Comparative study of analgesic efficacy after supraclavicular brachial plexus block with bupivacaine alone and with clonidine, fentanyl and midazolam additives

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Abstract

Background: Upper limb surgeries are mostly performed under peripheral blocks such as the brachial plexus block. This not only provide intraoperative anaesthesia but also extend analgesia in the post-operative period. Various adjuvants are used along with Bupivacaine to prolong the duration of analgesia. Aim: To compare the analgesic efficacy of adding additives like clonidine, fentanyl and midazolam to bupivacaine in brachial plexus blockade by supraclavicular approach. **Material and Methods:** A total of 60 adult patients posted for various types of upper limb surgeries were randomly allocated into 4 equal groups. BC group received 30ml of 0.25% Bupivacaine with 1mcg/kg of preservative free Clonidine to the maximum of 75 mcg. BF group received 30ml of 0.25% Bupivacaine with preservative free Fentanyl 1 mcg /kg to the maximum of 50 mcg. BM group received 30ml of 0.25% Bupivacaine with preservative free Midazolam 50 mcg/kg and B group received 30ml of 0.25% Bupivacaine. **Results:** Duration of sensory block was 602±6.54, 452±6.54, 421±6.54 and 332±6.54 min in group BC, BM, BF and B respectively. The mean duration of the sensory and motor blockade was significantly prolonged in group BC. The mean VAS score at 6 hrs was 0±0.260, 0.93±0.260, 3.2±0.260 and 5.46±0.260 in group BC, BM, BF and B respectively. The pain scores as assessed by the VAS were significantly lower in group I (BC) when compared to the other groups. **Conclusion:** Clonidine 1mcg/kg to a maximum of 75mcg added to 0.25% Bupivacaine solution for supraclavicular brachial plexus block improves the quality of postoperative analgesia when compared to fentanyl and midazolam group.

Keywords: supraclavicular brachial plexus block, Bupivacaine, clonidine, fentanyl, midazolam, analgesic efficacy

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INTRODUCTION

Regional nerve blockade avoids the unwanted effects of anesthetic drugs used during general anesthesia. It has

benefit of extended postoperative pain relief. In supraclavicular approach, the plexus is blocked where it is most compactly arranged at the level of the nerve trunks; as a result, a block with rapid onset can be achieved. Of the several local anaesthetic drugs used for brachial plexus block, Bupivacaine is used most frequently as it has a long duration of action varying from 3-8 hours. To prolong the duration of analgesia various drugs have been studied as adjuvants to local anaesthetic solution. These adjuvant drugs ideally are expected to prolong the analgesic effect without causing any systemic side effects or prolonging motor blockade. Commonly used additives to local anaesthetic solutions are epinephrine, clonidine and opioids, benzodiazepines and phenylephrine.^{1,2} Clonidine, an $\Box 2$ adrenergic agonist has

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been extensively studied as an adjunct to general and regional anaesthesia. It has been shown to produce this effect by activation of postsynaptic adrenergic receptors.3,4 Fentanyl an □-receptor agonist has also been used widely in intrathecal, extradural and peripheral nerve plexus blockade.^{2,5} Midazolam, a water soluble benzodiazepine, is known to produce antinociception and to enhance the effect of local anaesthesia when given epidurally or intrathecally.^{6,7} This study was intended to compare the analgesic efficacy of adding additives like clonidine, fentanyl and midazolam to bupivacaine in brachial plexus blockade by supraclavicular approach.

MATERIAL AND METHODS

In this prospective randomized comparative study, 60 adult patients posted for various types of upper limb surgeries at the Department of Orthopedics and Department of Plastic Surgery of a tertiary care teaching hospital formed the study group. After receiving the institutional ethical committee approval and informed consent, the patients were randomly allocated into 4 groups brachial plexus block with Nerve Stimulator was performed with supraclavicular block technique.

Study groups:

- 1. BC group: 15 patients received 30ml of 0.25% Bupivacaine with 1mcg/kg of preservative free Clonidine to the maximum of 75 mcg.
- 2. BF group: 15 patients received 30ml of 0.25% Bupivacaine with preservative free Fentanyl 1 mcg/kg to the maximum of 50 mcg.
- 3. BM group: 15 patients received 30ml of 0.25% Bupivacaine with preservative free Midazolam 50 mcg/kg.
- 4. B group: 15 patients received 30ml of 0.25% Bupivacaine.

