

# Comparison of Local Anesthetic Mixtures with Tramadol or Fentanyl for Axillary Plexus Block in Orthopaedic Upper Extremity Surgery

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## ABSTRACT

The local anesthetic mixtures are performed for peripheral nerve blocks to accelerate the onset time of sensorial and motor blocks. Also adjuvant agents can be added to local anesthetics to improve the quality and duration of plexus blocks. In this study, we compared the effect of tramadol and fentanyl as adjuvant agents to local anesthetic mixtures in axillary plexus block for orthopedic upper extremity surgery. After approval of hospital ethics committee and written patient consent, sixty patients were enrolled to the study in three groups; The Control Group (Group C, 40 mL of 0.25% levobupivacaine + 40 mg lidocaine n:20), the Fentanyl Group (Group F, 40 mL of 0.25% levobupivacaine + 40 mg lidocaine + 50 mcg fentanyl n:20), the Tramadol Group (Group T, 40 mL of 0.25% levobupivacaine + 40 mg lidocaine + 100 mg tramadol n:20) for axillary plexus block. Groups were compared for partial and complete motor and sensorial block, onset time, partial and complete motor and sensorial block recover time, and postoperative first analgesic requirement time (VAS >4). In Group T partial sensorial block onset time was shorter than Group C and complete sensorial block onset time was shorter than Group C and Group F. In Group T complete sensorial block recover time was longer than Group C and Group F. The postoperative first analgesic requirement time was significantly longer in Group T and F when compared with Group C and significantly longer in Group T when compared with Group F. We conclude that the addition of tramadol or fentanyl to local anesthetic mixtures as an adjuvant agent for axillary block provide better postoperative analgesia for orthopedic upper extremity surgery. Furthermore tramadol more improves the block quality than fentanyl.

**Key words:** Axillary block, local anesthetics, tramadol, fentanyl

## Ortopedik Üst Ekstremitte Cerrahisinde Aksiller Pleksus Blok için Fentanil veya Tramadol Lokal Anestetik Karışımlarının Karşılaştırılması

### ÖZET

Periferik sinir bloklarında duyuşal ve motor bloğun hızlı başlaması için lokal anestetikler birlikte kullanılabilirler. Pleksus bloklarının kalite ve süresini artırmak için lokal anestetiklere adjuvan ajanlar da eklenebilir. Bu çalışmada tramadol ve fentanilin ortopedik üst ekstremitte cerrahisi için aksiller pleksus blokta lokal anestetik karışımlara adjuvan ajanlar olarak eklenmesinin etkilerini karşılaştırdık. Hastane etik kurul onayı alındıktan ve hastanın yazılı onamından sonra 60 hasta çalışmaya dahil edildi. Hastalar 3 gruba ayrıldı. Kontrol Grubu (Grup C, 40 mL %0,25 levobupivakain + 40 mg lidokain n:20), Fentanil Grubu (Grup F, 40 mL %0,25 levobupivakain + 40 mg lidokain + 50 mcg fentanil n:20), Tramadol Grubu (Grup T, 40 mL %0,25 levobupivakain + 40 mg lidokain + 100 mg tramadol n:20). Gruplar parsiyel ve tam motor ve duyuşal blok, başlama, iyileşme süreleri ve postoperatif ilk analjezik gereksinim süreleri açısından karşılaştırıldı (VAS >4). Grup T'de parsiyel duyuşal blok başlama süresi Grup C'den kısa bulundu. Tam duyuşal blok başlama süresi Grup C ve Grup F'den kısadır. Grup T'de tam duyuşal blok iyileşme süresi Grup C ve Grup F'den uzundu. Postoperatif ilk analjezik gereksinim süresi Grup C ile karşılaştırıldığında Grup T ve F'de anlamlı derecede uzundu ve Grup F ile karşılaştırıldığında Grup T'de anlamlı derecede uzundu. Lokal anestetik karışımlara adjuvan ajan olarak tramadol ya da fentanil eklenmesinin ortopedik üst ekstremitte cerrahisi için daha iyi bir postoperatif analjezi sağladığı sonucuna vardık. Ayrıca, tramadolun blok kalitesini fentanilden daha fazla geliştirdiğini gözlemledik.

