İstanbul Med J 2023; 24(1): 83-7
DOI: 10.4274/imj.galenos.2023.37531

A Randomized, Prospective Evaluation the Effect of Oral Pregabalin in Forearm Surgery with Infraclavicular Nerve Block

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ABSTRACT

Introduction: The infraclavicular block method has been increasingly used in hand, wrist, and forearm surgery in anesthesia practice. Although the infraclavicular block method provides appropriate postoperative analgesic effect, patients still suffer from postoperative pain at high rates. Opioids are widely used for postoperative analgesia. There are many studies showings that taking oral pregabalin before the operation reduces postoperative pain and opioid use. In this study, we investigated the effect of preoperative use of 150 mg oral pregabalin on infraclavicular sensory block duration and opioid use.

Methods: Ethics committee approval and patient consents were obtained for the study. The study included 60 patients between the ages of 18 and 65 who would undergo an American Society of Anesthesiologists I-II hand, wrist or forearm surgery. The control group (group K) did not take medication before the operation. The pregabalin group (group P) took 150 mg of oral pregabalin an hour before the operation. Ultrasound-guided infraclavicular block was applied to both groups. Patients were observed for 24 hours per operatively and postoperatively in terms of analgesic medication needs and complications.

Results: Postoperative analgesic use was observed to be higher in group K ($p<0.05$). There was no significant difference in sensory block and motor block initial durations in group K and group P ($p>0.05$). However, the sensory block completion time was statistically significantly longer in group P than in group K ($p<0.05$). There was no statistically significant difference between the motor block ending times of both study groups in terms of side effects ($p>0.05$).

Conclusion: In this study, we concluded that a single dose of 150 mg oral pregabalin treatment applied before the operation prolongs the infraclavicular sensory block duration and reduces the need for analgesic drugs in the first 24 hours postoperatively.

Keywords: Infraclavicular block, pregalabalin, postoperative analgesia

Introduction

Recently, peripheral nerve blocks have been frequently used in anesthesia practice. Infraclavicular block practice is actually a type of brachial plexus block that is used safely and effectively in both anesthesia and postoperative analgesia management in hand, wrist, and forearm surgeries (1). The World Health Organization classifies the relief of pain as a human right (2). Successful pain management ensures early patient ambulation and shortens the duration of hospital stay. It is also a quality indicator (1).

Despite significant advances in analgesia techniques, surgical procedures still cause moderate to severe postoperative pain in 50-70% of patients (3). Postoperative pain includes both inflammatory and neuropathic components (3). Pregabalin is an anticonvulsant agent that is widely used as an analgesic with membrane-stabilizing and antinociceptive effects for neuropathic pain. It is rapidly absorbed through the intestine and reaches its highest plasma concentration with 90% bioavailability after about an hour (4). Pregabalin is an anti-epileptic, analgesic, and anxiolytic agent. It binds to the α-2-δ subunit of voltage-gated calcium channels. Reduces the release of various excitatory neurotransmitters such as glutamate and prevents the development of hyperalgia (5). In doing so, it inhibits central sensitization and progression of pain (6). In this way, it can be used for perioperative and postoperative analgesia. Opioids are also frequently used in postoperative pain management despite numerous side effects (7). Use of Pregabalin has been found to reduce postoperative opioid consumption and opioid side effects in many surgical operations (3). The increase in opioid consumption led to increasing side effects and complications resulting from opioids.

We investigated the effect of preoperative use of 150 mg oral pregabalin on infraclavicular sensory block duration and opioid use (8). The hypothesis of this randomized controlled trial is that a single dose of 150 mg oral pregabalin will prolong the duration of infraclavicular sensory

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Cite this article as: Deligöz Ö. A Randomized, Prospective Evaluation the Effect of Oral Pregabalin in Forearm Surgery with Infraclavicular Nerve Block. İstanbul Med J 2023; 24(1): 83-7.

Received: 26.12.2022
Accepted: 30.01.2023

blockade, reduce the need for peroperative and postoperative opioids, and mitigate the side effects that may develop due to opioid use.

