

Effectiveness of addition of neostigmine or dexamethasone to local anaesthetic in providing perioperative analgesia for brachial plexus block: A prospective, randomized, double blinded, controlled study

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Abstract

Background: Various local anaesthetic agents are used for brachial plexus block. We compared effectiveness of addition of Dexamethasone versus Neostigmine to Lignocaine, adrenaline admixtures for Brachial plexus block in providing perioperative analgesia.

Methods: Ninety patients were randomized in three groups and were received 24ml of study drugs. The group A [Lignocaine with adrenaline (1.5%)], group B [Lignocaine with adrenaline (1.5%)] +500µg Neostigmine, and group C (Lignocaine with adrenaline (1.5%) +4mg Dexamethasone) for brachial plexus block through supraclavicular approach. The observed parameters were onset of analgesia, completion of sensory and motor blockade, Duration of analgesia, Surgeon's score, side effects, number of supplemental analgesics doses and Visual analogue scale (VAS) score for pain in 12 hour of post-operative period.

Results: Mean onset of analgesia 4.6±1.1, 4.4±0.8, 3.8±1.8 mins in group A, B and C respectively and the Mean onset of motor blockade were 7.7±2.0, 7.0±1.8, 6.0±2.1 mins in group A, B and C respectively. Similarly Mean Complete sensory block in 10.6±3, 10.4±2.5, and 8.9±2.2 mins and Mean complete motor block in 17.3±4.3, 17.2±4.0 and 14.7±3.5 mins in group A, B and C respectively were achieved. Duration of analgesia was 176.5±53.5, 225.7±53.3 and 454.2±110.7 mins in group A, B and C respectively. Duration of analgesia in group C was statistically significant in comparison with other groups. The number of mean analgesic requirement by group C (0.9±0.4) was significantly (p=0.005) lower. The mean VAS was significantly lower in group C in 12 hours post-operatively.

Conclusion: The onsets of action, duration of analgesia were better in dexamethasone group and also need less number of rescue analgesics requirement.

The recent emergence of pain management as formal subspecialty and increasing importance of outpatient (Ambulatory) surgery in anaesthetic practice have further bolstered interest in peripheral nerve blocks. The peripheral nerve block may be used for surgical anaesthesia alone or, in conjunction with general anaesthesia and for the acute and chronic pain management. Many studies have been carried out for the search of better quality of analgesics in per-operative as well as in post operative period and it has been found that regional anaesthesia provides better result¹.

Brachial plexus block is an easy and relatively safe procedure for upper limb surgeries though there are different approaches to it, out of which supraclavicular approach is most consistent and widely used method for anaesthesia and peri-operative pain management in surgery below shoulder joint

So the provision of good quality of analgesia during and post-operative period is important not only to ease

patients suffering and induce sense of well being but also improve the ability to ambulate early and thereby reducing post operative complication².

Various local anaesthetic agents are used for Brachial Plexus Block but most commonly used drugs are; Bupivacaine, and Lignocaine. Bupivacaine is long acting where as Lignocaine is short acting drug. Novel adjuncts studied to date include opioids, Clonidine, Neostigmine, Tramadol, Midazolam, Dexmedetomidine etc.

Dexamethasone is very potent and highly selective glucocorticoid. Basically it is used as anti-inflammatory and immunosuppressant. Its potency is about 40 times

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that of hydrocortisone. Clinical Uses of Dexamethasone are for treatment of many inflammatory and autoimmune conditions but Glucocorticoid are also used to treat patients suffering from neuropathic pain and complex regional pain syndromes (CRPS). So, steroids have anti-inflammatory as well as analgesic effects³.

Neostigmine is a parasympathomimetic, specifically, a reversible cholinesterase inhibitor. By interfering with the breakdown of acetylcholine, neostigmine indirectly stimulates both nicotinic and muscarinic receptors. Clinical Uses of neostigmine are to improve muscle tone in people with myasthenia gravis and routinely in anesthesia at the end of an operation to reverse the effects of non-depolarizing muscle relaxants. Apart from this it has been also used as additives to local anesthetics to get prolong analgesic effect. Although there is good evidence for a spinal action of neostigmine, a rationale for a peripheral mechanism of action is lacking^{4,5}.

