



## Original Research

# Prolonged Analgesic Efficacy of Articaine with the Addition of Tramadol in Axillary Brachial Plexus Block

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### Abstract

**Objectives:** Articaine is a rapid-onset, short-duration, local anesthetic. The aim of this study was to study the effect of adding tramadol to articaine in an axillary block to prolong the analgesic effect.

**Methods:** This study was conducted with 60 patients of American Association of Anesthesiologists classification I or II and aged 18 to 60 years who underwent hand or forearm surgery with an axillary plexus block using a nerve stimulation technique. The patients were randomized into 2 groups: Group A (n=30) received 40 mL 1% articaine and Group AT (n=30) was administered 40 mL 1% articaine with 100 mg tramadol. The onset of sensory block, motor block, duration of sensorial block and motor block, duration of analgesia and hemodynamic parameters were recorded before the block and 5, 10, 20, 30, 60, 120, 180 minutes after the local anesthetic injection.

**Results:** The sensory block duration in Group AT (187.5±13.0 min) was significantly longer than that of group A (140.78±8.74 min) ( $p<0.02$ ). The motor block duration in Group AT (137.4±3 min) was significantly longer than that seen in Group A (93.71±9.6 min) ( $p<0.01$ ). The duration of analgesia was longer in Group AT (218.8±18.2 min) than in Group A (170.8±17.2 min) ( $p<0.05$ ). In group AT, 2 patients experienced the side effect of nausea and 1 patient had hypotension in the postoperative period.

**Conclusion:** This study demonstrated that the addition of 100 mg of tramadol to articaine used for an axillary plexus block prolonged analgesia.

**Keywords:** Articaine; axillary nerve block; Tramadol.

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Brachial plexus block is a recommended and reliable technique for upper limb surgeries and helps to avoid general anesthesia. An ideal drug should have a quick sensory onset, release the motor block before the sensory block, and provide prolonged analgesia.<sup>[1,2]</sup>

A number of short-acting local anesthetic drugs have been found to be useful for brachial plexus block, such as lidocaine, prilocaine, and articaine.<sup>[3-5]</sup> Articaine is a rapid-on-

set, short-acting, local anesthetic.<sup>[6]</sup> Articaine is less cardiotoxic and neurotoxic than lidocaine or bupivacaine.<sup>[7]</sup>

Adjuncts, such as opioids, clonidine, tramadol, and dexmedetomidine, are commonly used with local anesthetics for peripheral plexus blockade to enhance the quality and duration of anesthesia and postoperative analgesia.<sup>[8-11]</sup> Tramadol is a synthetic 4-phenyl-piperidine analogue of codeine. It is active at central and peripheral m-opioid

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and monoaminergic receptors. Tramadol also exhibits local anesthetic properties.<sup>[12, 13]</sup> Fewer side effects have been reported with tramadol than clonidine and sufentanil.<sup>[14]</sup> There is no clinical trial that has evaluated the influence of the addition of tramadol to articaine in an axillary brachial plexus block.

The aim of the present study was to investigate the addition of tramadol to articaine to determine if it increased the duration of sensory and motor blocks or prolonged analgesia during a brachial plexus block.

## Methods

This study was carried out between June 2004 and August 2004 in accordance with the principles of the Declaration of Helsinki and after receiving approval from the ethics committee of Sisli Hamidiye Etfal Education and Research Hospital 06.12.2004/32. In this prospective, randomized, double-blind study, 60 patients scheduled for forearm and hand surgery under axillary brachial plexus block were studied. The inclusion criteria were: age between 18 and 65 years and American Society of Anesthesiologists (ASA) status I-III. Exclusion criteria were: chronic medication with tramadol, pregnant women, and patients with a history of cardiac, respiratory, hepatic, or renal failure, as well as those with peripheral neuropathy or hypersensitivity to local anesthetic agents.

