

Original Article

Anaesthetic and analgesic effects of adding fentanyl to bupivacaine-lignocaine mixtures in supraclavicular brachial plexus block – a comparative study with or without fentanyl

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Abstract

Brachial plexus block is gaining popularity day by day for upper extremity surgery because it has manifold advantages. Supraclavicular approach offers a high success rate for elbow, forearm, hand surgery. Different mixtures of local anesthetics are intended to provide faster block onset than long-acting agents and to extend the duration typically seen with intermediate or short-acting agents. This prospective, randomized comparative study was conducted to compare the onset time of sensory block, onset time of motor block and time to achieve complete block, duration of analgesia adding fentanyl with bupivacaine-lignocaine mixtures in supraclavicular brachial plexus block. A total of 60 patients fulfilling the inclusion and exclusion criteria were selected for the study & divided into two groups. Group A received lignocaine-bupivacaine mixtures (1% lignocaine, 0.25% bupivacaine) and was considered control; group Group B received fentanyl (100µg) with the local anaesthetic mixtures (1% lignocaine, 0.25% bupivacaine). The mean onset of sensory and motor block were significantly early in group B compared with that of group A. The mean time to achieve complete block and duration of analgesia were significantly longer in group B. It was revealed in the study that patients of group B had no pain up to 4 hrs, there was first reporting of pain (VAS >4) around 5 hrs, the worst pain was

experienced after 8 hrs, first dose of analgesic was administered according to patient's request. The patients of group A had no pain up to 3 hrs. Thereafter pain intensity increased at 4 hrs, around 6 hrs postoperatively the patients experienced the worst pain. This feature reveals a significantly longer duration of analgesia in group B. This study revealed that addition of fentanyl significantly causes early onset of anaesthesia and longer duration of analgesia without any side effects.

Keywords : Supraclavicular brachial plexus block, fentanyl, bupivacaine

Introduction

Regional nerve blockade avoids the unwanted effects of anaesthetic drugs used during general anaesthesia and beneficial for the patients with various cardio-respiratory co-morbidities.¹ Various approaches (interscalene, supraclavicular, infraclavicular, axillary) can be used to block brachial plexus providing anaesthesia and analgesia for upper extremity surgery.² 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. This approach also offers a high success rate for elbow, forearm, hand surgery because all the branches of the brachial plexus can be reliably blocked.³ Mixtures of local anesthetics are intended to provide faster block onset than long-acting agents and to extend the duration typically seen with intermediate-acting or short-acting agents. Bupivacaine is the most commonly administered drug in brachial plexus blocks, introduced by Ecknstrom in 1957 and used clinically by Telivuo since 1963.² The presence of peripheral opioid receptors is shown in immune cells and primary afferent neurons in animals.⁴ Study has demonstrated the presence of peripheral opioid receptors that mediate analgesia by endogenous as well as exogenous opioid agonists.⁵ It was speculated that the peripheral administration of opioids provides stronger and longer lasting analgesia with a lower dose of opioid without central side.⁵ Fentanyl could act directly on the peripheral opioid receptor as primary afferent tissues (dorsal roots) have been found to contain opioid binding sites.⁶ Fentanyl is reported to have a local anaesthetic action⁷ & also potentiate local anaesthetic action via central opioid receptor-mediated analgesia by peripheral uptake of fentanyl to systemic circulation.⁸ It appears that local

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anaesthetics and opioids exert their action independently via different mechanisms. Local anaesthetics block propagation and generation of neural action potentials by a selective effect on sodium channels, whereas opioids act on the opioid receptors creating an increase in a potassium conductance. This action results in hyperpolarization of the nerve cell membrane and a decrease in excitability.⁹ Although sodium channel block is proposed to be the primary mode of action, local anaesthetics also have an effect on synaptic transmission. In contrast, in addition to the considered primary mode of action, opioids were found to directly suppress the action potential in nerve fibers. This study was conducted to compare the onset time of sensory block, onset time of motor block and time to achieve complete block, duration of analgesia adding fentanyl with bupivacaine-lignocaine mixtures in supraclavicular brachial plexus block.