Methods

The Recep Tayyip Erdoğan Training and Research Hospital Ethics Committee approval was obtained for this study (approval number: 137, date: 07.08.2019). All patients were evaluated and then were explained the procedure preoperatively. Oral and written consent were obtained from the patients. Sixty patients between the ages of 18 and 65 who were planned to undergo the hand, wrist, elbow, and forearm bone surgeries within the scope of American Society of Anesthesiologists (ASA) I and II were included in the study. Patients with hypersensitivity to the drugs to be used in the study or the substances in their composition, patients with severe cardiac, hepatic, renal disorders, patients who did not want to participate, and who did not allow infraclavicular blocking were excluded from the study. Patients were randomized in a computer environment and divided into two groups. The group that was not administered any medication before the operation was named the control group (group K), and the group that was orally administered 150 mg pregabalin 1 h before the operation was named the pregabalin group (group P). The study was planned as a prospective and double-blind study. Preoperative randomization was done by a computer. Postoperative follow-ups were performed by different physicians. Age, gender, body mass index (BMI), type of surgery, and duration of surgery were recorded in all patients. In the first 24 postoperative h, motor block and sensory block return times and analgesic needs of the patients were recorded. Again, possible side effectsand complications within 24 h peroperatively and postoperatively were noted.

An hour before the operation, the patients were taken to the preoperative room of the operating theater. Group P was administered 150 mg of oral pregabalin with a small amount of water. Patients underwent standard monitoring with electrocardiogram, peripheral oxygen saturation, and noninvasive arterial pressure. The vascular route was opened with 18/20 G cannula and 500 mL 0.9% isotonic solution was inserted. The necessary space cleaning was performed using 10% povidone-iodine in the supine position. Then, the axillary artery and brachial plexus cords were imaged in both groups under ultrasound guidance using a linear probe (Philips-Sparq device, high-speed 5.2 mHz). Following up, ultrasonography (USG)-guided peripheral block needle (Stimuplex ultra360, 22G*80mm) was used to perform infraclavicular blocking. 30 mL of local anesthetics, which consisted of 15 mL 0.5% bupivacaine and 15 mL 2% Lidocaine, were administered in a way to spread in a U-shaped manner to the posterior, lateral, and medial cords of the brachial plexus observed around the axillary artery. Modified Bromage Motor Scale (4. normal muscle strength, 3. muscle strength decreased but overcomes resistance, 2. muscle strength unable to overcome resistance but gravity, 1. tremor style muscle strength, 0. no muscle strength) was used for motor block. The initial motor block duration was determined as the duration between the time of local anesthetic administration and the time of scale 1. A pin - Prick test (0-no sensory block, 1-tactile sensation without pain, 2-no tactile sensation and pain) was used for sensory block. The onset duration of sensory block was determined between the time of local anesthetic administration and the time of Pin - Prick test 1. Motor and sensory block onset time was recorded.

In the peroperative period, it was planned to administer fentanyl (50 µgr + 50 µgr) IV in case the patient felt pain. The time of fentanyl administration and the total amount administered were recorded. Patients who still felt pain after 100 h of fentanyl administration were treated with deep sedo-analgesia and were excluded from the study.

Postoperatively, patients were followed up in the orthopedics and traumatology service for the first 24 h. The full return of muscle strength was the return of the motor block. The onset of pain was also considered to be the time of sensory block recovery. Both time were recorded. Numerical rating scale (NRS) number 11 (0=no pain, 10=very severe unbearable pain) was used as a pain scale. It was planned to administer paracetamol 500 mg orally up to NRS 3 in case the patient-required analgesics. Administration of tramadol HCL 1-2 mg/kg i.v. was planned in case of insufficient paracetamol or NRS above 4.

Statistical Analysis

Statistical analyses were performed using the NCSS 2007 Statistical Software (Utah, USA) package software. In addition to descriptive statistical methods (mean, standard deviation) in the evaluation of the data, the distribution of the variables was examined using the Shapiro-Wilk normality test, an independent t-test was used in the comparison of the binary groups of the variables with normal distribution, chi-square and Fisher reality test were used in the comparisons of qualitative data. $P<0.05$ was considered significant.