To achieve the better quality of anaesthesia and analgesia per-operative as well as postoperative with minimal side-effect, various studies have been done on additives to local anesthetics. So the purpose of our study was to compare the effectiveness of neostigmine vs. dexamethasone when added to 1.5% of Lignocaine with adrenaline admixture for Brachial Plexus Block.

Aims and objectives

To compare the effectiveness of addition of Neostigmine versus Dexamethasone to Lignocaine Adrenaline admixture for Supraclavicular Brachial plexus block in providing analgesia in perioperative phase.

Materials and methods

This was a prospective, randomized, controlled, double blinded study. An ethical approval was obtained from B. P. Koirala Institute of Health Sciences (Dharan) ethical committee. Written informed consent was taken for the procedure from the patient.

A total of 90 adult subjects of ASA (American Society of Anesthesiology) 1 and 2 of either sex undergoing forearm or, hand surgery were enrolled in the study. The Patients with history of neurological, psychiatric, neuro-muscular disease, respiratory compromised patient, drug abuser, pregnant or, lactating women, uncontrolled systemic disease (e.g. diabetes, hypertension, ischemic heart disease and acid peptic disease), were excluded from the study.

Groups of patients

Ninety patients were randomly allocated in group A, B, and C. Thirty patients in each study group.

Group A- Lignocaine (1.5%) with adrenaline (1:200,000) (1.5%) (24 ml)

Group B- Lignocaine (1.5%) with adrenaline (1:200,000) (1.5%) +Neostigmine (0.5mg) (24ml)

Group C-Lignocaine (1.5%) with adrenaline (1:200,000) (1.5%) +Dexamethasone (4mg) (24 ml)

The total volume of study drug was 24 ml in each group. As Lignocaine with adrenaline is marketed in 2% concentration so, 18 ml (360mg) of drug diluted to 24 ml with normal saline to get 1.5% concentration of Lignocaine with adrenaline for control group. Similarly total Volume was kept 24 ml in additive groups as well [i.e. Neostigmine 500µg (1 ml) and Dexamethasone 4 mg (1 ml) groups].The study drug was prepared by trained anaesthesia technician who was not involved in this study.

Patient preparation

Standard supra-clavicular Brachial Plexus Block (BPB) technique were performed with nerve stimulator (0.5mA, stimulex, B Braun) in all cases after pre-anaesthetic evaluation with monitoring instrument¹. During injection of drugs negative pressure aspiration was performed after every 5-6 ml to avoid intra-vascular injection. Sensory and motor block of all four nerve territories i.e. radial, ulnar, median, musculocutaneous were assessed.

- Sensory block was tested by PIN-PRICK TEST⁶
- Motor Block was determined by according to modified LOVETT rating scale⁷
- Time to onset of nerve blockade⁶ was defined as
- For sensory - Time from injection for Brachial plexus block to reduction in sensibility to 30% or less. (Considered as onset of analgesia)
- For motor - Time from injection for BPB to reduction of muscle power less than or, equal to 3 (Lovett rating scale).
- Complete nerve blockade⁶
- For sensory - Time from injection for BPB to reduction in sensibility to zero (pin prick test)
- For motor - Time from injection for BPB to reduction of muscle power less than or equal to zero (Lovett rating scale).
- If planned for tourniquet during surgery 1.5% Lignocaine with adrenaline 10 ml was infiltrated sub-cutaneously over axillary level for the Intercosto- Brachial nerve. Adequacy of block for surgery was considered only after achieving complete sensory blockade.

Patients was evaluated for pain relief, related side effect (nausea and vomiting) in postoperative period at 1 min, 15 min, 30min, 1hr, 2hr, 3hr, 6hr 9hr and at12 hour.

Assessment of pain was done by subjective method. Subjective assessment was done by VAS.

The pain assessment was done for 12 hours in post operative period with an aim to keep VAS less than 3. The patient was evaluated if he/she complained of pain of VAS 3-5, Tablet Diclofenac 50 mg P/O but if VAS \geq 6 Injection Diclofenac 75 mg IM was given. Time of first perception of pain was also recorded.

Duration of analgesia was defined as the time between onsets of analgesia to first pain perception by patient.

Amount of muscle relaxation and the ease of performing the surgery in operative field will be measured by the surgeon score (in VAS 0---10 cm).

