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## **ORIGINAL ARTICLE**

## A Comparative Study on the Effects of Adding Fentanyl and Buprenorphine to Local Anaesthetics In Brachial Plexus Block

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#### ABSTRACT

**Objective:** To evaluate the efficacy of fentanyl and buprenorphine in improving the blockade characteristics when used as an additives in supraclavicular block.

**Study Design:** Prospective, randomized, double blind trial conducted over a period of twelve months (July 09- June 10).

**Material and Methods:** A total 75 adult patients of either sex with ASA health status I-III, who were selected for elective upper limb surgery under supraclavicular brachial plexus block were randomly divided into three equal Groups A, B and C. Group A received a mixture of lignocaine (2%) with adrenaline (1:2,00,000) 10ml + bupivacaine (0.5%) 20 ml + distilled water 10 ml, to make a total volume of 40 ml. Group B received 1 ml (0.3 mg) buprenorphine and Group C received 1ml (50 µgm) fentanyl in addition to the above local anaesthetics in the same volumes and concentrations. The onset time of the sensory and motor blocks; the time required for complete sensory and motor blocks; the total duration of analgesia, the haemodynamic changes and side effects were noted and compared in both the groups.

**Results:** The onset time of the sensory and motor blocks was delayed in the fentanyl group  $(4.4 \pm 1.41 \text{ min and } 3.04 \pm 1.31 \text{ min respectively})$ , with no significant benefits on the duration of analgesia. In group C, buprenorphine, when added to local anaesthetics, prolonged the duration of analgesia by more than 1.5 times as compared to group A. Addition of fentanyl and buprinorphine to local anaesthetics in the brachial plexus block had no significant effects on the respiratory and haemodynamic parameters, except with minimal incidence (5.33%) of nausea and vomiting with the use of buprenorphine.

**Conclusion:** We conclude that the addition of buprenorphine to local anaesthetics provides long lasting analgesia without any significant increase in complications and recommend its incorporation in the routine anaesthesia practice.

**Keywords:** Peripheral nerve block (PNB), Supraclavicular brachial plexus block, fentanyl, buprenorphine

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### Introduction

It has been suggested since long, that peripheral nerves possess opioid receptors, and this has tempted clinicians to add narcotics to local anaesthetics to prolong the analgesic effects of these solutions. To date, the results of studies evaluating the efficacy of opioids and local anaesthetic combinations in the brachial plexus are inconclusive [1-4]. However, over the past 20 years, several studies have suggested that the addition of certain opiates to the local anaesthetics which are used for brachial block provide may effective. long-lasting postoperative analgesia [3],[4]. Some studies have indicated that the agonist-antagonist, buprenorphine, when added to bupivacaine, provided a longer period of postoperative analgesia than the traditional opiates. This practice can be of particular benefit to patients undergoing ambulatory upper extremity surgery, by providing prolonged analgesia after discharge from the hospital. [5-8]

This study was conducted to compare the effects of adding fentanyl and buprenorphine to local anaesthetics in the supraclavicular brachial plexus block (SBPB) by using nerve stimulators. The features of the blockade which were observed were the onset time of the sensory and motor blocks, the time of complete sensory and motor blocks and the duration of analgesia and motor blocks, along with any side effects or complications.

#### **Material and Methods**

The study was conducted in our institute in 75 patients who were undergoing elective upper limb surgery over a period of one year (July 2009- June 2010), with prior permission from the institute's ethics committee. Patients aged18 years and above, of both sexes and with ASA physical status I to III, were enrolled for the study after taking their written informed consent. The exclusion criteria included patient refusal, infection at the proposed site of injection, history / findings of allergy to local anaesthetics, medical disorders like diabetic neuropathy, psychiatric illness, coagulopathy and bleeding disorders or any other contraindication to PNB.

The patients were randomly divided into 3 equal groups by drawing out any one of the three labelled cards (A, B and C) from a sealed opaque envelope. The anaesthetist performing the randomization and preparation of the drug solution was not involved in the process of performing blocks or in the evaluation and recording of the study parameters and thus, the study was double blinded. The composition of the drugs in the various groups included:

**Group A:** 10ml of lignocaine (2%) with adrenaline (1:2,00,000) + 20 ml of 0.5% bupivacaine diluted with 10 ml distilled water.

**Group B:** 10ml of lignocaine (2%) with adrenaline (1:2,00,000) + 20 ml of 0.5% bupivacaine + buprenorphine (0.3 mg) 1 ml diluted with 9 ml distilled water

**Group C:** 10ml of lignocaine (2%) with adrenaline (1:2,00,000) + 20 ml of 0.5% bupivacaine + fentanyl 50µg 1 ml diluted with 9 ml distilled water.

