Original Article

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Evaluation of Fentanyl as an Adjuvant in Ultrasound Guided Supraclavicular Brachial Plexus Block

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Abstract

Background & Objectives: Supraclavicular brachial plexus blocks have been performed effectively using local anaesthetic agents alone for upper limb surgeries. The Primary objective of this study is to determine whether the addition of fentanyl to a supraclavicular brachial plexus block improves the success rate, block time, duration and quality of postoperative analgesia. Secondary objective is can fentanyl be recommended as a safe adjuvant to local anaesthetic agents for peripheral blocks.

Design & Methods: The study was conducted on ASA I-III patients who were randomly divided into Group I (Control) and Group II (Study). Patients in the control group received 20 ml 0.5% bupivacaine, 10 ml 2% lidocaine and 2 ml normal saline. The study group received 20 ml 0.5% bupivacaine, 10 ml 2% lidocaine and 2 ml fentanyl (100 μg). Onset times for sensory and motor block were recorded. Post-operatively patients were followed over a 24 h period at 2hr interval for any breakthrough pain, and the intensity of pain was determined using Verbal Rating Score (VRS) system.

Results: Fifty patients were studied with 25 in each group. The overall mean Verbal Rating Score for immediate postoperative pain in the fentanyl group was 2.6 compared to that of the control group which was 3.8 ($p<0.001$). 24 h post-operatively at 2hr intervals, the VRS ranged between 1 and 8; the mean VRS in control group was 5.7 while it was 3.8 in the study group ($p<0.001$). There was also a significant reduction in the incidence of breakthrough pain in the fentanyl group ($p<0.0001$) at the end of 24 hrs.

Conclusions: The study found that the addition of 100 μg fentanyl in supraclavicular brachial plexus block prolongs the duration of analgesia without any side effects. Fentanyl may be used as a safe adjuvant for supraclavicular brachial plexus blocks to improve the quality of analgesia.

Keywords: Fentanyl; Brachial Block; Ultrasound.

Introduction

All major upper limb surgeries are associated with severe postoperative pain [1]. The supraclavicular approach of the brachial plexus block has a high success rate including blockade of the ulnar and musculocutaneous nerve, which can be missed respectively with the interscalene and axillary approach [1,2]. At the level of the supraclavicular fossa, the plexus is most compactly arranged.

Antinociceptive effects of opioids at the central and/or spinal cord level are well known [3]. However, evidence from recent experimental studies have shown that by activation of peripheral opioid receptors by exogenous opioid drugs antinociception can be initiated [4,5]. Opioids are used as an adjuvant with local anaesthetic drugs to prolong analgesia during post-operative period. Fentanyl a synthetic opioid is approximately thirty times more potent than morphine because of its high lipophilicity. Fentanyl causes less nausea and decreased histamine release so less itching in relation to morphine. Fentanyl has been shown to be of benefit in central neuraxial blocks and other regional blocks by increasing the duration of pain relief [6,7]. Hence we decided to use fentanyl in this study because of its potent effect and relatively less systemic side

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effects.

The addition of narcotic analgesic in brachial plexus block has improved success rate and postoperative analgesia [8-12]. However the results are conflicting with some authors showing favorable response, whereas others have found no effect [13-15].

With this background, the current study was conducted to determine if addition of fentanyl as an adjuvant to the local anaesthetic agents during brachial plexus blocks would improve the quality of analgesia postoperatively.

Methods and Materials

Description of Study

The protocol of this prospective, randomized, double-blind study was approved by the Ethics Committee and the Institutional Review Board. All participants fulfilling inclusion criteria were explained about procedure, and written informed consent was obtained from them.

Sample Size was Calculated using the Following Formula

Desired power of study = 0.8

P value = 0.05

Effect size = 30% reduction in pain in the study group compared to control group.

The following formula was used to calculate the sample size which yielded 25 patients in each group.

$$n = \frac{2(\bar{p})(1-\bar{p})(Z_{\beta} + Z_{\alpha/2})^2}{(p_1 - p_2)^2}$$

(where p is the effect size, Z_{β} is the desired power, Z_{α} is the level of statistical significance)

Inclusion Criteria

1. ASA grade I, II, and III posted for elective operations on elbow, forearm and hand, ele
2. Age group: 17 to 70 years
3. Sex: Either gender.