**Key words:** Aksiller blok, lokal anestetik, tramadol, fentanil

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## **INTRODUCTION**

The axillary approach to the brachial plexus is a commonly used and efficient analgesia technique for hand wrist and/or forearm surgery (1,2). Local anesthetics, are often used in axillary block application. Considerable research has been conducted in order to determine the ideal drug or combination. An ideal drug would have a fast sensory onset time and a differential offset, with an earlier offset of motor rather than sensory blockade, thus enabling patients to move their arms while enjoying continued analgesia. Combinations of local anesthetics are employed for peripheral nerve blocks to accelerate the onset time of sensorial and motor blocks (3).

In addition, adjuvant agents are used to improve the quality and duration of nerve blocks and to reduce the need for supplementary analgesics for postoperative pain. There have been several studies concerning opioids, and particularly the use of fentanyl as an adjuvant agent. Fentanyl has been added to local anesthetics, with different results, increase the success rate of sensory blockade and prolong the duration of analgesia in contrast did not find any effects on the time to onset of nerve block or time to first request for postoperative pain medication. being obtained (4-6). Tramadol, a synthetic codeine analogue, has been used as an adjuvant to improve peripheral block quality in peripheral nerve block and to extend postoperative analgesia (7,8).

In this study, we compared the effect of sensorial onset, recovery and postoperative first analgesic requirement time of tramadol and fentanyl as adjuvant agents to local anaesthetic mixtures (lidocaine and levobupivacaine) in axillary plexus block for orthopedic elective hand, wrist and forearm surgery.

## **MATERIALS AND METHODS**

This prospective, randomized, double-blind study designed following institutional review board approval, written informed consent was obtained from patients undergoing elective surgery of the hand, wrist, or forearm under axillary block using the nerve stimulation technique. Sixty American Society of Anesthesiologists (ASA) physical status I or II patients of aged between 18 and 60 were randomly allocated to one of three groups using sealed envelopes for this prospective, randomized, double-blind study.

Our exclusion criteria were; central or peripheral neuropathies; pregnancy; a history of allergic reaction to any of the study drugs; cardiac, respiratory, hepatic and/or renal failure; regional anesthesia being contraindicated; coagulation defects and infection at the puncture site were not included.

Patients were randomly allocated into one of three groups: the control group (Group C, 40 mL of 0.25% levobupivacaine+2 mL (40 mg) lidocaine+2 mL saline, n:20), the fentanyl group (Group F, 40 mL of 0.25% levobupivacaine+2 mL (40 mg) lidocaine+2 mL (50 mcg) fentanyl, n:20), or the tramadol group (Group T, 40 mL of 0.25% levobupivacaine+2 mL (40 mg) lidocaine+2 mL (100 mg) tramadol, n:20) for axillary plexus block. Patients were not pre-medicated prior to the block. Details of the anesthetic technique, the study protocol and visual analogue scales were fully explained during the preoperative visits, and written consent was obtained from each patient before enrollment in the study. After the insertion of an intravenous catheter and neurological examination, patients were monitored using electrocardiography, pulse oximetry, heart rate and non-invasive blood pressure measurements (Datex-Ohmeda Cardiocap 5). The same axillary block was employed in all patients. The arm to be operated on was abducted to at least 90°, with the forearm in 90° flexion. The injection site was then subcutaneously infiltrated with 1 mL of 2% lidocaine. A 22-gauge, 40-mm, short bevelled, insulated, unipolar cannula (Pajunk, Geisingen, Germany) was connected to a nerve stimulator (Stimuplex HNS11TM, B. Braun, Melsungen, Germany) and inserted immediately above the artery until the brachial plexus was located. Block was then applied with only local anesthetic, fentanyl or tramadol according to the study groups. The anesthetist performing the block was aware of the site of surgery, although other staff members unaware of the patient's group status evaluated the sensory and motor block. Sensory block was graded according to the following scale (9): 0:No block (normal sensation), 1:Partial block (decreased sensation) 2:Complete block (no sensation).