Fully satisfied = 0, Not satisfied = 10.

- Hypotension treated with intravenous fluid (crystalloids) and / or Mephenteramine when indicated.
- Nausea vomiting score 2^s or more and unrelated to hypotension was treated with injection Metoclopramide 10 mg IV.

Analysis

Parametric or nonparametric data were collected and were entered in master chart in Microsoft Excel worksheet. Data were analyzed by epi Info 2002 (version 3.3.2) software. The significant difference of mean between the groups was calculated using ANOVA test and for discrete variables, chi square test was used. For all the purpose probability value was considered significant when P-value was less than 0.05 and was considered highly significant when P-value was less than 0.001.

Results

A total of 90 cases were involved in our study, 30 in each group. Age ranges between 18-60 yrs. In group A age (32.1 \pm 12.2 yrs), sex (M: F = 23:7), in group B age (30.1 \pm 10.9 yrs), sex (M: F= 22: 8), and in group C age (31.1 \pm 11.7 yrs), sex (M: F= 23: 7) were not significant (p-value – 0.781) (Table 1A)

Similarly individual statistical analysis demonstrated no significant difference in distribution of age, sex, tourniquet application, duration of surgery and tourniquet duration among groups. (Table 1B)

Surgeries of less than 2 hours duration like Wound debridement and repair of muscles and tendons was most frequent surgery in our study followed by open reduction internal fixation of fractured bones forearm and hand. Distributions of types of surgeries were comparable among different groups. (Table 1C)

After brachial plexus block, time to onset of sensory and motor block were assessed and it was found onset of sensory block was faster in group C (3.8 \pm 1.8 min) than group B (4.4 \pm 0.8 min) and group A (4.6 \pm 1.1 min). Similarly onset of motor block was also faster in group C (6.0 \pm 2.1 min) than group B (7.0 \pm 1.8 min) and group A (7.7 \pm 2.0 min). So, time to onset of sensory and motor block as well as complete sensory and motor block were significantly lower in group C as compare to group A and group B. These were statistically significant. (Table 2A, 2B)

Regarding Surgeons Score, measured in VAS (cm) was statistically significant in inter group comparison. It showed surgeons were highly satisfied with the block in group C than in group A. But there was no difference between group A and B or group B and C. (Table 2C)

The duration of analgesia was maximum in group C (454.2 \pm 110.7 mins) followed by in group B (225.7 \pm 53.3) and minimum in group A (176.5 \pm 53.5min) Which is statistically significant (P=0.0001). It shows significant longer duration of analgesia in group C in comparison with group A and B. Similarly the duration of analgesia was statistically significant in group B in comparison with group A (P=0.016). (Table 2D)

Table 2 E showing minimal analgesic was received by patients of group C (0.9 \pm 0.4). The inter group statistical analysis showed group C was statistically significant (p=0.0001), suggest group C required minimal analgesic in 12 hours of post-operative period than group A and B. And there is also less number of analgesic required in group B when compare to group A which was also statistically significant (p=0.008).

Similarly types of analgesics (Tablets, Injection or both) required over 12 hours were statistically significant between groups. In group C (16.7%) patients did not require any analgesic in 12 hours, where as only (3.3%) of patient did not required analgesic in group B but in group A all of them received some form of analgesics. Most of the patients of group A and group B received, both forms of analgesics (oral + intramuscular) that is 83.3% and 53.3% respectively where as in group C only 6.7% of patient received both forms of analgesics. The P-value was <0.05 in all group and was statistically significant. (Figure 2A)

The VAS score (in 0-10cm scale) for pain was recorded over 12 hour post operatively showed no statistically significance till first 30 min, then VAS at 1 hr, 2 hr and 3 hr were statistically significant out of which VAS at 2 hr and 3 hr were highly significant (P=0.0001). It suggested that patients in group C had significantly low VAS-scores till 3 hours of post operative period. (Fig 2B)

VAS at 6 hr, 9hr and 12hr were statistically not significant

There were no complications or any significant change in vitals during peri-operative period.