Methods

This prospective, randomized, comparative, single-blinded (patients only) clinical study was carried out in the Department of Anaesthesiology and Intensive Care Medicine, BSMMU, Dhaka from jan to july. A total of 60 patients of ASA (American society of anaesthesiology) grade I and II undergoing elective operation for upper limb distal to midarm (elbow, forearm and hand) were excluded. Patient with coagulopathy, history of allergy to local anaesthetics, history of hypertension, history of peripheral neuropathy, history of COPD, psychological disorder, anatomical distortion, infection at the site of injection & patients who refused to enroll themselves in the study were excluded. Patients were divided in to two groups, A & B, consisting of 30 patients each. Group-A received inj. bupivacaine (0.25%) 19 ml+ inj. lignocaine

(1%) 19ml + inj. Normal saline (0.9%) 2ml (total 40 ml) where as group-B received Inj. bupivacaine (0.25%) 19ml + Inj.lignocaine (1%) 19ml+ inj. fentanyl 100ug (2ml) (total 40ml). All the relevant data were compiled on a master chart first. Onset time of sensory block, onset time of motor block and time to achieve complete block & duration of analgesia were compared between two groups.

Statistical analyses were done using SPSS-V18. The continuous data were expressed as mean ± SD. The categorical data were expressed as numbers and percentages and analysed with the Chi-Squared test. An unpaired Student’s t test was used to test for differences in means for continuous variables.

Written informed consent was obtained from each patient. Study protocol was approved by ethical committee of the institution.

Results

The mean duration of surgery (min) in group B (110.50±15.31) was slightly higher than that in group A (109.47±19.24), but the difference was statistically non-significant (p=0.819). The mean onset of sensory block (min) was significantly early in group B (5.30±0.95) (p<0.001) compared with that of group A (12.17±2.35). The mean onset of motor block (min) was significantly early in group B (4.35±0.63) compared with that of group A (8.97±1.81). The mean time to achieve complete block (min) was significantly early in group B (17.80±2.95). (Table-I) The mean duration of analgesia (min) was significantly longer in group B (551.33±44.34) compared with that of group A (373.33±12.68). (Table-I & Figure-1)

Table-I: Comparison of anaesthesia related data among the study groups (n=30 patients in each group)

	Study Groups	Mean	SD	P	
Duration of Surgery (Minutes)	Group A	109.47	19.24	0.819	NS
	Group B	110.50	15.31		
Onset of Sensory Block (Minutes)	Group A	12.17	2.35	0.000	S
	Group B	5.30	0.95		
Onset of Motor Block (Minutes)	Group A	8.97	1.81	0.000	S
	Group B	4.35	0.63		
Time to achieve complete Block (Minutes)	Group A	23.03	2.70	0.000	S
	Group B	17.80	2.95		
Duration of Analgesia (Minutes)	Group A	373.33	12.68	0.000	S
	Group B	551.83	44.34		

NS = Non- significant (P > 0.05) ; S = Significant (P < 0.001) in unpaired Student’s t test of significance

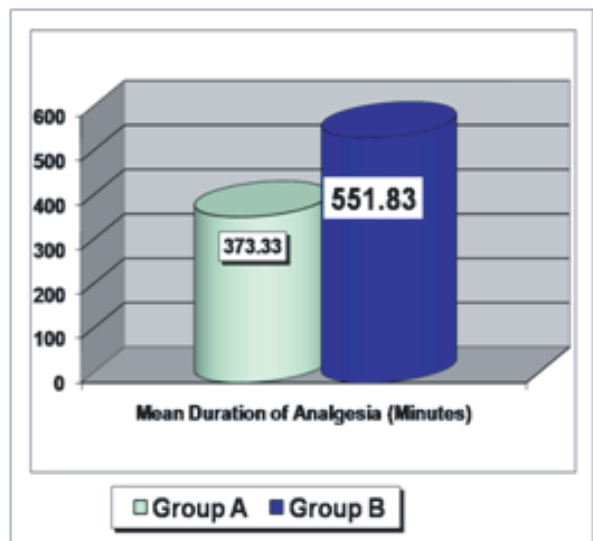


Figure-1: Mean duration of analgesia (minutes) among the study groups

The baseline vital signs remained stable and within physiologic ranges throughout anaesthesia and postoperatively as well. It was revealed in the study that patients of group B had no pain up to 4 hrs, there was first reporting of pain (VAS >4) around 5 hrs, the worst pain was experienced (mean VAS 8.57±0.93) after 8 hrs. First dose of analgesic was administered according to patient's request. The patients of group A had no pain up to 3 hrs. Thereafter pain intensity increased (mean VAS 4.93±1.23) at 4 hrs, around 6 hrs postoperatively the patients experienced the worst pain (9.17±0.79). This feature reveals a significantly longer duration of analgesia in group B (P=<0.001) (Table-II)