Duration of sensory block, defined as a return of sensation to pinprick in all nerve distributions, was also measured. Motor block was graded according to the following scale: 0: No block (full muscle activity), 1: Partial block (decreased muscle activity), 2: Complete block (no muscle activity)

**Table 1.** Demographic data of patients in the three groups (mean  $\pm$  SD)

	Group C	Group T	Group F
Age (yrs)	45 $\pm$ 9.96	42 $\pm$ 14.8	38 $\pm$ 15.5
Weight (kg)	69 $\pm$ 10.8	74 $\pm$ 14.9	65 $\pm$ 15.4
Height (cm)	165 $\pm$ 7.1	167 $\pm$ 7.2	160 $\pm$ 13.9
Male/Female	14/6	12/8	12/8

Time to onset of motor block (time to onset of Grade 1 motor block in any nerve distribution) duration of motor block (time from onset to a motor block score of 0 for all activities), and the proportion of patients reaching each grade of motor block were measured. If the block was not complete, the surgeon infiltrated 1% lidocaine at the incision site. If the patients experienced pain, 0.5-1 mcg/kg of fentanyl was administered intravenously.

Patients who experienced anxiety were given midazolam 1-2 mg i.v. or a propofol i.v. infusion. Those patients who had already requested sedation for the time of surgery were administered a continuous i.v. infusion of propofol. If, in spite of an additional infiltration of lidocaine and i.v. fentanyl, the patient experienced pain, a general anaesthetic with propofol was to be administered and a laryngeal mask airway (LMA) employed. At the end of surgery the patients were told to note the time at which, in their opinion, the arm was fully recovered from the block. Blood pressure, heart rate (HR), peripheral oxygen saturation (SpO<sub>2</sub>) were measured at the same time points. Additional adverse effects (i.e. nausea and vomiting, pruritus) were also recorded throughout the study period. Patients'

**Table 3.** Adverse effects observed throughout the study

	Group C	Group T	Group F
Nausea/Vomiting	0	2/0	1/0
Pruritus	0	0	0
Tinnitus	0	0	0

conditions were checked by phone visits, or personally if the patient was still in hospital, at 8–11 a.m. by one of the investigators, blinded to which local anesthetic had been used. The next morning, all patients were interviewed again by telephone. The time to the first requirement for an analgesic (non-steroidal anti-inflammatory drug or paracetamol) was also recorded, as well as the time to the first analgesic. In addition, patient and surgeon were asked about their own personal degrees of satisfaction with the quality of the brachial plexus block for producing anesthesia and postoperative analgesia, and this was rated on a 2-point scale, 'satisfied' or 'dissatisfied'.

#### Statistical analyses

The Kolmogorov-Smirnov test was used for normality and homogeneity of data distribution. Parametric data (age, weight, height, onset and complete of sensory and motor blocks, postoperative first analgesic requirement times) were compared with one-way ANOVA. Post hoc comparisons were performed with Dunnett two-tailed t-test by using control as the reference control group. Discrete variables (sex, side effects) were compared by

**Table 2.** Block characteristics and quality of analgesia

	Group C	Group T	Group F	p value
<b>Time to onset</b>				
Partial sensory block (mins)	9 $\pm$ 4.45	5 $\pm$ 3.94*	7 $\pm$ 3.73	<0.001
Complete sensory block (mins)	18 $\pm$ 6.14	11 $\pm$ 5.47 <sup>a</sup>	15 $\pm$ 5.08	<0.001
<b>Time to onset</b>				
Partial motor block (mins)	11 $\pm$ 3.73	9 $\pm$ 6.6	10 $\pm$ 6.68	ns
Complete motor block (mins)	18 $\pm$ 3.37	18 $\pm$ 7.42	14 $\pm$ 8.2	ns
<b>Time to recover</b>				
Complete sensory block (hours)	4 $\pm$ 1.32	11 $\pm$ 5.67 <sup>#</sup>	8 $\pm$ 2.83	<0.001, < 0.05
Complete motor block (hours)	4 $\pm$ 1.14	10 $\pm$ 5.32	7 $\pm$ 2.57	ns
Postoperative first analgesic requirement time (hours)	5 $\pm$ 1.40	19 $\pm$ 6.34 <sup>§</sup>	9 $\pm$ 1.88 <sup>€</sup>	<0.001

\*Significance between Group T and Group C, <sup>a</sup>Significance between Group T and Group C,F, <sup>#</sup>Significance between Group T and Group C,F, <sup>€</sup>Significance between Group T and Group C,F, <sup>§</sup>Significance between Group F, and Group C, ns:non-significant

using ki-square-test. All data are presented as means (SD) or number. A p value <0.05 was considered as statistically significant. Calculation of number of patients is based on postoperative first analgesic requirement time. Power of study was used for power -Analysis programme The power of study was 99%  $\alpha$ :0.05.