Exclusion Criteria

1. ASA grades IV and V
2. Age below 17 or above 70 years
3. Patients who had history of significant neurological, psychiatric, neuromuscular disease as well as pregnant or lactating women.
4. Known hypersensitivity to local anaesthetic drugs and history of coagulation disorders
5. Local infection.

All enrolled patients received supraclavicular brachial plexus block which were performed by an experienced anaesthetist guided by sonographical images and nerve stimulator. A different anaesthetist assessed the patient during the postoperative period. Both the anaesthetists were blinded .

After standard anesthesia monitoring , Blocks were performed on all the patients in either lying or semi-supine position. The head of the patient was rotated either to right or left side, opposite to the side of block. All aseptic precautions were taken prior to performing the block. A 50 mm, 22 gauge Teflon-coated short-bevel peripheral nerve stimulator needle (Pajunk, Geisingen, Germany; or B. Braun Bethlehem PA), Stimuplex (Braun Germany) nerve stimulator and Ultrasound (Siemens, Acuson X 150) guidance was used during the procedure.

Subcutaneous injection of 2mL of 1% lidocaine was administered at the needle insertion site. After locating the end point and observing the response using ultrasound landmarks,using in plane approach and a distal motor response with an output lower than 0.5 mA, following negative aspiration the solution containing local anaesthetic combined with either fentanyl or normal saline was administered as follows:

Group I (control): bupivacaine 0.5% 20 mL + lidocaine 2% 10 mL + NS 2 mL

Group II (study): bupivacaine 0.5% 20 mL + lidocaine 2% 10 mL + fentanyl 2 mL (100μg).

Mild sedation was administered after evaluation of block was complete, so that constant verbal contact can be maintained with the patient.

Any clinical evidence suggesting local anaesthetic toxicity, in addition to possible side effects like nausea, vomiting, and systemic effects of fentanyl was recorded, which is routine after all regional anaesthetic techniques such as brachial plexus blocks.

Outcomes Measured Include the Following

- Time of onset of sensory and motor block of the area of distribution of the brachial plexus block.
- The duration of post block analgesia, defined as

the interval between block completion and requirement of first postoperative analgesic and incidence of post block neurologic and respiratory complication were recorded.

Evaluation of sensory block was performed every 5 minutes in the dermatomal areas corresponding to median nerve, radial nerve, ulnar nerve and musculocutaneous nerve over a 30 minute period after the completion of the block procedure. Onset of sensory blockade was determined by the pin prick method, and evaluation was made based on the findings when there is a dull sensation to pin prick along the distribution of any of the above nerves.

Rating of the block was quantified as, no block (sharp pin sensation felt), partial block (dull sensation felt), or complete block (no sensation felt).

The block was considered successful when there was complete loss of sensation to pin prick. Motor block was evaluated using forearm flexion-extension, thumb and second digit pinch, and thumb and fifth digit pinch, and scored as follows: no loss of force (no block); reduced force compared with the contralateral arm (partial block); incapacity to overcome gravity (complete block). Patients were assessed for sensory and motor blockade at regular intervals intraoperatively and postoperatively over period of 24 hours at 2hr intervals. Patients were instructed pre-operatively about use of the Verbal Rating Scale (VRS) for pain assessment. Where patients were asked to verbally rate their perceived pain intensity on a numerical scale from 0 to 10, with the zero representing "no pain" and the 10 representing the extreme pain ("the worst pain possible"). If any potentially surgical territory was not completely anaesthetised at the time of surgery around the elbow or wrist, general anaesthesia was induced and patients were excluded from the study.

During Postoperative Period Following Assessments was Made:

1. First analgesia for breakthrough pain
2. Duration of time- the regions of the arm remain insensible or weakened
3. Respiratory Rate

Table 1: Types of surgeries in the study subjects

Surgery	Frequency (%)
ORIF forearm bones	19 (38)
AV Fistula	18 (36)
K wiring	5 (10)
Exploration surgery	3 (6)
Excision of bony cyst	2 (4)
Tendon repair	1 (2)
Synovectomy	1 (2)
Ulnar artery repair	1 (2)

Results

Data were collected and entered in Microsoft Excel software. Statistical analyses were performed by using computer software package Statistical Package for Social Sciences (SPSS)-version 16.