Standard monitoring was established in the operating room (OR) with peripheral oxygen saturation, respiratory rate, electrocardiography, and noninvasive measurement of arterial blood pressure. A 20-G cannula was placed in a peripheral vein in the contralateral arm and oxygen was delivered via a face mask at a rate of 2 L/minute. Every patient was premedicated with an intravenous (iv) dose of midazolam (0.02 mg/kg-1) (Dormicum; F. Hoffmann-La Roche AG, Basel, Switzerland) in the OR. The patients were monitored and the results were recorded every 5 minutes until end of the surgery.

Patients were separated into 2 equal groups based on a computer-generated list of random numbers that were placed in opaque sealed envelopes.

From the list of random numbers, instructions for randomization were prepared in sealed envelopes for each patient before the start of the study. The drug solutions were prepared by an anesthesiologist not involved in the study. The patients were allocated to 1 of 2 groups to receive an axillary block. Group A patients (n=30) received 40 mL of group (Ultracaine; Sanofi Aventis, Paris, France) 10 mg.mL<sup>-1</sup> mixed with 2 mL of isotonic sodium chloride solution, and the AT group (n=30) received articaine+tramadol (Contra-

key) 40 mL of articaine 10 mg.mL<sup>-1</sup> mixed with 2 mL (100 mg) of tramadol.

The patient was in a supine position. The operated arm was abducted at a 90° angle and externally rotated. An axillary block was performed in aseptic conditions by a single experienced anesthesiologist who was unaware of the injected solutions. A 24-G, 50-mm, insulated, short-bevel needle and a nerve stimulator (Stimuplex HNS 11; B. Braun Melsungen AG, Melsungen, Germany) was used for nerve localization. The stimulation frequency was set at 2 Hz, and the duration of stimulation was set at 0.3 milliseconds. The intensity of the stimulating current, initially set to deliver 1 mA, was gradually decreased to <0.5 mA after the appropriate motor response was observed with intermittent aspiration, and the total volume was subsequently injected into the perivascular area.

Sensory block (of all nerves) was assessed by pinprick test using a 3-point scale: 0=no block, 1=analgesia (loss of sensation of pinprick), and 2=anesthesia (loss of sensation of touch). Motor block was evaluated by asking the subject to flex and extend their wrist and fingers. A 4-point scale was used for assessment: 0=no motion, 1=only elbow motion, 2=reduced motion of fingers and wrist, and 3=total motion of fingers and wrist. The block was evaluated and recorded every 5 minutes (following local anesthetic injection) up to 30 minutes and hourly after the surgery for a period of 24 hours by the anesthesiologist who performed the block.

The onset time of the sensory block was defined as the time between the completion of the local anesthetic injection and the loss of pinprick sensation; the onset time of the motor block was defined as the time between the completion of the local anesthetic injection and achieving complete motor block. The duration of the sensory block was defined as the time interval between the completion of the local anesthetic administration and the complete resolution of anesthesia in all nerves. The duration of the motor block was defined as the time interval between completion of the local anesthetic administration and recovery of complete motor function of the hand and the forearm. The time between the finalization of the local anesthetic administration and the first analgesic request was recorded as the duration of analgesia. A neurological assessment was recorded at 1, 2, 3, 6, 12, and 24 hours postoperatively by a blinded anesthesiologist. If anesthesia was insufficient after 30 minutes and 1 or more distal nerve blocks was performed, the patient was excluded from the research and replaced in the randomization list.

The presence of side effects (nausea/vomiting, hypotension, bradycardia, sedation) and antiemetic administration in the immediate 24-hour period) were recorded. Hypoten-

sion, bradycardia, and sedation were defined and managed using the criteria of a decrease of more than 25% in mean systemic arterial blood pressure compared with baseline values, increments of ephedrine 3 mg iv every 2 minutes, heart rate <45 bpm, a 0.5 mg iv bolus of atropine, and blood oxygen saturation <90% using an oxygen flow of 6 L/minute. Heart rate (HR), and mean arterial blood pressure (MAP) were recorded before the axillary block and 5, 10, 20, 30, 60, and 120 minutes peroperatively and at 1, 2, 3, 6, and 24 hours postoperatively. Postoperative rescue analgesia in the form of nonsteroidal anti-inflammatory drugs (injection diclofenac sodium 75 mg) was provided when the patient indicated a pain score of VAS >4.