Inclusion criteria

- Both sexes
- ASA I and II.
- Age Group 20-60 years
- Weight 40-70 kgs
- Surgeries of the upper limb.

Exclusion Criteria

- Patients refusal
- Coagulopathy
- Infection at injection site

Methodology

Patients were all pre-operatively evaluated, clinically examined and investigations done prior to assessment Procedures were explained in detail and written consent obtained. Initially the pre procedure parameters were recorded i.e., pulse rate, blood pressure, SPO2, ECG. Then block was administered. All through the study, these parameters were monitored continuously except the NIBP which was recorded intermittently. Post-operatively they were monitored for 24 hours. Patients were observed vigilantly for development of various complications. The skin and subcutaneous tissue was infiltrated with local anaesthetic solution. The subclavian artery was palpated above the medial third of the clavicle. A 35mm 21G insulated needle was attached to the nerve locator set at 1-5mA and inserted through the weal created in downward, inward and backward direction, so that it was pointing to the spine of second to fourth thoracic vertebra. The superior trunk of the brachial plexus was usually located first. The needle position was adjusted while decreasing the current to 0.9mA with maintenance of the muscle response. The response that results in the greatest block success was muscle contraction below the shoulder. A cough from the patient is a warning sign that the pleura is being contacted by the needle. Incremental injection of local anaesthetic was made with repeated aspiration. After injecting the local anaesthetic the block was tested for both sensory (using pin prick) and motor (using muscle power) and is compared with same stimulation or power in the contralateral arm. Motor block was evaluated by thumb abduction (Radial nerve), thumb adduction (Ulnar nerve), thumb opposition (Median nerve) and flexion of the elbow in supination and pronation of the forearm (Musculocutaneous nerve). The Hollmen's scale was used in the study for assessing both sensory and motor blockade. Evaluation was carried out for every minute after completion of injection and the time of onset was noted both for sensory and motor blockade. Onset of blockade both sensory and motor was defined as a minimum of grade 2 in Hollmen's scale. Block was considered complete when sensory and motor scores were at least grade 3 in Hollmen's scale. Only patients with complete block were included in the study. Duration of sensory blockade was considered as the time interval between local anaesthetic administration and the onset of paresthesia, while the duration of motor block was defined as the time interval between local anaesthetic administration and recovery of the block. Sedation was assessed using Sedation scores by Culebras et al where sedation was graded on a scale of 1-5. Baseline vital signs were recorded and monitored every 5 mins till the procedures was over and thereafter every hour for 24 hours. Onset, completion of blockade, duration of blockade was assessed. Pain was assessed using visual analog scale (VAS).

Statistical analysis

Quantitative variables were compared by mean and standard deviation, using Independent sample t-test. Categorical variables were compared by using Chi square test. P value < 0.05 was considered as statistically significant.

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RESULTS

The minimum age of the patient was 20 years and the maximum age was 65 years. The distribution of demographic and baseline characters of the patients in all the groups were comparable.

_	Table 1: Demographic profile of the patients in study groups								
	Characteristics	Group BC	Group BF	Group BM	Group B				
	Age group								
	20-25 yrs	04	06	02	01				
	26-35 yrs	04	02	06	04				
	36-45 yrs	01	02	02	05				
	46-55 yrs	03	05	03	03				
	56-65 yrs	03	00	02	02				
	Sex								
	Male	10	12	10	10				
	Female	05	03	05	05				
		1	101.0	1					

Duration of sensory block was 602±6.54, 452±6.54, 421±6.54 and 332±6.54 min in group BC, BM, BF and B respectively. The duration of motor block was 557.3±7.24, 414±7.24, 389±7.24 and 292±7.24 min in group BC, BM, BF and B respectively.

Table 2: Onset and duration of sensory and motor block in study groups								
Onset and duration of sensory and motor block	Group BC	Group BF	Group BM	Group B				
Sensory block								
Onset Mean±SD (min)	4.73±0.19	6.46±0.19	5.8±0.19	7.6±0.19				
Duration Mean±SD (min)	602±6.54	452±6.54	421±6.54	332±6.54				
Motor block								
Onset Mean±SD (min)	6.26±0.25	7.73±0.25	7.73±0.25	10.13±0.25				
Duration Mean±SD (min)	557.3±7.24	414±7.24	389±7.24	292±7.24				

The pain scores as assessed by the visual analog scale were significantly lower in group I (BC) when compared to the other groups (Table 3).