Descriptive analyses of all the demographic as well as clinical parameters were done. The numerical variables were expressed in mean and standard deviation as well as median and interquartile ranges. The verbal rating Score which is ordinal scale were compared between the groups using Mann- Whitney U test. Chi-square test was used to analyse the difference between groups for categorical data such as gender, breakthrough pain etc. Statistical significance was fixed at the level of $p<0.05$.

A total of 50 patients who were scheduled for upper limb surgery were included in this study. The study compared intra-operative and post-operative analgesic effects after performing supraclavicular brachial plexus block using 0.5% bupivacaine and 2% lidocaine in Group I (control) and 0.5% bupivacaine, 2% lidocaine and 100 µg fentanyl in Group II (study).

The age of patients ranged from 17 to 70 with a mean of 44.5 [16.5 (SD)]. 60% of the study subjects were males. The gender was equally distributed between groups

Brachial plexus blocks were performed for different upper limb procedures. The denomination of surgeries is given in Table 1.

Majority of the patients (54%) did not receive any supplemental sedation during procedures, while in 46% of the patients mild sedation was provided with

midazolam.

Overall 58% of the patients did not have any breakthrough pain and 42% were recorded to have experienced it at the end of 24 Hrs.Those with pain were treated with Inj.Pethidine.

The onset time of sensory block ranged from 10-45 min, the median was 20 min. The onset time for motor block ranged between 15 to 60 min, the median was 24.5 min. The surgical duration ranged from 35 to 180 min, the median being 90 min. The Verbal Rating Score (VRS) during immediate post-operative period ranged between 1-6, the median was 3 and VRS after 24 hours ranged between 1-8, the median being 5.

Table II shows that the mean age in control group was 38.9 years where as in study group it was 50.2 years. The difference was statistically insignificant. The onset time for sensory block varied between 10 minutes to 45 minutes but the mean was 21 minutes in control group and in study group it was 20.5 minutes respectively. This was not much different between the groups and was statistically insignificant. The onset time for motor block ranged between 15 minutes to 60 minutes, however the mean motor block time in study group 25.8 minutes which was less when compared to control group which was 26.4 minutes but was statistically insignificant. The surgical duration varied between 35 minutes to 180 minutes which was based on the different type of surgeries. The statistical comparison of the surgical duration was insignificant in both groups. The Verbal Rating score (VRS) was in range of 1- 6 during post operative period but the mean in control group was 3.8 and study group was 2.6 which was statistically

Table 2: Comparison of variables between groups

Variable	Control group Mean (SD)	Study group Mean (SD)	P value
Age	38.9 (14.8)	50.2 (16.3)	0.015*
Onset time – sensory block (min)	21 (6.8)	20.5 (8.4)	0.470
Onset time- motor block (min)	26.4 (8.1)	25.8 (10.7)	0.470
Surgical duration (min)	96 (33.3)	86.4 (27.4)	0.445
VRS postoperative	3.8 (1.2)	2.6 (0.8)	0.001*
VRS 24 hours	5.7 (1.4)	3.8 (1.1)	<0.001*

VRS Verbal Rating Score for pain
*Statistically significant by Mann-Whitney U test

Table 3: Comparison of breakthrough pain

Study Group	Breakthrough pain		Total
	No	Yes	
I (Control)	4(mean-24hrs)	21(mean-12 Hrs)	25
II (Fentanyl)	25(mean-24hrs)	0	25
Total	29	21	50

Chi-square value 36.2; df: 1; p<0.0001

significant. The VRS 24 hours postoperative period at 2hr interval ranged between 1- 8 and the mean was 5.7 in control group and 3.8 in study group which was again statistically significant with p value <0.001. Vital parameters like pulse rate, systolic blood pressure, respiratory rate, and oxygen saturation did not show any significant fluctuation in both the groups.

14 patients in Control group received sedation and only 9 patients in study group received sedation, whereas 11 patients in control group and 16 patients in study group did not receive any sedation during surgical procedure. Even though sedation requirement in control group was higher compared to study group still the results were not statistically insignificant.