Results

Seventy-eight patients were enrolled in the study. Sixty eligible patients were analyzed. All details about the inclusion of patients in the study are presented in the CONSORT flowchart (Figure 1).

There was no statistically significant difference between the two groups in the demographic data of the patients such as age, gender, BMI, ASA, duration of surgery, and type of surgery (Table 1).

There were no statistical differences in the time and dose of fentanyl use during the operation in both study groups. Likewise, the time of the first postoperative analgesic use and the dose of paracetamol and tramadol were not found to be significant (Table 2). However, postoperative analgesic use was higher in the control group ($p=0.01$) (Table 2, Figure 2).

In the control group and pregabalin group, the onset durations of sensory block ($p=0.641$) and motor block ($p=0.570$) were not significant (Table 3). Sensory block ending the duration of the pregabalin group ($p=0.0001$) (1098±470.87 min) was statistically significantly shorter than in the control group (606.67±399.19 min) (Table 3, Figure 3). There were no statistical differences between the motor block -ending durations of both study groups ($p=0.231$) (Table 3, Figure 3).

There were no statistical differences between the two groups in terms of complications and side effects during the process of performing block procedures in the peroperative and postoperative periods (Table 4).

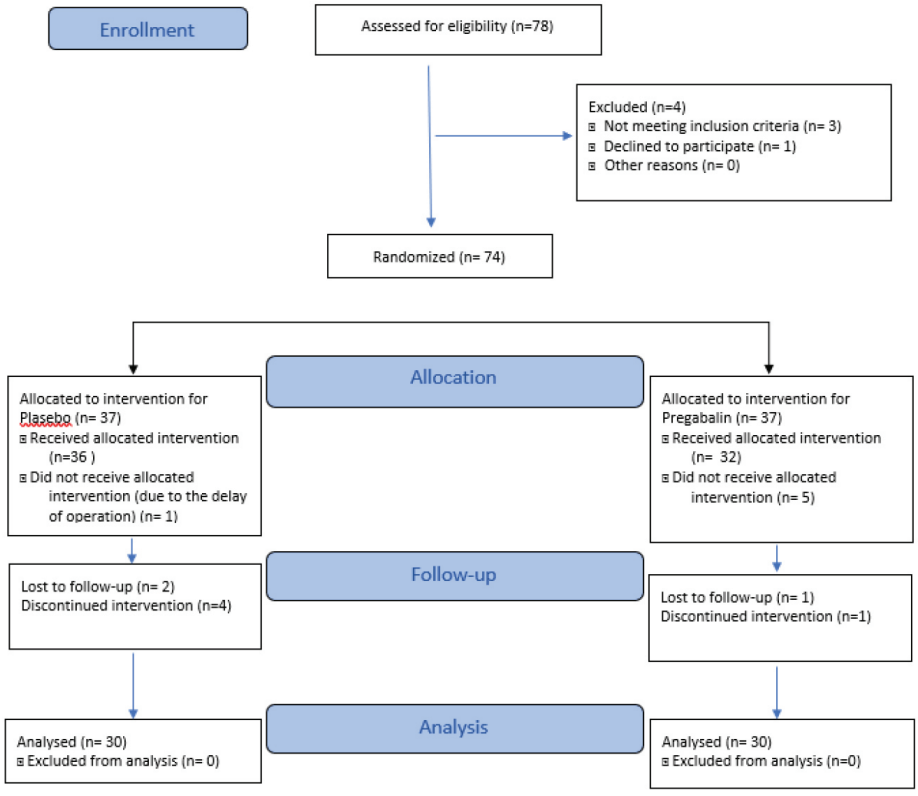

Figure 1. CONSORT 2010 flow diagram

Table 1. Demographic and clinical characteristics in the study groups

		Control group		Pregabalin group		p
Age (years)		43.93±16.62		49.83±15.89		0.165*
Gender	Male	20	(66.67%)	19	(63.33%)	0.787+
	Female	10	(33.33%)	11	(36.67%)	
BMI		23.3±2.63		24.65±3.74		0.110*
ASA Class	Class I	8	(26.67%)	3	(10.00%)	0.095+
	Class II	22	(73.33%)	27	(90.00%)	
Surgery duration (min)		94.53±36.7		109.67±33.81		0.102*
Type of surgery	Wrist	2	(6.67%)	0	(0.00%)	0.117+
	Hand	2	(6.67%)	0	(0.00%)	
	Forearm	26	(86.67%)	30	(100.00%)	