Table 3: VAS in study groups								
Group BC	Group BF	Group BM	Group B					
U.	V. C							
0±0.260	0.93±0.260	3.2±0.260	5.46±0.260					
4±0.16	5.3±0.16	6.2±0.16	7.8±0.16					
	Group BC	Group BC Group BF 0±0.260 0.93±0.260	Group BC Group BF Group BM 0±0.260 0.93±0.260 3.2±0.260					

DISCUSSION

Brachial plexus blockade offers an excellent alternative technique to general anaesthesia for upper limb surgical procedures. Various approaches for successful performance of the blocks and for reducing the complication have been described. Supraclavicular technique was chosen for this study because it provides a rapid onset, dense and predictable anaesthesia with a high success rate. Clonidine an □2-adrenergic agonist has been extensively used an adjunct to general anaesthesia and regional anaesthesia. When added to 1% mepivacaine with 1:2,00,000 epinephrine 150mcg of clonidine prolongs the duration of both anaesthesia and analgesia after axillary brachial plexus blockade.8 The minimum dose of clonidine required to prolong significantly the duration of analgesia and anaesthesia for brachial plexus block with 1% mepivacaine is respectively 0.1mcg/kg and 0.5mcg/kg.9 At this dose, clonidine may be used without important reported adverse effects even in outpatients. In this study, 1mcg/kg to the maximum of 75mcg of clonidine was used. It is postulated that clonidine added to local anaesthetics for peripheral nerve block prolongs postoperative analgesia and duration of block owing to a direct action on the nerve.^{10,11} Two mechanisms of action may be proposed. This effect might be due to clonidine mediated activation of postsynaptic adrenergic receptors leading to vasoconstriction thus prolonging local anaesthesia by decreasing the systemic absorption of the local anaesthetic. When applied on the rabbit cornea, clonidine is approximately 140 times more potent as a surface anaesthetic than procaine. This might indicate that C fibers or $A\Box$ fibers, which exclusively innervate the rabbit cornea are especially sensitive to clonidine. Butterworth and Strichartz hypothesized that

analgesia seen after neuraxial application of clonidine might result from direct inhibition of impulse conduction in primary afferent nerve fibres. They speculate that part of the efficacy of 2-adrenergic agonists at producing analgesia after their regional injection may result from their local anaesthetic actions on A \square and especially C fibers.¹² Fentanyl, a synthetic opioid and a \Box receptor agonist has been extensively studied for its use in brachial plexus block.^{2,5} Nishikawa et al² have concluded in their study that fentanyl improves analgesia but prolongs the onset of brachial plexus block by peripheral mechanism. Mostafa *et al*¹³ have studied the effects of addition of fentanyl to local anaesthetic in peribulbar block and concluded that addition of fentanyl to local anaesthetic mixtures fastens the onset and prolong the duration of akinesia and improve the quality of postoperative pain in peribulbar block. Karakaya et al⁵ have studied the analgesic and anaesthetic effects of fentanyl with 0.25% bupivacaine and concluded that addition of 100 mcg/ml fentantyl to 0.25% bupivacaine almost doubles the duration of analgesia following axillary brachial plexus block when compared to 0.25% bupivacaine alone. Midazolam as an additive to local anaesthesia has been studied in intrathecal, epidural and caudal routes. It has been proved in these studies that midazolam is as useful additive by way of improved analgesia and with sedation. 50mcg/kg midazolam in central neuraxial blockade did not produce any significant adverse effects. Studies in animals have showed no neurotoxic effects of intrathecally administered midazolam.^{14,15} Potentiation of analgesic effects of intrathecal fentanyl with midazolam in labouring patients has been demonstrated.¹⁶ Intrathecal midazolam 2mg did not increase the occurrence of neurologic or urologic symptoms. Hence, 50 mcg/kg dose was chosen in this study. In present study, the onset and completion of the sensory and motor blockade was quicker in group I (Bupivacaine+clonidine) followed by group II (Bupivacaine+fentanyl) and group III (Bupivacaine+midazolam). Similarly, the duration of sensory block was prolonged to last longer than motor block in group I (BC) followed by group II (BF) and group (III) (BM). This is in line with the observations made by Dejong *et al*¹⁷ who explained that large fibers require a higher concentration of local anaesthetic than small fibres. The minimum 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. In this study, the pain scores as assessed by the visual analog scale were significantly lower in group I (BC) when compared to the other groups.