Discussion

Brachial plexus block is widely employed regional anaesthesia for upper limb surgery. Brachial plexus block offers many advantages over general anaesthesia for upper limb surgeries such as sympathetic block, better

Table-II: Comparison of visual analog scale (VAS) at different times among the study groups (n=30 patients in each group)

VAS	Study Groups	Mean	SD	Range	P
At 30 Minutes	Group A	0.00	0.00	0 – 0	-
	Group B	0.00	0.00	0 – 0	
At 60 Minutes	Group A	0.03	0.18	0 – 1	0.321 NS
	Group B	0.00	0.00	0 – 0	
At 2 Hours	Group A	0.27	0.69	0 – 2	0.565 NS
	Group B	0.17	0.65	0 – 3	
At 3 Hours	Group A	2.33	1.49	0 – 4	0.000 S
	Group B	0.43	1.22	0 – 5	
At 4 Hours	Group A	4.93	1.23	3 – 7	0.000 S
	Group B	1.70	1.98	0 – 6	
At 5 Hours	Group A	7.17	1.18	5 – 9	0.000 S
	Group B	3.90	1.54	2 – 7	
At 6 Hours	Group A	9.17	0.79	8 – 10	0.000 S
	Group B	6.10	1.06	5 – 8	
At 8 Hours	Group A	2.43	1.55	0 – 4	0.000 S
	Group B	8.57	0.93	7 – 10	
At 10 Hours	Group A	4.90	1.24	3 – 7	0.000 S
	Group B	0.90	2.25	0 – 9	
At 12 Hours	Group A	7.10	1.15	5 – 9	0.000 S
	Group B	1.70	1.60	0 – 5	

post-operative analgesia and fewer side effects.⁹ Bupivacaine is the most commonly administered drug, but it is cardiotoxic and its delayed onset of action is the limiting factors and duration of action is 2-4 hrs.¹⁰

Nowadays, different drugs have been used as adjuvants to achieve quicker onset, dense and prolonged block.¹¹ Adjuvants improve analgesia, reduce systemic side-effects and reduce total dose of local anaesthetics required.¹²

In our study, the mean onset of sensory block (min) was significantly early in group B (5.30 ± 0.95) ($P < 0.001$) compared with that of group A (12.17 ± 2.35), the mean onset of motor block (min) was significantly early in group B (4.35 ± 0.63) ($P < 0.001$) compared with that of group A (8.97 ± 1.81) ($P < 0.001$), the mean time to achieve complete block (min) was significantly early in group B (17.80 ± 2.95) ($P < 0.001$). This result nearly matched with another randomized double blind control study undertaken by SP Singh and colleagues to compare the effect of plain bupivacaine, alkalized bupivacaine and fentanyl-bupivacaine mixture in supraclavicular brachial plexus blocks. The quality of block (assessed by VAS) was significantly improved in the alkalized bupivacaine group and fentanyl-bupivacaine group as compared to the control group ($p < 0.05$).²² Minimum time was required to achieve complete block with alkalization of the bupivacaine (control 25.6 ± 7.8 , alkalized bupivacaine 17.4 ± 3.8 and fentanyl-bupivacaine = 21.8 ± 4.6 , $p < 0.001$). The duration of analgesia was maximum with the addition of fentanyl (7.28 ± 0.55 hrs) as compared to control (4.45 ± 0.43 hrs) and alkalized bupivacaine (5.33 ± 0.59 hrs) and the difference was statistically significant among all the three groups ($p < 0.001$).

Not all studies support the same feature. However, other studies reported conflicting claims. A randomized double-blind study by Kardash and Schools examined the effects of adding fentanyl to mepivacaine in supraclavicular blocks on block characteristics and postoperative analgesia. There was no statistically significant difference between the two groups in sensory or motor block characteristics.²² However, the onset time of analgesia was prolonged in every nerve distribution by adding fentanyl to lignocaine for axillary brachial plexus block in a double-blinded study performed by Nishikawa and team. The success rate of sensory blockade for radial and musculocutaneous nerves and the duration of the sensory blockade significantly increased in patients receiving lignocaine and $100 \mu\text{g}$ fentanyl (323 ± 96 min) as compared with the patients receiving lignocaine and normal saline (250 ± 79 min). The researchers concluded that the addition of fentanyl to lidocaine causes an improved success rate of the sensory blockade, but a delayed onset of analgesia, although this may be accounted for by the decreased pH caused by the fentanyl.²² The onset of motor block was faster than the sensory block in either of the group in this study. As described by Winnie in 1977 the outer motor fibers are blocked earlier than the sensory fibers which are situated deeper in the brachial plexus at the level of the trunk and division. Our study showed the same result that the motor block was quicker than the sensory block. Hickey et al

compared 0.25% ropivacaine with 0.25% bupivacaine for brachial plexus block for upper limb surgery, and showed that although motor onset was quicker in the bupivacaine group, there was no significant difference in terms of onset of sensory block.²⁴