*Independent t-test, +chi-square test, BMI: Body mass index, ASA: American Society of Anesthesiologists

Table 2. Per operative and postoperative analgesic use in the study groups

	Control group		Pregabalin group		p
First fentanyl time (min)	71±29.24		71±31.9		1*
Second fentanyl time (min)	40±		85±63.64		0.667*
Per operative fentanyl dose (µg)	60±22.36		70±27.39		0.545*
Presence of analgesic use	19	(63.33%)	9	(30.00%)	**0.01**+
The first analgesic use time (min)	585±254.42		553.89±256.22		0.765*
Total dose of paracetamol (mg)	791.67±334.8		583.33±204.12		0.184*
Total dose of contramal (mg)	68.75±37.2		75±28.87		0.776*

*Independent t-test, +chi-square test

Discussions

Peripheral nerve blocks are widely used in anesthesia applications. Especially with the introduction of ultrasonography, the success of blockade has increased, and complications have decreased significantly (9). Pain is a complex structure formed because of transmissions to the central and peripheral nervous systems (1). Local anesthetics infiltrate around the nerves and block pain transmission to the brain for several hours. For this reason, peripheral nerve block duration may be insufficient for the postoperative period and postoperative pain management remains an important problem (1).

We aimed to determine the effect of premedication of pregabalin on the sensory and motor block time of infraclavicular block and on analgesic needs. In the results of our study, oral pregabalin prolonged sensory block duration and did not affect motor block duration. There was no difference in the peroperative and postoperative opioid requirements in the pregabalin and non-pregabalin groups. However, more analgesics were used in the control group in the postoperative 24-h period.

In previous studies, oral pregabalin had been administered in the dose range of 75-600 mg, sometimes as a single dose and sometimes with added doses 1-2 h before surgery. Postoperative 12th and 24th h were compared with the placebo group. A 150 mg dose of pregabalin was observed to provide adequate postoperative analgesia and opioid-protective effect (8-10). In addition, high doses of pregabalin have more side effects (3). We used 150 mg oral pregabalin, as recommended in the literature (8-10). We also administered pregabalin to patients preoperatively, 1 h before surgery, to reach the maximum plasma concentration (30 min - 2 h) during surgical stimulation (10).

A objective of preoperative pregabalin use is to increase the duration of sensory block. They reported that preoperative 150 mg oral pregabalin contributed to postoperative sensory and motor block (11). Cegin et al. (9) reported that 150 mg and 300 mg oral pregabalin increased the motor block onset duration and sensory block ending duration before administering infraclavicular block and that there was no difference between these two doses (9). Omara et al. (11) reported that