CONCLUSION

In conclusion, clonidine 1mcg/kg to a maximum of 75 mcg added to 0.25% Bupivacaine solution for supraclavicular brachial plexus block, quickens the onset of sensory and motor blockade, prolongs the duration of sensory blockade, improves the quality of postoperative analgesia when compared to fentanyl and midazolam group.

REFERENCES

- Power I, Brown DT, Wildsmith JA. The effect of fentanyl, meperidine and diamorphine on nerve conduction in vitro. Reg Anesth. 1991 Jul-Aug;16(4):204-8.
- 2. Nishikawa K, Kanaya N, Nakayama M, *et al.* Fentanyl improves analgesia but prolongs the onset of axillary brachial plexus block by peripheral mechanism. Anesth Analg 2000;91(2):384-387.
- Duma A, Urbanek B, Sitzwohl C, Kreiger A, Zimpfer M, Kapral S Clonidine as adjuvant to local anaesthetic axillary brachial plexus block. A randamized controlled study. Br J Anaesth 2005 Jan; 94(1):112-6.
- Bhatnagar S, Mishra S, Madhurima S, Gurjar M, Mondal AS Clonidine as an analgesic adjuvant to continuous paravertebral bupivacaine for post thorocotomy pain. Anaesth Intensive Care 2006 Oct;34(5):581-91.
- Karakaya D, Buyukgoz F, Baris S, Addition of fentanyl to Bupivacaine doubles the duration of analgesia following axillary brachial plexus block. Reg. Anaesth Pain Med 2001 Sep – Oct. 26(5). 434-8.
- Yegin A, Sanli S, Dosemecil, Kayacarin, Akbas M, Karsli B. The analgesic and sedative effects of intrathecal midazolam in perianal surgery. Eur J Anaesthsiol 2004 Aug; 21(8):658-62.
- Nishiyama T, Yokoyama T, Haraoka K. Midazolam improves postoperative epidural analgesia with continuous infusion of local anaesthetics. Can J Anaesth 1998;45(6):551-5.
- Erlacher W, Schuschnig C, Koinig H, Marhofer P, Mayer N, Kapral S. Clonidine as adjuvant for mepivacaine, ropivacaine, bupivacaine in axillary perivascular brachial plexus block. Can J Anaesth. 2001 Jun; 4(6):522-5.
- Singelyn FJ, Gouverner JM, Rober A. A minimum dose of clonidine added to mepivacaine prolongs the duration of anaesthesia and analgesia after axillary brachial plexus block. Anaesth Analg 1996 Nov; 83(5):1046-50.
- Singelyn FJ, Dangoisse M, Bartholomes S, Gouverneur JM. Adding clonidine to mepivacaine prolongs the duration of anaesthesia and analgesia after axillary brachial plexus block. Reg Anesth 1992;17:148-50.
- 11. Eledjam JJ, Deschodt J, Viel EJ, *et al.* Brachial plexus block with bupivacaine: effects of added alphaadrenergic agonists: comparison between clonidine and epinephrine. Can J Anaesth 1991; 38:870-5.
- 12. Butterworth JF, 5th, Strichartz GR. The alpha 2adrenergic agonists clonidine and guanfacine produce tonic and phasic block of conduction in rat sciatic nerve fibers. Anesth Analg. 1993;76:295–301.

- Mostafa Abdee Hamid Abo Eltnin, Ismail Eiwis. Effect of fentanyl addition to local anaesthetic in peribulbar block. IJA 2009;5(1):57-63.
- Serrao JM, Mackenzie JM, Goodchild CS, Gent JP. Intrathecal midazolam in the rat; an investigation of possible neuroloxic effects. EurJ. Pharmcol. 1990; 7; 115-22.
- 15. Schweiger IM, Jerg-Costa M, Pizzolato GP, Foster A, Morel DR. Intrathecal midazolam reduces isoflurane.
- 18.

MAC and increases the apnoecic threshold in rats. Canj Anaesth 1994; 41:144-8.

- Tucker AP, Mezzatesta J. Nadeson R, Goodchild CS. Intrathecal midazolam II: Combination with intrathecal fentanyl for labour pain. Aanesth Analg 2004; 98:1521-7.
- De Jong RH, Wagman IH. Physiological mechanisms of Peripheral nerve block by local anaesthetics. Anaesthesiology 1963; 24:684-727.

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