Table 3 shows the comparison of the incidence of breakthrough pain between the groups. There was statistically significant reduction in the incidence of breakthrough pain in the fentanyl group compared to the control group at the end of 24 hrs postoperative period. 25 patients in fentanyl group had no breakthrough pain where as only 4 patients in control group had no breakthrough pain. None of the patients in fentanyl group complained of breakthrough pain where as 21 patients in control group complained of breakthrough pain at mean of 12 hrs postoperatively. 75 mg of pethidine was administered intramuscularly to all the patients who complained of breakthrough pain, and VRS in these patients was >5.Surprisingly none of the patients in study group had breakthrough pain even after 24 hrs.

Discussion

This study demonstrates the efficacy of adding fentanyl as an adjuvant to local anaesthetic drug in ultrasound guided brachial plexus block for upper limb surgeries. A comparison was made to determine effect of fentanyl in prolonging the analgesia during immediate postoperative period and over 24 hr period in Group I (Control) and Group II (Study group). Statistically significant difference in analgesia was observed postoperatively using Verbal Rating Score. However, fentanyl did not prolong the onset time of the sensory and motor block according to our study.

Addition of fentanyl to lidocaine for brachial blocks improved the success rate of sensory blockade [7,9,16,17]. Morphine and buprenorphine are reported to cause analgesia with or without local anaesthetic drugs when used for brachial plexus block [18]. Studies performed using agents such as tramadol, clonidine, dexamethasone and dexmedetomidine as an adjunct in brachial blocks have demonstrated significant increase in sensory and motor blockade when used with local anaesthetic solution [19-22]. Study conducted by Karakaya et al [9] showed that the duration of sensory block, motor block and analgesia was longer when fentanyl was added to bupivacaine, the duration was almost double when compared to the group in which Bupivacaine alone was administered. Similar finding were demonstrated by Nishikawa et al. in their study where fentanyl was administered with lidocaine in epinephrine 1: 200000 for axillary blocks [23]. There was increase in success rate and the duration of blockade there by prolonging postoperative analgesia.

Some authors have postulated the mechanism of action by which fentanyl improved analgesia on peripheral administration. First, fentanyl could act directly on the peripheral opioid receptor. Secondly presence of primary afferent tissues (dorsal root) have known to contain opioid binding sites [9,10] and the presence of bi-directional axonal transport of opioid binding protein has been shown [24], so fentanyl may penetrate the nerve membrane and act at the dorsal horn. This could have also accounted for the prolonged analgesia. However, some authors have reported of fentanyl also has a local anaesthetic like action [9]; Gormley et al [11] suggested that alfentanil also prolonged postoperative analgesia by local anaesthetic action. In animals presence of peripheral opioid receptors has been reported [25-27]. As it is still unclear if functional opioid receptors exist in human peripheral tissue various studies were conducted in past to determine if addition of opioids to local anaesthetic drugs would improve the quality of regional blocks [10]. However, further studies are required comparing the effects of fentanyl on brachial plexus block using solution of different pH and quantity. But from our study 100 μg of fentanyl did prolong the sensory block significantly there by prolonging analgesia. However, not all studies confide with our findings.

Contradicting results were published by Fletcher et al. which showed no change in the success rate, onset time, or duration of analgesia when fentanyl was used for axillary brachial plexus block [13,15]. Study by Racz et al [14] demonstrated that addition of morphine to local anaesthetic solution neither changed the onset time nor quality of postoperative pain relief. Kanaya et al [27] in his study demonstrated that addition of fentanyl to axillary brachial plexus block prolonged the onset time of sensory block in every trunk; This effect was contributed due to change in pH on addition of fentanyl to the local anaesthetic solution [16-27]. It is well know that change in pH of an anaesthetic drug can alter the action of local anaesthetic. However there was no increase in onset time in our study.We had included different types of upper limb surgeries as mentioned in Table 1, so that the intensity of pain based on severity of procedure could be evaluated and efficacy of fentanyl in brachial blocks for different surgery could be determined on assessment using VRS. In other studies the choice of procedure was selective there by assessment of pain using subjective scoring system could be influenced by various factors [2].

Conclusion

Our sample size was relatively small, and this smaller sample size may contribute to the statistical misappropriations and may overstate the benefits from the addition of drugs to brachial plexus blocks.In conclusion, addition of fentanyl to local anaesthetic solution does prolong the sensory block there by prolonging the duration of analgesia which was evident in our study when assessed in immediate postoperative period and at regular intervals over a period of 24 hrs. However there was no increase in duration of motor blockade and neither did it affect the onset time after the block was performed.

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