blockade with 0.25% bupivacaine and 15.4 minutes as the time to achieve maximum sensory anaesthesia. They also showed that concentrations in venous blood, measured after 100-150 mg bupivacaine in various types of blocks, have been less than 1µg/ml, which is a safe level to be used. 9, 10 Cunningham and Kaplan reported 6 ± 1 minute as onset of sensory block with 30 ml of 0.5% bupivacaine. 11 The values in various studies confirm to the present time of onset of

8.40±1.90.minutes, in group S, using only 30 ml of 0.5% bupivacaine.

The onset of sensory block was prolonged in group P where phenylephrine 150 µg was given along with bupivacaine, the mean time being 9.74±1.8 minutes. The difference here is statistically significant, though prolongation of the time to onset of block is undesirable. The reason here probably is the intense local vasoconstriction by phenylephrine, as it is highly α-1 selective.

Onset of motor blockade was similar in both Groups. One patient, in group P, failed to develop any block up to 30 minutes after injection of drugs. It was considered as failure of procedure and that patient was excluded from the study. The success rate of supraclavicular brachial plexus block using a nerve stimulator, in our study, was calculated to be 97.25 per cent. It is in accordance to the success rate of other workers. Yasuda I et al observed that the block was successful in 98% of patients when the stimulation was felt in the index, middle or ring finger, but was often incomplete when felt in the thumb or little finger. Riegler FX reported a success of 97% with the aid of nerve stimulator. 12, 13

Total duration of analgesia for group S was 483.50 ±87.37 minutes and for group P was 748.42 ± 133.219 minutes. Neil RS observed 405.3 ± 60.1 minutes duration of sensory block after bupivacaine, which is in agreement with the mean duration in group S.^[14]

The duration of analgesia was increased in group P, using phenylephrine as an adjuvant. There are various reports of its use in neuraxial blockade where phenylephrine has been found to prolong spinal anaesthesia using tetracaine and lidocaine, though wide variations in its effect have been seen. It was seen that both phenylephrine and epinephrine increased the duration of bupivacaine at various segmental levels but these only reached statistical significance with regard to total duration with the epinephrine-containing solution. It was in contrast to another study that used tetracaine and found that phenylephrine produced greater prolongation of spinal anaesthesia.^[15,16]

Eledjam JJ et al compared clonidine and epinephrine in supraclavicular brachial block n concluded that the injection of clonidine into the brachial plexus sheath is an attractive alternative to epinephrine to prolong the duration of analgesia following upper limb surgery under conduction anaesthesia.^[17]

Baba H, Shimoji K and Yoshimura M, found direct action of noradrenaline on substantia gelatinosa neurons in augmentation of GABA-ergic and glycinergic inhibitory transmission, in spinal cord. This augmentation was mimicked by α-1 receptor agonist, phenylephrine and blocked by a selective α-1 blocker like prazosin. Considering the evidence that phenylephrine does not affect the clearance of local anaesthetics, the action of phenylephrine in spinal anaesthesia must be caused by a direct action on

spinal neurons via α -1 receptors, thus accounting for an alternate mechanism of action.^[18]

Brown DA and Marsh S demonstrated presence of GABA receptors in mammalian peripheral nerve trunk also. It was further demonstrated that axonal GABA receptors are present on both normal and regenerated sensory fibres in rat peripheral nerve.^[19,20] Cairns BE, Sessle BJ, Hu JW observed the presence of GABA receptors within the temporomandibular joint and that its activation could decrease the transmission of nociceptive signals.^[21] Based on these observations, presence of GABAergic receptors on peripheral nerves and their augmentation by α -1 agonists could be a possible explanation for the prolongation of duration of analgesia seen in the group of patients receiving phenylephrine, which is highly specific for α -1 receptors.

Lepner U, Goroshina J and Samarütel J used 80 ml bupivacaine 0.125% with 5 mg, in a randomised prospective double-blind clinical trial, for control of postoperative pain relief after laparoscopic cholecystectomy by wound infiltration and found it effective in reducing the intensity of abdominal pain for up to 24 hours after laparoscopic cholecystectomy. So, it is in accordance with the speculation that phenylephrine may have some other direct actions on peripheral nerves too, apart from the vasoconstrictive action.^[22]

The results in our study showed, that sensory block tended to last longer as compared to motor block which agrees with the observation by De Jong RH, 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.^[23]

The effect of the procedure and drugs on the hemodynamic parameters was also studied in both the groups. Pulse rate and mean arterial blood pressure in group S and P were comparable at all times, with no statistically significant difference.

As seen from the data provided above, pain scores were significantly lower in patients who received phenylephrine in addition to bupivacaine. The number of patients who required rescue analgesia, 45% in group S and 5.2% in P, were significantly lower at eight hours postoperatively, in group P, with a p value of 0.01 (<0.05). The mean number, of supplemental analgesic boluses required, was also significantly lower in patients in Group P.

The systemic effect of the vasopressors is of clinical importance, as one may anticipate some pressor effects, but no major complications were seen in our study. Only one patient in group S experienced nausea about eight hours postoperatively. This was probably a result of repeat antibiotic injection that was administered to the patient, rather than per se

because of the procedure or any of the drugs used for the block. One patient had failure of block in group P. Rest of the patients had an uneventful course.

The administration of phenylephrine 150 mcg, along with bupivacaine, in brachial plexus block in this study, did not increase the occurrence of neurologic or vasopressor symptoms. Bray et al also observed the same, when 5 mg phenylephrine was used in spinal anaesthesia. They found that the phenylephrine caused no significant elevation in blood pressure and in no instance was there, evidence of any neurological complication.^[24]

From this study, in conclusion, phenylephrine 150 μ g, may be used as an adjuvant to 0.5% bupivacaine, in supraclavicular brachial plexus block. When added, it prolongs the duration of both the sensory and motor block thus enhances analgesia, reduces the rescue analgesic requirements and does not cause sedation, is devoid of any hemodynamic or neurological side effects, though further studies, more validation and research is suggested.

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