## RESULTS

There was no difference between the groups in terms of age, weight, height and sex. (Table 1). Surgical procedures were similarly distributed among the three groups. Block characteristics are shown in Table 2.

### Onset of sensorial block

#### *Partial sensorial block onset time*

Partial sensorial block onset time in Group T was shorter than in Group C ( $p$ :0.01).

#### *Complete sensorial block*

Complete sensorial block onset time in Group T was shorter than in Group C and F ( $p$ =0.0006,  $p$ =0.03, respectively).

### Onset of motor block

There was no significant difference between the groups in terms of onset of partial and complete motor block, recovery of sensation, return of full motor block.

### Postoperative first analgesic requirement time

The postoperative first analgesic requirement time was significantly longer in Group T and F compared with Group C ( $p$ =0.0001,  $p$ :0.0001, respectively), and significantly longer in Group T compared with Group F ( $p$ =0.0001). In no case was propofol administration or general anesthesia required to complete surgery. Only two patients complained of pain (one patient in group C). The surgeon infiltrated 1% lidocaine at the incision site, iv fentanyl 1mcg/kg were given in this patients. Nausea was observed in two patients in group T and in one in group F (Table 3). These side effects were mainly of gastrointestinal origin. They were also transient and of short duration (maximum duration was 15 min in one patient in group F), and did not require any therapeutic intervention. Heart rate, non-invasive blood pressure, peripheral oxygen saturation exhibited no significant inter-group differences. No patients showed any signs of local anesthetic toxicity, inflammation of the punc-

ture site or nerve lesion. No episodes of hypotension, bradycardia or hypoxemia as defined previously were observed in any group throughout the study. Patient acceptance was good in all the patients studied, and no complications were observed at postoperative follow-up. The telephone follow-up interview conducted after discharge revealed neither persistent nor recurrent side effects, and no post-block neurological complications were observed among the three groups. One of the patients in control group was dissatisfied. In all cases, surgeon satisfaction was obtained and two patients were dissatisfied.

## DISCUSSION

This study showed that the addition of tramadol or fentanyl to local anesthetic mixtures as an adjuvant agent for axillary block provide better postoperative analgesia for orthopaedic upper extremity surgery. Furthermore tramadol more improves the block quality than fentanyl.

Due to their long term impact, local anesthetics are frequently used in axillary blockade (9,10). Levobupivacaine, an analogue of S(-) bupivacaine, is used as alternative local anesthetic in peripheral blockade due to its reduced toxic effects. The toxicity of levobupivacaine to the cardiovascular and central nervous system has been reported to be less than bupivacaine (11,12). Therefore levobupivacaine was preferred to use as the major local anesthetic in our study. Low dose lidocaine was used for the purpose of to accelerate sensorial onset time. In order to improve patient comfort, and particularly to maintain and prolong postoperative analgesia adjuvant agents (tramadol and fentanyl) were added to local anesthetics. Several studies have indicated that fentanyl and tramadol, a synthetic codeine analogue, increase the quality of peripheral blockade and improved the duration of postoperative analgesia (6,7).

Opioids are frequently used in regional anesthesia as an adjuvant agent. The introduction discovery of opioid receptors in the peripheral nervous system has led to research into opioid use as an adjuvant in peripheral blockade applications such as brachial plexus blockade. Gobeaux et al. added 100 mcg of fentanyl to adrenalinized lidocaine for brachial plexus block and reported that when fentanyl was added this enhance-

ment of intensity and duration of sensory and motor nerve blocks allowed a reduction in the amount of lidocaine required and shortened the delay between injection and complete blockade (6). They suggested that this result might be related to the peripheral effects of opioids. The lipid solubility of fentanyl is thought to have had a perineural effect. Our study also supports the idea that the addition of fentanyl to local anesthetic combinations improves postoperative analgesia quality. The postoperative first analgesic requirement time was significantly longer in Group T and F compared with Group C. In another study, Nishikawa et al. evaluated the effects of 100 mcg of fentanyl added to lidocaine for axillary brachial plexus block and achieved an improved and prolonged sensory blockade (13).