A minimum sample size of 28 patients was determined based on a preliminary study that examined the statistical significance of the changes in the duration of analgesia. The duration of analgesia was ensured at a level of A error of 0.05 and a B error of 0.8. A total of 60 patients were

selected for the study and written informed consent was obtained from each patient.

The statistical analysis was performed with SPSS for Windows, Version 16.0 (SPSS Inc., Chicago, IL, USA). All of the data were assessed for normal distribution using the Kolmogorov-Smirnov test and a histogram. The patient demographic data and the onset and duration of blocks were compared using the Mann-Whitney U-test or Student's ttest, as appropriate. Categorical data were analyzed using a chi-square test or Fisher's exact test. The data were presented as mean±SD. Statistical significance was considered to be a p value of <0.05.

## Results

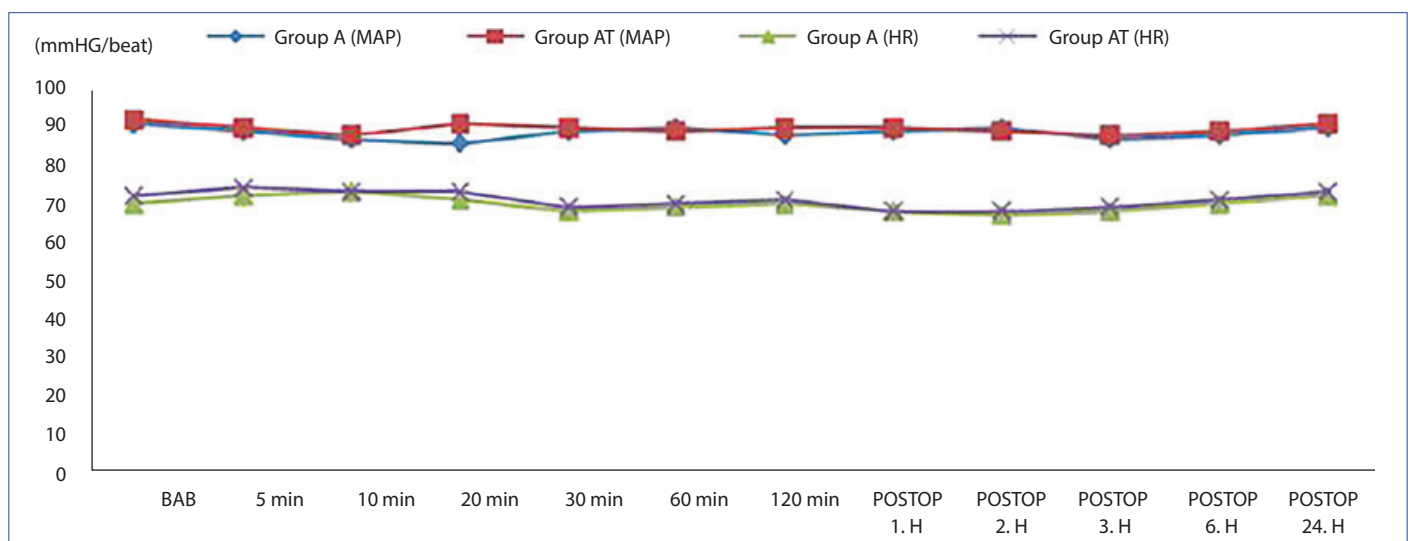
Sixty patients were enrolled in the study; two patients in Group A were later excluded. There were no significant differences in the demographic data or surgical characteristics between the 2 groups ( $p>0.05$ ) (Table 1). The he-

**Table 1.** Demographic data and surgical characteristics

	American Society of Anesthesiologists (n=28)	Group AT (n=30)	p
Age (years)	32.8±10.7	31.1±9.9	$p>0.05$
Weight (kg)	63.3±5.3	66.2±7.1	$p>0.05$
Height (cm)	169.1±3.7	169.2±3.5	$p>0.05$
ASA I/II	18/10	24/6	$p>0.05$
Gender (Female/male)	8/20	7/23	$p>0.05$
Duration of surgery (min)	91.0±13.4	89.5±13.2	$p>0.05$
Duration of tourniquet time (min)	78.2±12.96	76±12.46	$p>0.05$

Data are expressed as mean±SD.