Thus, the total volume of the drug solutions which were prepared in all the three groups was 40 ml, to ensure their blinding from the investigator who was performing the block.

On the day of surgery, the Visual Analogue Scale (VAS) was explained in detail to the patients, but not the process of Bromage evaluation.

In the operating room (OR), after achieving asepsis, the site of stimuplex needle insertion was identified and marked as per surface anatomical landmarks [Table/Fig. 1].



[Table/Fig. 1]: Anaesthetist-2 performing the block procedure

The stimuplex needle was connected with the Nerve stimulator, with the current output set at 1.0 mA and repeat twitch mode selected by the assistant under the guidance of an anaesthetist. On needle insertion, a twitch of the upper trunk (shoulder) was considered as the evidence of the needle approaching the brachial plexus. Wrist flexion and extension of the fingers were taken as acceptable responses and the current was gradually reduced between 0.2 to 0.5 mA, whereby maintaining the visible twitches. As per the card of the randomization process, the total volume of the anaesthetic solution was injected at an incremental dose of 5ml each, preceded by negative aspiration in each group.

Following completion of the LA injection, the sensory block was evaluated by a Hollmen scale Score [1] = Normal sensation of pinprick; [2] = Weaker sensation of pin prick felt as compared with other upper limb; [3] = Pin prick recognized as touch with blunt object; [4] = No perception of pin prick. The findings were recorded at an interval of 2 min till a complete sensory block was achieved i.e Hollmen Score=4 [10].

The onset time of the sensory block (OTSB) was taken as the time interval in minutes from time-0 till the sensory block started appearing i.e Hollmen score > 1, while the time for the complete sensory block (TCSB) was taken from time-0 till the complete sensory block was achieved i.e Hollmen Score=4. The total duration of the Sensory Block (TDSB) was taken as the duration of the time in minutes between TCSB till the time when the Hollmen score reached <4 in the postoperative period.

The motor block was evaluated by using the Modified Bromage Scale (MBS) for the upper extremity and the finding was recorded from time-0 till the complete loss of the motor power was achieved i.e MBS Score=3[11]. The onset time of the motor block (OTMB) i.e MBS score=1 and the time for complete motor block (TCMB) i.e MBS score=3 were also recorded in all cases.

The adequacy of the block was evaluated by asking the patients whether they felt any discomfort when pressure was applied with the Allis clamp at the area of the surgical field. The block was considered to have failed if complete sensory and motor block was not achieved after 30 min and the failed block was converted to GA and it was recorded. Intra-operative complications, if any, including vessel injury, haematoma, nausea and vomiting, dyspnea, fall in respiratory rate or oxygen saturation, any symptom/sign of LA toxicity, ECG changes, Horner's syndrome, sedation, etc were recorded, with their respective management.

Postoperatively, on complaint of pain (i.e. VAS>4), systemic analgesics were supplemented as per the individual requirement and the total time of the sensory block was recorded. VAS scale consisted of a 10 cm line, where the patients were asked to mark the pain intensity on the line in between 0 (no pain) to 10 (worst possible pain).

**Statistical analysis:** The results were presented as Mean  $\pm$  Standard Deviation (SD) for parametric data and as percentage for nonparametric data. The data were analyzed by using Microsoft Office Excel 2007 and SPSS version 14 software (Chicago ltd). The difference between the two groups was analysed by using the unpaired t-test and one way ANOVA and between the three groups by using the Kruskal-Wallis test. A *P*-value <0.05 was considered to be significant.

#### Results

There was no significant difference in the demographic data or the duration of surgery in all the three groups.

[Table/Fig 2]. Demographic data of all patients

Patient characteristic	Group A	Group B	Group C
S			
Pt. age (yrs)	18-80	18-80	18-80
Mean±SD	40.64±19.32	37.96±15.82	40.68±19.3
			8
Male: female	17(68%):	19(76%):	20(80%):
	8(32%)	6(24%)	5(20%)
Weight(kg)	50-80	50-80	50-100
mean± SD	$62.36 \pm 7.39$	$61.28 \pm 7.75$	$63.4 \pm 11.4$

Height(cm) mean±SD	151-180 164.92 ± 9.54	151-180 167.88 ± 11.56	151-180 165.32 ± 10.66
Duration of surgery	59.56 ± 33.65	$72.60 \pm 26.38$	67.96 ± 32.68