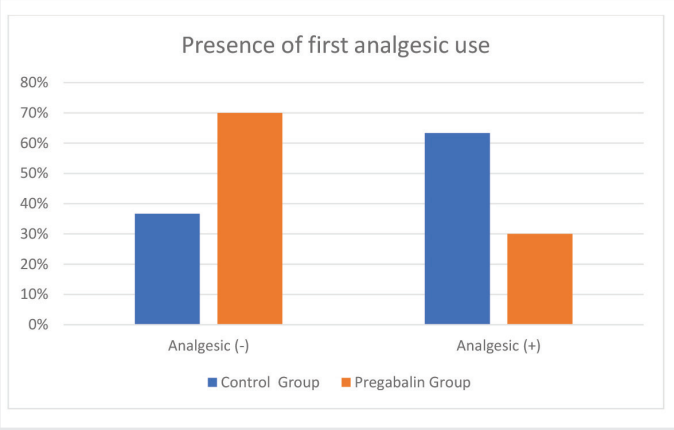

Figure 2. Presence of postoperatif analgesic use

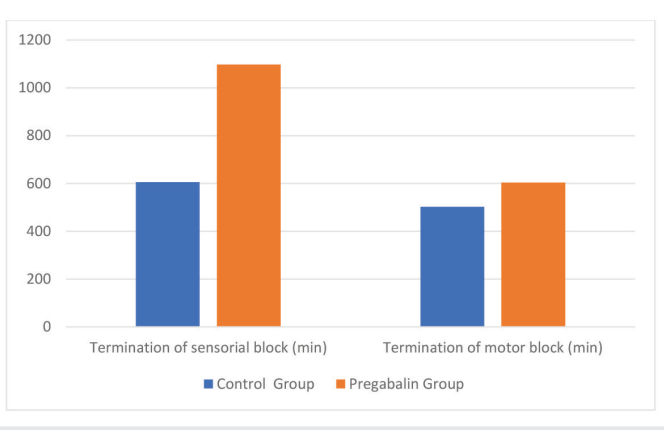

Figure 3. Termination of sensorial and motor blocks in the study groups

Table 3. Comprasion of sensorial and motor block initiation and termination durations in the study groups

	Control group	Pregabalin group	p
Initiation of the sensorial block (min)	3.1±3.21	2.77±2.21	0.641*
Initiation of motor block (min)	13.9±9.67	15.33±9.76	0.570*
Termination of the sensorial block (min)	606.67±399.19	1098±470.87	**0.0001***
Termination of motor block (min)	502±256.28	604.5±386.24	0.231*

*Independent t-test

Table 4. Side effects recorded in the study groups

		Control group		Pregabalin group		p
Block complications		3	10.00%	2	6.67%	0.640+
Peroperative complications		0	0.00%	0	0.00%	-
Postoperative complications	Nausea	7	23.33%	3	10.00%	0.166+
	Vomiting	5	16.67%	5	16.67%	1+
	Pruritus	5	16.67%	1	3.33%	0.085+
	Dizziness	5	16.67%	3	10.00%	0.448+
	Others	1	3.33%	1	3.33%	1

*Independent t-test, +chi-square test

administration of 150 mg oral pregabalin 1 h before spinal anesthesia in patients undergoing orthopedic surgery prolonged the durations of sensory and motor blocks. They reported that this contributed to sleep quality on the first postoperative night (11). Panse et al. (10) found that there was no difference in the onset durations of motor and sensory blocks in patients who underwent spinal anesthesia, as in our study, but the duration of sensory motor block was prolonged. Unlike our study, they also reported that the duration of motor block was prolonged (10). In our study, we found that the duration of sensory block was prolonged, and motor block was not added to this prolongation. Kushwaha et al. (12) also found that in brachial plexus block with oral pregabalin, the duration of sensorial block prolonged and the duration of motor block was not affected, as we did. We believe that a prolonged duration of postoperative sensory block and a non-prolonged duration of motor block will increase the postoperative satisfaction of patients.

The side effects of pregabalin are dose-dependent and usually transient (13). Similar to other studies, nausea, vomiting, pruritus and dizziness were the most frequently observed effects in our study (13,14). However, there is no difference in side effects between the groups (13-15). There was no difference between the peroperative and postoperative complications and side effects of both groups. The onset durations of motor and sensory block were similar in both groups.

Study Limitations

Our study is subject to certain limitations. First, although 150 mg oral pregabalin was shown to be sufficient preoperatively in previous studies, using only 1 dose (150 mg) of pregabalin and not comparing it with other doses was a limitation. Second, the preoperative anxiety scores and pain level of the patients were not analyzed. Pregabalin may affect the preoperative pain and anxiety scores.

Conclusion

In this study, we found that a preoperative single dose of 150 mg oral pregabalin prolonged the duration of sensory block without affecting the duration of motor block and reduced the need for analgesic use in the first 24 h postoperatively in patients undergoing the hand, wrist, elbow, and forearm bone surgeries with infraclavicular block. We believe that further studies and experience are needed to support these results.

Ethics Committee Approval: The Recep Tayyip Erdoğan Training and Research Hospital Ethics Committee approval was obtained for this study (approval number: 137, date: 07.08.2019).

Informed Consent: Oral and written consent were obtained from the patients.

Peer-review: Externally and internally peer-reviewed.

Financial Disclosure: The author declared that this study received no financial support.

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