A: Articaine; ASA: American Society of Anesthesiologists; AT: Articaine and tramadol.



**Figure 1.** Heart rate and mean arterial pressure changes.

A: Articaine; AT: Articaine and tramadol; BAB: Before axillary block; HR: Heart rate; MAP: Mean arterial pressure.

**Table 2.** Block characteristics

	Group A (n=28)	Group AT (n=30)	p
Onset time of sensory block (min)	10.89±3.2	12±2.8	p>0.05
Onset time of motor block (min)	17.2±3.9	18.3±4.0	p>0.05
Duration of sensory block (min)	140.78±8.74	187.5±13.0	p<0.02
Duration of motor block (min)	93.71±9.6	137.4±3	p<0.01
Duration of analgesia (min)	170.8±17.2	218.8±18.2	p<0.05

Data are expressed as mean±SD.

A: Articaïne; AT: Articaïne and tramadol.

**Table 3.** Side effects

	Group A (n=28) (%)	Group AT (n=30) (%)	p
Nausea	0 (0)	2 (6.6)	p>0.05
Hypotension	0 (0)	1 (3.3)	p>0.05
Bradycardia	0 (0)	0	p>0.05

Data are expressed as a number.

A: Articaïne; AT: Articaïne and tramadol.

mo-dynamic parameters (MAP and HR) were similar in both groups (p>0.05) (Fig. 1).

The sensory and motor block onset time was similar between groups; no significant differences were revealed (p>0.05) (Table 2). The sensory block duration in group AT (187.5±13.0 minutes) was significantly longer than that of Group A (140.78±8.74 minutes) (p<0.02) (Table 2). The motor block duration in group AT (137.4±3 minutes) was significantly longer than that observed in Group A (93.71±9.6 minutes) (p<0.01) (Table 2). The duration of analgesia was longer in Group AT (218.8±18.2 minutes) than in Group A (170.8±17.2 minutes) (p<0.05) (Table 2).

Hypotension and nausea were more frequently recorded in Group AT. We found no significant difference in the side effects experienced in the groups (p>0.05) (Table 3).

## Discussion

Our study demonstrated that a mixture of 100 mg tramadol and articaïne 1% injected perineurally for axillary brachial plexus block prolonged the duration of sensory and motor block.

Articaïne is commonly used for dental anesthesia and outpatient surgery due to the rapid onset of anesthesia and the short duration of the motor block.<sup>[15]</sup> It has a similar analgesic efficacy to lidocaine.<sup>[16]</sup> It has a lower central nervous system toxicity and a rapid hydrolysis of the ester group in tissues, with a lower allergic potential than lidocaine.<sup>[17]</sup>

Simon et al.<sup>[16]</sup> demonstrated that lidocaine and articaïne had a similar anesthetic effect in an axillary block. They found that the mean onset time of sensory block of the median nerve with both lidocaine and articaïne was approximately 10 min. In another study, 2% articaïne and 2% articaïne with 100 µg fentanyl were compared in an ultrasound-guided axillary block. The authors reported that adding fentanyl to articaïne prolonged the sensorial block duration and first analgesic requirement time.<sup>[5]</sup> Hyperbaric articaïne 80 mg has demonstrated a shorter recovery in spinal anaesthesia during lower limb surgery when compared with plain bupivacaine 15 mg.<sup>[15]</sup> Yurtlu et al.<sup>[18]</sup> implied that a combination of 2% articaïne and 0.75% ropivacaine was superior to 0.75% ropivacaine alone in epidural anesthesia during a cesarean section. We used articaïne as a local anesthetic for a brachial plexus block due to the faster onset of action, rapid recovery from the sensory and motor effects, and faster penetration through bone and soft tissue than other local anesthetics. An axillary block using a large volume of local anesthetic may lead to local anesthetic toxicity. Articaïne has a shorter elimination time, a lower peak plasma concentration, and minimal effect on cardiovascular parameters. These qualities make articaïne a better choice for an axillary brachial plexus block. The maximum dose of articaïne for an adult patient is 500 mg (6.6-7 mg/kg-1), which is the same as the maximum lidocaine dose.<sup>[19]</sup> We used 400 mg articaïne at our study. Our findings were similar with literature: We found an onset time of sensory block and motor block of 10.89±3.2 and 17.2±3.9 minutes, respectively, a duration of sensory block of 140.78±8.74 minutes, and a duration of analgesia of 170.8±17.2 minutes in the articaïne group.