Table 1 A: Showing distribution of demographic data of patients

Parameters	Group A (n=30)	Group B (n=30)	Group A (n=30)	P value
Age (18-60 yrs.)	32.1±12.2	30.1±10.9	31.8±11.7	0.781
Sex (M/F)	23/7	22/8	23/7	0.942 X ² =0.120

Table 1B: Showing clinical data comparison to each group and except Tourniquet application which is in frequency. P value of <0.05 is considered to be significant.

Parameters	Group A (n=30)	Group B (n=30)	Group A (n=30)	P value	
Toruniquet	Applied	7	11	13	0.252 X ² =2.765
	Not applied	23	19	17	
Surgery Duration (mins)	73.5±16.3	81.1±18.7	82.01±6.8	0.120	
Toruniquet Duration (mins)	38.5±7.4	45.4±10.1	44.2±10.9	0.349	

Table 1C: Showing types of surgeries in each group in percentage with p-value

Types of surgery	Group A (n=30)	Group B (n=30)	Group A (n=30)	P value
Wound debridement (W.D.) and repair	10 (33.3%)	7 (23.3%)	7 (23.3%)	0.194 X ² = 13.564
Wound debridement (W.D.) and external fixation	2 (6.7%)	8 (26.7%)	8 (26.7%)	
Wound debridement (W.D.) and external fixation	4 (13.3%)	2 (6.7%)	4 (13.3%)	
Open reduction and internal fixation (ORIF)	7 (23.3%)	9 (30.0%)	7 (23.3%)	
Implant removal	2 (6.7%)	3 (10.0%)	4 (13.3%)	
Others	5 (16.7%)	1 (3.3%)	0 (0.00%)	

Table 2 A: Showing time to onset of sensory and motor block were significantly lower in group C as compared to group A and group B

Parameters	Group A (n=30)	Group B (n=30)	Group A (n=30)	P value
Sensory onset (mins)	4.6±1.1	4.4±0.8	3.8±1.8	0.024*
Motor onset (mins)	7.7±2.0	7.0±1.8	6.0±2.1	0.007*

Table 2B: Showing time to complete sensory and motor block significantly lower in group C as compared to group A and group B

Parameters	Group A (n=30)	Group B (n=30)	Group A (n=30)	P value
Sensory complete block (mins)	10.6±3.0	10.4±2.5	8.9±2.2	0.028*
Motor complete block (mins)	17.3±4.3	17.2±4.0	14.7±3.5	0.020*

Table 2 C: Showing surgeon's score with highly satisfied in group C than A and B

	Group A (n=30)	Group B (n=30)	Group A (n=30)	P value
Surgeon's score	0.8±0.8	0.5±0.6	0.2±0.4	0.006*

Table 2 D: Showing significant longer duration of analgesia required in group C in comparison to other groups

Parameter	Group A (n=30)	Group B (n=30)	Group A (n=30)	P value
Duration of analgesia	176.5±53.5	225.7±53.3	454.2±110.7	0.001*

Table 2E: Showing minimal no. of analgesia required in 12 hours post-operatively in group C

Parameter	Group A (n=30)	Group B (n=30)	Group A (n=30)	P value
Numbers of analgesia in 12 hrs.	1.8±0.3	1.5±0.5	0.9±0.4	0.001*

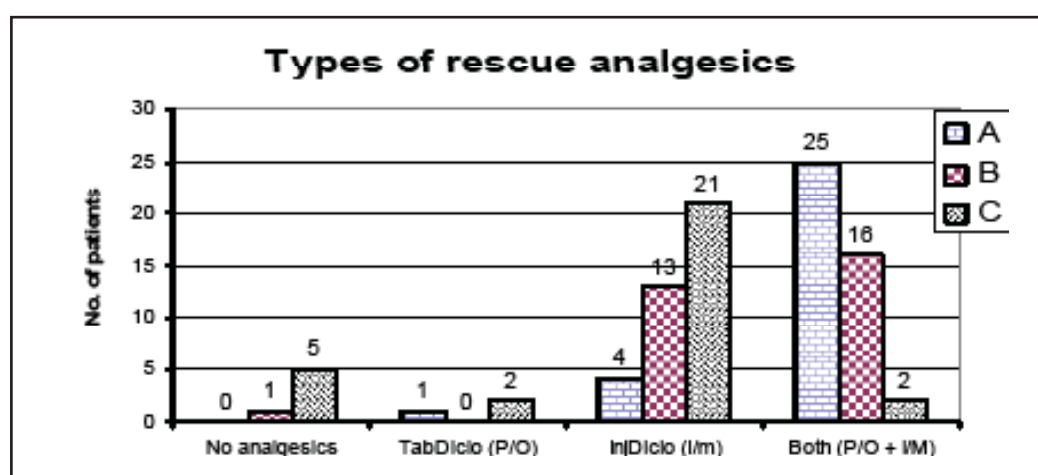


Fig 2A: Types of analgesic required in 12 hours post-operatively in each group.