The onset time of the sensory block (OTSB) and the onset time of the motor block (OTMB) were the earliest in Group A>B>C when compared groups (2.88>3.28>4.4 among the min respectively) [Table/Fig 3]. Intergroup comparison showed a non-significant difference (P > 0.05) between Groups A and B, a significant difference (P < 0.05) between Groups B and C and a highly significant (P < 0.001) difference between Groups A and C. OTMB was earlier and significant (P < 0.05) in Group A than in Groups B or C and non significant (P > 0.05)between Group A vs. C and Group B vs. Group C. The time for the complete sensory block (TCSB) and the complete motor block (TCMB) were the earliest in Group A>B>C. TCSB, when compared between Groups A and B, showed a non-significant difference, but it was significantly delayed (P < 0.001) in Group C as compared to Group A or B. The time for complete motor block (TCMB) was significantly less (P < 0.05) when compared between Groups A and B and highly significant (P < 0.001) between Group A vs. C and Group B vs. C [Table/Fig 3].

[Table/Fig 3]: Time of onset and achievement of complete sensory and motor blockade in groups A, B & C.



\*: Onset Time of Sensory Block (OTSB); +: Onset Time of Motor Block (OTMB); §: Time required for Complete Sensory Block (TCSB); €: Time required for Complete Motor Block (TCMB)

The total duration of the Sensory and motor blocks (TDSB and TDMB) and Analgesia

(TDA) were all significantly prolonged in Group B as compared to the other groups [Table/Fig 4]. TDSB and TDMB were statistically non significant (P > 0.05) between Groups A and C.

Analgesia	(TDA) in	all the	3 groups.
Group	A	В	C
TDSB (min)*	217.28 ± 48.56	261.84 ± 53.30	225.12 ± 34.06
TDMB (min)*	287.76±44.62	328.32 ± 47.94	294.16 ± 55.69
T DA (min)*	448.32±147.69	698.64±189.48	493.28±152.45

[Table/Fig 4]: Total Duration of Sensory & Motor Block (TDSB & TDMB) and Total Duration of Analgesia (TDA) in all the 3 groups.

\*: Values expressed in Mean ± SD

Out of 75 patients, 5 (6.7%) patients had vessel injury, of which 1 (4%) was in Group-B and 2 (8%) were in Groups A and C (1 in each). They were managed by a little withdrawal and repositioning of the needle and antiseptic pressure dressing after completion of the block. Four (5.33%) cases, all from Group-B, complained of nausea and vomiting in the postoperative period and were managed with injection ondensetron 4 mg intravenously. No serious complication was observed in the perioperative period in any of the groups.

#### DISCUSSION

We designed this prospective randomized double blind study to identify the outcome of adding fentanyl and buprenorphine to local anaesthetics in the brachial plexus block. We observed a 100% success rate in our study and none of our patients were supplemented with general anaesthesia. This is comparable to the study by Jeon DG et al, wherein they concluded that the elicitation of a twitch on the fingers was more effective in increasing the success rate (93.7% versus 75.0%) and reducing the onset time  $(14.4\% \pm 6.0 \text{ min versus } 15.3 \pm 6.7 \text{ min})$ than the elicitation of a proximal response (arm or elbow) [19]. In Borgeat et al's study, the success rates were 97% when a distal response was elicited and 44% when a proximal response was observed in the infraclavicular block [20].

In our study, adjuvants to the local anaesthetics which were used were buprenorphine, which is a

lipid soluble opioid agonist- antagonist and fentanyl, which is a pure agonist. The onset time of LA is greatly influenced by the relative amounts of the ionized and the non ionized forms of the drugs which are present in the solution.

In our study, the onset time of the sensory and the motor blocks was delayed in the fentanyl group, they being  $4.4 \pm 1.41$  min and  $3.04 \pm 1.31$ min, respectively. The time required for the complete sensory and the motor blocks were  $11.44 \pm 1.47$  min and  $14.16 \pm 1.40$  min, respectively. This does not correlate with the study done by Kardash K et al, who achieved the onset of the sensory and the motor blocks at  $2.9 \pm 1.9$  min and  $4.0 \pm 3.1$  min, respectively and the complete sensory and the motor blocks at  $18.2 \pm 7.5$  min and  $13.5 \pm 7.3$  min, respectively [21]. As compared to the study done by Nishikawa K et al [22], who used100 µgm of fentanyl in 40 ml of 1.5% lidocaine with 1:2,00,000 epinephrine in the brachial plexus block by the axillary approach, we found a similar delay in the time which was required for the complete sensory block. They concluded that the decrease in pH of lignocaine from 6.2 to 5.2 by the addition of 100 µgm of fentanyl may have reduced the rate of nerve penetration of lidocaine, thus resulting in a slower onset of analgesia.