The results of some recent studies have indicated that adding 100 mg tramadol to mepivacaine in an axillary brachial plexus block prolongs sensory and motor block duration.<sup>[20, 21]</sup> Kaabachi et al.<sup>[10]</sup> compared the effect of adding 100 mg and 200 mg tramadol to lidocaine in an axillary brachial plexus block. The duration of the sensory block was greater in both tramadol groups. The benefit of block prolongation associated with the addition of 200 mg tra-

madol to lidocaine during axillary block is limited by the slow onset of the block. In a supraclavicular brachial plexus block, 100 mg tramadol with bupivacaine was evaluated to have reduced the onset time of motor and sensory block and enhanced the duration of sensory block, motor block, and postoperative analgesia.<sup>[22, 23]</sup> Tramadol has also been used as an adjunct with ropivacaine and levobupivacaine in a brachial plexus block. The study results demonstrated that tramadol significantly reduced the onset time of the brachial plexus block and prolonged the duration of anesthesia and postoperative analgesia.<sup>[14, 24, 25]</sup> Two additional studies examined the addition of tramadol to ropivacaine and levobupivacaine for axillary brachial plexus block but no beneficial effects were found.<sup>[26, 27]</sup> Tramadol has been used as an adjunct to peripheral plexus anesthesia in recent publications and adding tramadol to a local anesthetic prolonged motor and sensorial block duration as well as the duration of analgesia. We elected to add tramadol as an adjunct to a local anesthetic for a peripheral plexus blockade; it offers long-lasting analgesia with less of a respiratory depressant effect. Our study results were similar to those of the literature: adding tramadol for an axillary plexus block prolonged sensory and motor block duration, as well as the first analgesia requirement.

Few studies have reported adverse effects when tramadol was added to a local anesthetic as an adjuvant in a brachial plexus block. Robaux et al.<sup>[21]</sup> reported that nausea/vomiting and drowsiness were seen more frequently in all tramadol groups. Kirksey et al.<sup>[28]</sup> concluded that tramadol increased postoperative nausea and vomiting when added to a peripheral nerve block. In our study, 2 patients experienced nausea and 1 patient had hypotension, but there were no significant statistical differences between the 2 groups. The patients who experienced nausea were treated with a rescue antiemetic on time and fluid was administered to the patient with hypotension. Our findings were similar to those currently in the literature.

## Conclusion

The addition of tramadol to articaine increased the duration of sensory and motor blocks and prolonged analgesia during a brachial plexus block.

## Disclosures

**Ethics Committee Approval:** Ethics committee of Sisli Hamidiye Etfal Education and Research Hospital 06.12.2004/32.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** There are no conflicts of interests among the authors.

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**Authorship Contributions:** Concept – L.K.; Design – L.K., S.Ç.; Supervision – S.Ç.; Materials – L.K., S.Ç., H.Ş.T.; Data collection &/ or processing – L.K., H.Ş.T.; Analysis and/or interpretation – L.K., S.Ç., H.Ş.T.; Literature search – L.K., S.Ç., H.Ş.T.; Writing – L.K., H.Ş.T.; Critical review – L.K., S.Ç.

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