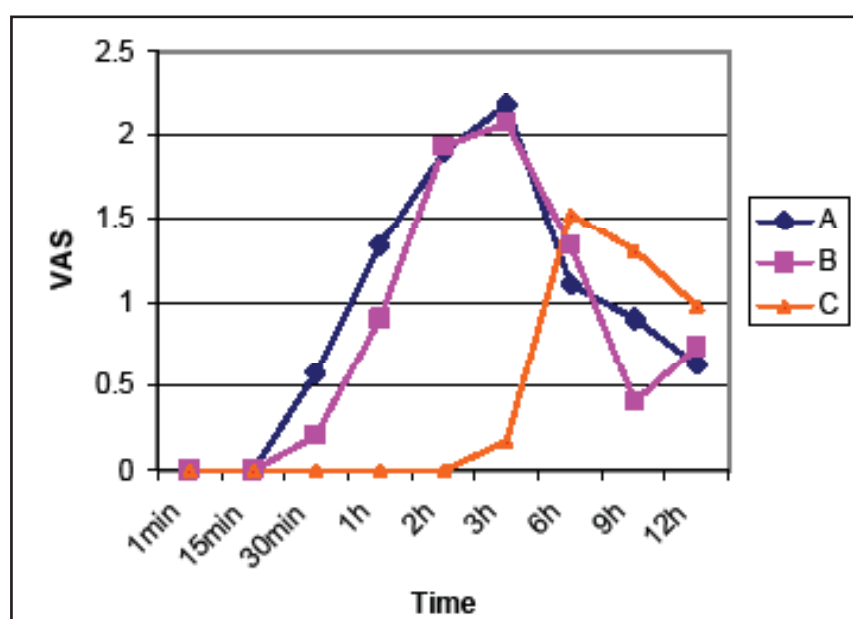


Fig 2B: VAS (cm) of patients in 12 hours of post-operative period showing group C patients had significantly low VAS-scores till 3 hours of post operative period

Discussion

In this study each patient of different groups had received in total equal volume of drugs through supraclavicular approach for brachial plexus block to avoid bias and alteration in concentration of local anesthetics.

Commonly long acting local anesthetics like Bupivacaine is most commonly used to get long duration of anaesthesia and analgesia, but in our study we had chosen Lignocaine with adrenaline to avoid delayed onset of action as well as delayed recovery from motor block by long acting local anesthetics (Bupivacaine) which may have interfered with the neurological assessment of limb post operatively⁹.

Our findings are comparable with the study conducted by Shrestha B.R et al¹⁰ in 40 patients, they found complete sensory block in Dexamethasone Group (mean 14.5 ± 2.10 mins) which was statistically significant in comparison with controlled group. They had used a mixture of lidocaine 2% with 1:200,000 adrenaline and Bupivacaine 0.5% for a total volume of 40-50 ml. Dexamethasone 4-8mg was added to the local anaesthetic solution in the steroid group. Time to complete sensory blockade was delayed in their study, it could be due to use of mixture of Lignocaine and Bupivacaine which might have altered individual concentration, pKA's and the pH of the solutions. Regarding duration of analgesia it was found prolonged in Dexamethasone group (12.75 ± 5.33 hours) Vs (3.16 ± 0.48 hrs) in local anaesthetic group which was statistically significant, similar to this in our study duration of analgesia was significant in dexamethasone group (454.2 ± 110.7 mins) among groups but it was less. This could be due to use of mixture of Lignocaine 2% with 1:200,000 adrenaline and Bupivacaine 0.5% in larger volume.