Jadon A *et al* [10] examined the benefit of adding buprenorphine to 30 ml of 0.3% bupivacaine in the supraclavicular block. In their study, the onset time of the motor block ( $4.05 \pm 0.94$  min) was significantly faster than the onset of the sensory block ( $6.65 \pm 1.18$  min), which does not correlate with those found in our study. This can be explained by the "core and mantle concept" of Winnie [23]. The earlier time to achieve the complete sensory and motor blocks in our study, as compared to theirs, can be attributed to the mixture of local anaesthetics which were used.

Sahu DK *et al*, in their study on supraclavicular brachial plexus block, used a mixture of 15 ml of 1.5% lignocaine and 15 ml of 0.325% bupivacaine and found that the average time for complete analgesia was  $7.61 \pm 2.82$  min and that for motor loss was  $11.70\pm2.50$  min [24].

Similarly, in our study, the time for the onset of complete sensory block was faster than that required for complete motor block in all the three groups, with the earliest sensory and motor block onset times being observed in Group A i.e  $8.88 \pm 2.59$  min and  $11.04 \pm 1.93$  min, respectively. A similar sequence i.e sensory onset time faster than motor onset time was also observed by Misiolek HD et al [25]. Klein SM et al, in their study, observed that the mean onset time for both the motor and sensory blockade was < 6 min when 30 ml of 0.5% bupivacaine, 0.5% ropivacaine and 0.75% ropivacaine was used in 3 different groups in the interscalene block. They premedicated their patients with IV midazolam (1-5 mg) and fentanyl (50-250 µgm), which probably enhanced the onset of the block, which does not correlate with our study [26].

[Table/Fig 5]: Duration of analgesia in other studies on Brachial Plexus Block by adding Fentanyl or Buprenorphine (Buprenor.) with LA

Investigat or	Drugs Used	Vol ume	Approa ch	Duration of Analgesia
Present Study	2% Lig. with Adr. 1:2000000 + 0.5% Bupiv. + 0.3mg Buprenorp.	40 ml	Supracla vicular	698.64 ± 189.48 min
Bazin JE et al <sup>17</sup> 1997	0.5% Bupiv. 1mg/kg + 1% Ligno. 2mg/kg with Adr. 1:200000+ Buprenor. 3μgm/kg		Supracla vicular	20 hr
Nishikawa et al <sup>8</sup> 2000	1.5% Lig. with Adr. 1:200000 + 100µgm Fentanyl	40 ml	Axillary	323 ± 96 min
Singh SP et al <sup>16</sup> 2009	0.25% Bupi. + 75 μgm fentanyl	30 ml	Supracla vicular	7.28 ± 0.55 hr
Jadon A et al <sup>9</sup> 2009 Buniy: Bu	0.3% Bupiv. + 3μgm/kg Buprenor.	31 ml	Supracla vicular	680.6 ± 86.27 min

Bupiv: Bupivacaine; Ligno: Lignocaine; Buprenor: Buprenorphine; Adr: Adrenaline

In our study, the duration of analgesia was maximum in the buprenorphine group ( $698.64 \pm 189.48 \text{ min}$ ), as compared to that in Group-A ( $448.32\pm147.69 \text{ min}$ ), which was 1.5 times that found in Group-A, whereas the fentanyl group did not show any significant prolongation of analgesia.

Jadon A et al [10] noted that the total duration of motor block with buprenorphine was  $329.2 \pm 28.4$  min, whereas in our study, it was  $328.32 \pm 47.94$  min, which is comparable. This can be

explained by the fact that bupivacaine, a long acting LA, was used and buprenorphine as such, does not have effect on the motor block.

From the above findings, we can suggest that opioids can be safely and effectively used in the brachial plexus block for post operative analgesia even in day care surgery. The more lipophilic the opioid (buprenorphine>fentanyl,) the longer the effect seems to last.

A limitation of our study was that a larger sample size could have added more precision to our results. Secondly, the incorporation of an ultrasound guided block localization technique could have drastically decreased the total volume of the local anaesthetics which were administered and this could have added new dimensions to our study. Future trials can explore the minimal safe doses of newer opioid additives by using an ultrasound guided method of nerve localization in the brachial plexus block.

#### Conclusion

We conclude that the addition of buprenorphine to local anaesthetics provides a significantly longer duration of analgesia by more than 1.5 times than when local anaesthetics are used alone in the supraclavicular block. The addition of opioids to local anaesthetics in the brachial plexus block has no significant adverse effect on the respiratory and haemodynamic parameters when used in prescribed doses and has a minimal incidence of nausea and vomiting or other minor side effects.

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