The mean duration of analgesia (min) was significantly longer in group B (551.33 ± 44.34) ($P < 0.001$) compared with that of group A (373.33 ± 12.68) in this study. Bazin et al reported sustained analgesic effect from opioids used in supraclavicular brachial plexus block which outlasted the local anesthetic action of bupivacaine. Patients reported prolonged satisfactory analgesia with buprenorphine, morphine and sufentanil compared with saline.²⁵ The control group received mixtures of lignocaine and bupivacaine. Others received same mixture combined with morphine, buprenorphine and sufentanil respectively. Analgesia lasted significantly longer in morphine [$21(8-27\text{hr})$], buprenorphine [$20(14-34\text{hr})$] and sufentanil [$24.5(11-38\text{hr})$] group than in the controls [$11.5(7-16\text{hr})$]. This result nearly matches with our study. Similar result was depicted in a comparative study carried out by Chavan and colleagues to evaluate the analgesic efficacy and side effects of addition of fentanyl to local anaesthetics (bupivacaine 0.5% and lignocaine 2%). The study revealed that mean duration of analgesia (695 ± 85 min) is extended if fentanyl is added to local anaesthetics without increasing the side effects, however onset time of analgesia was prolonged. This may be accounted for by the decreased pH caused by fentanyl.²⁶ In this study the intensity of pain was measured on visual analogue scale at different time intervals postoperatively. It is revealed in the study that patients of group B had no pain up to 4 hrs, then there was first reporting of pain (VAS > 4) around 5 hrs, the worst pain was experienced (mean VAS 8.57 ± 0.93) around 8 hrs, first dose of analgesic was administered according to patient's request (VAS > 7). The patients of group A had no pain up to 3 hrs. Thereafter pain intensity increased (mean VAS 4.93 ± 1.23) around 4 hrs, around 6 hrs postoperatively the patients experienced the worst pain (9.17 ± 0.79). This feature reveals a significantly longer duration of analgesia in group B ($P = 0.000$) which nearly matches with the effects of adding fentanyl with mepivacaine in supraclavicular block by Kardash and Schools. There was a significantly lower VAS score among the patients with fentanyl added to their blocks within the first hour after the operation (1.3 ± 1.5 cm versus 3.8 ± 3.1 cm; $P < .05$), but subsequent VAS scores and total 24-hour patient-controlled analgesia requirements were no different.²⁷

In this study, no side effect was seen during anaesthesia and postoperative period as well. Since the introduction of

long acting local anaesthetics with better safety profiles as well as the availability of better equipment, the usage of peripheral nerve blocks has increased. Levobupivacaine, the S-enantiomer of bupivacaine, is the latest local anaesthetic agent introduced into clinical practice. It is less cardiotoxic compared to racemic bupivacaine. Ropivacaine, the S-enantiomer of S-1-propyl-2,6-pipecoloxylidide, is an amino-amide local anaesthetic with chemical structure similar to that of bupivacaine. Ropivacaine has been shown to produce less cardiac and central nervous system toxic effects, less motor block and similar duration of sensory analgesia when compared to bupivacaine. In a comparative study by Mageswaran and Choy, it is postulated that there were statistically significant differences in the onset-time for sensory (11.1 ± 2.6 minutes) ($p=0.003$) and motor block (17.1 ± 2.6 minutes) ($p=0.013$) in group receiving 0.5% levobupivacaine.²⁷ Although the clinical advantage of levobupivacaine is not substantial, its safety profile becomes a major consideration in the choice of local anaesthetic for brachial plexus block where a large volume is required for an effective result.

This prospective, randomized comparative study of supraclavicular brachial plexus block with local anaesthetic mixtures, with or without fentanyl revealed that addition of fentanyl significantly causes early onset of anaesthesia and longer duration of analgesia without any side effects. On the basis of the results of the present study, integrated with understanding from the available literature it may be recommended that, this technique will open new perspective for upper limb surgery under regional anaesthesia.

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