Ali movafegh et al¹¹ in 60 adults had used either 34 ml local anesthetics Lignocaine (1.5%) with 2 mL of isotonic saline chloride (control group, n =30) or 34 mL Lignocaine (1.5%) with 2 mL of dexamethasone (8 mg) (dexamethasone group, n= 30). The duration of analgesia was comparable with our study. They observed prolonged duration of analgesia with dexamethasone group (242 ± 76 mins) Vs control group (98 ± 33 mins) which was statically significant. The duration analgesia was less when compare with dexamethasone group of our study, it could be due to presence of local anaesthetic with adrenaline admixture and placement of position of needle of nerve stimulator while performing block. In their study position of needle was considered to be acceptable when distal motor response was observed with output current of less than/equal to 0.7mA where as in our study position of needle was considered to be acceptable when distal motor response was observed with output current of less than/equal to 0.5mA. So,

deposition of local anaesthetic was closer in vicinity of brachial plexus, as well as presence of local anaesthetic with adrenaline admixture could be the explanation for prolonged analgesic effect of our study. Apart from this addition of 2 ml dexamethasone might have altered the concentration of local anesthetics of their study drug could be another possibility of less duration of analgesia in their study.

It has been also observed that addition of small amounts of dexamethasone to local anesthetics prolonged duration of analgesia after subcutaneous, intercostals blockade, intra-articular and epidurally^{12, 13, 14, 15}. In few study it was observed that systemic administration of Dexamethasone reduced pain^{16, 17}.

Though actual mechanism of Dexamethasone in producing rapid block and prolonging duration of analgesia is not well understood but by reviewing various previous studies, the reason of prolongation of analgesia in our study could be due to local action of dexamethasone on nerve as well as systemic anti-inflammatory effect after being observed from peripheral site (BPB site) to systemic circulation. Other possibilities are alteration in $k \pm$ channel of nerve cell thereby synergistic action with local anesthetics or, the action on corticosteroid receptor present in brain after being absorbed from periphery to systemic circulation^{18, 19, 20}.

Our study findings were found to be similar to study by Boudierka M.A et al²¹, in which Bupivacaine were randomly assigned to one of 3 groups 30 in each. Group 1 received saline solution (1 ml) in the axillary plexus; group 2 received 500 μ g (1 ml) neostigmine in the axillary plexus and group 3 received 500 μ g neostigmine subcutaneously. Neostigmine (500 μ g) was added to Bupivacaine in axillary brachial plexus block showed lower VAS score as well as significant decrease the consumption of post-operative analgesic requirement. Apart from brachial plexus block, systemic administration and addition of neostigmine to local anesthetics for or other regional anaesthesia had shown analgesic effect. Like systemically²², intra-articular^{23, 24}, caudal block^{25, 26}, epidurally^{27, 28, 29, 30, 31, 32} and intrathecally³³.

There are good evidences for a spinal action of neostigmine; a rationale for a peripheral mechanism of action is lacking. The inhibition of spinal cholinesterase results in an increase of endogenous acetylcholine, which is most likely released from intrinsic cholinergic neurons within the dorsal horn of the spinal cord³⁴. And Nagui B.M and Yaksh TL suggested analgesic effects are likely mediated by spinal M1, and or, M3 receptor sub type³⁵.

So, prolongation of duration of analgesia in our study in neostigmine group in comparison with control group could be due to stimulation of muscarinic receptors in peripheral nerves may be having antinociceptive action as well as systemic action of peripherally administered Neostigmine for BPB can potentiate the analgesic action of local anesthetics.

Conclusion

Thus, in our study addition of Dexamethasone (4mg) to local anesthetics had fastest onset as well as complete blockade of sensory and motor nerves in comparison to other groups. It also showed prolonged duration of analgesia without side effects. Similarly, addition of Neostigmine (0.5 mg) to local anesthetic also prolonged duration of analgesia in comparison with control group without any side effects where as time to onset and complete block were comparable. As both Dexamethasone (4mg) and Neostigmine (0.5mg) were found to be effective in prolonging duration of analgesia when combined with Lignocaine with adrenaline admixture (1.5%) in comparison to control group so, addition of these drugs can be useful and safe adjunct to Lignocaine with adrenaline admixture for Brachial plexus block in patients undergoing forearm hand surgeries.

As far as the quick onset of action, duration of analgesia and number of analgesics required are concerned dexamethasone group appeared to be better than the neostigmine group.

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