In contrast, Morros Viñoles et al. concluded that the addition of fentanyl 100 mcg to mepivacaine in the axillary blockade of the brachial plexus did not alter the anesthetic characteristics nor the time of postoperative analgesia (5). Fletcher et al. were similarly unable to demonstrate any clinical benefits resulting from the addition of fentanyl to local anesthetic for axillary brachial plexus block (14). Fanelli et al. added fentanyl 1 mcg/mL to ropivacaine 7.5 mg/mL and determined that this did not improve the nerve block characteristics of axillary brachial plexus anesthesia for orthopedic procedures involving the hand (15).

We similarly observed that the addition of fentanyl did not affect block characteristics but did extend initial analgesia requirement time. Different results can be obtained with the effect of perineural fentanyl on postoperative initial analgesia requirement duration. Fentanyl was used in this study 50 mcg because we want to examine the effect of opioids in minimal dosages. The goal of this study was to observe the addition of adjuvant to local anesthetic mixtures, not that of adjuvant to a single local anesthetic.

Tramadol exhibits both opioid and non-opioid activities. Recent clinical and laboratory studies have concluded that tramadol displays a peripheral local anesthetic effect (17,18). Tramadol has been used as an adjunct to peripheral plexus anesthesia in recent publications. The results of our study showed that the addition of 100 mg of tramadol to local anesthetic mixtures for axillary brachial plexus block improves the speed of block onset and increases the duration of sensory block.

Kapral et al. demonstrated that the addition of 100

mg of tramadol to mepivacaine 10 mg/mL for axillary brachial plexus block resulted in a significant increase in the duration of the block, whereas intravenous tramadol (100 mg) exhibited no effect. Consequently, the results of that study suggest that tramadol has a specific analgesic effect on peripheral nerves (7). In a study in which it was added to 20 mL of ropivacaine 7.5 mg/mL, conducted by Antonucci, tramadol was shown to significantly reduce the onset time of brachial plexus block and to prolong the duration of anesthesia and postoperative analgesia (18). In our study, and similarly to that of Antonucci, we added 100 mg of tramadol to levobupivacaine and lidocaine and observed a longer analgesia duration.

Kaabachi et al. investigated the addition of varying doses of tramadol to lidocaine 1.5% (epinephrine 1/200.000) solution and reported that the benefit of block prolongation associated with the addition of 200 mg of tramadol to lidocaine during axillary block was limited by the slow onset of the block (19). In our study, we found that the addition of 100 mg of tramadol to a local anesthetic mixture significantly shortened complete sensorial block onset duration compared with both the fentanyl and control groups and that it maintained prolonged postoperative analgesia. Similarly, Robaux et al. added different doses of tramadol to mepivacaine 15 mg/mL for axillary brachial plexus block and reported that tramadol extended the duration and improved the quality of post-operative analgesia in a dose-dependent fashion (8).

In contrast, Kesimci et al. reported that the addition of 100 mg of tramadol to 7.5 mg/mL of ropivacaine, for axillary brachial plexus block, does not prolong the duration of motor and sensory block and analgesia (20). The reason may be addition to single local analgesic. In our study we added tramadol to levobupivacaine and lidocaine mixture. Similarly, Sarsu et al. performed axillary blockade by adding 100 mg of tramadol to combination levobupivacaine and lidocaine. They reported that tramadol was not effective on sensorial and motor block durations, onset time, and analgesia duration (21). The reason for this may be the higher dosage of lidocaine (200 mg) than we've used in our study (40 mg). It seems that there are many factors affecting the characteristics of block in axillary application. Different results related to adjuvant agents appear in the literature. This may be due to the use of local anesthetics, experience of the practitioner etc.



In conclusion, the addition of tramadol or fentanyl to local anesthetic mixtures as an adjuvant agent for axillary block provide better postoperative analgesia for orthopedic upper extremity surgery. On the other hand tramadol addition is seemed superior than fentanyl ad-dition. Of course, in order to support this statement further studies must perform related this topic.

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