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Is Pregabalin Addition to Infraclavicular Block, Effective in Distal Radius Surgery?

İnfraklaviküler Bloğa İlave Edilen Pregabalin Distal Radius Cerrahisinde Etkili midir?

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ABSTRACT

Objective: Our study evaluated the effects of pregabalin (PR) on wrist function and chronic post-surgical pain (CPSP) following infraclavicular brachial plexus block for surgical repair of distal radius fractures.

Methods: Adult patients who underwent ultrasound-guided infraclavicular blockade (IB) plus surgical repair of a distal radius fracture between 2012 and 2017 were evaluated from hospital medical records retrospectively. Two different treatment protocols were used for postoperative analgesia. Group IB received standard analgesia protocol as 15 mg/kg IV paracetamol 4 times a day ±2 mg/kg IV tramadol and group PR received oral PR plus the standard protocol. The frequency of Tramadol use during hospital stay (TCHS) was also evaluated. The disability of the arm shoulder and hand (DASH) score and Mayo wrist score (MWS) were used to assess wrist function and a visual analog scale (VAS) was used for subjective pain severity assessment. CPSP and its neuropathic component were evaluated using the douleur neuropathique 4 (DN4) and Self-completed Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) pain scales.

Results: A total of 122 patients with a mean age 39.4±11.5 years were included in the study (group IB, n=62 and group PR, n=60). The TCHS of group PR was significantly lower than group IB (p=0.030). Better VAS, DASH and MWS scores were found in group PR at months 3, 6, and 12 (p=0.002, p=0.007, p=0.02 for VAS; p=0.01, p=0.01, p=0.01 for DASH; p<0.001, p<0.001, p=0.01 for MWS). The ratio of neuropathic pain according to DN4 and S-LANSS scores of group PR was also significantly lower than group IB at 6- and 12- month visits (p=0.21, p=0.023 for DN4; p=0.034, p=0.038 for S-LANSS).

Conclusion: The administration of low dose PR for 2 weeks following distal radius fracture surgery is beneficial for wrist function, chronic pain, and opioid consumption.

Keywords: Pregabalin, distal radius fracture, infraclavicular block, postoperative analgesia, chronic post-surgical pain, visual analog scale

ÖZ

Amaç: Çalışmamızda, distal radius kırıklarının cerrahi onarımı ve infraklaviküler brakiyal pleksus bloğunu takiben pregabalin (PR) verilmesinin bilek fonksiyonu ve kronik cerrahi sonrası ağrı (CPSP) üzerindeki etkileri değerlendirildi.

Yöntemler: Bu çalışmada, 2012-2017 yılları arasında ultrason eşliğinde infraklaviküler blok (IB) ve distal radius kırığına cerrahi onarım uygulanan erişkin hastalar hastane kayıtlarından geriye dönük olarak değerlendirildi. Postoperatif analjezi için iki farklı tedavi protokolü kullanıldı. Grup IB günde 4 kez 15 mg/kg IV parasetamol ±2 mg/kg IV tramadol olarak standart analjezi protokolü aldı ve grup PR oral PR artı standart protokol aldı. Hastanede kalış sırasında tramadol tüketimi (TCHS) insidansı da değerlendirildi. El bileği fonksiyonunu değerlendirmek için kol omuz ve el yetersizliği (DASH) skoru ve Mayo bilek skoru (MWS) ve subjektif ağrı şiddetini değerlendirmek için görsel analog skala (VAS) kullanıldı. CPSP ve nöropatik bileşeni, douleur neuropathique 4 (DN4) ve Self-completed Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) ağrı skalaları kullanılarak değerlendirildi.

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Bulgular: Çalışmaya yaş ortalaması 39,4±11,5 yıl olan toplam 122 hasta dahil edildi (grup IB, n=62 ve grup PR, n=60). Grup PR'nin TCHS'si grup IB'den anlamlı derecede düşüktü (p=0,030). Grup PR'de 3., 6. ve 12. aylarda daha iyi VAS, DASH ve MWS skorları tespit edildi (VAS için p=0,002, p=0,007, p=0,02; DASH için p=0,01, p=0,01, p=0,01; p<0,001, p<0,001, MWS için p=0,01). Goup PR'nin DN4 ve S-LANSS skorlarına göre neoropatik ağrı oranı da 6. ve 12. ay vizitlerinde Grup IB'den anlamlı derecede düşüktü (DN4 için p=0,21, p=0,023; S-LANSS için p=0,034, p=0,038).

Sonuç: Distal radius kırığı cerrahisini takiben 2 haftalık düşük doz PR kullanımı el bilek fonksiyonu, kronik ağrı ve opoid tüketimi için açısından olumlu etki gösterebilmektedir.

Anahtar kelimeler: Pregabalin, distal radius kırığı, infraklaviküler blok, cerrahi sonrası analjezi, kronik cerrahi sonrası ağrı, görsel analog skala

INTRODUCTION

Chronic post-surgical pain (CPSP) is defined as the pathological pain that persists beyond 2 months after surgery despite a lack of any local complications (1). Nearly one-third of patients present with varying degrees of CPSP at the end of 1st year following surgical procedures (1). Many factors are considered responsible for the development of CPSP. Among these, the presence of perioperative pain and its intensity are recognized as the most important patient-related factors. Effective control of perioperative and postoperative pain may improve patient satisfaction, early rehabilitation, and functional outcomes.

Brachial plexus block is a commonly preferred technique in surgical procedures of the upper extremity not only for improving intraoperative comfort by providing regional anesthesia but also for offering postoperative analgesia (2). This includes interscalene, infraclavicular, or supraclavicular blockade depending on the anatomic site to which it is applied. Major advantages of regional anesthesia include effective postoperative pain control, reduced need for opioids, and faster recovery after surgery than is offered by general anesthesia (3,4).

Pregabalin (PR) is a gabapentinoid derivative that has widespread use in the management of acute and chronic pains. PR reduces sensitization at peripheral neuron terminals and central neurons by decreasing calcium influx into the terminal presynaptic area (5). In addition, as PR decreases the need for opioids, opioid complications are decreased (6-8).

The aim of our study was to evaluate the effects of PR on wrist function and CPSP in patients who underwent infraclavicular brachial plexus block for surgical repair of distal radius fracture, retrospectively. We hypothesized that in distal radius fracture surgery, oral PR administration that was added to the infraclavicular block (IB) for multimodal pain control would decrease the risk of chronic pain by enhancing the effects of the block.

METHODS

Current study was conducted in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975, as revised in 2000.

After obtaining approval from the University of Health Sciences Turkey, Okmeydanı Training and Research Hospital Ethics Committee (decision no: 807, date: 09.01.2018), adult patients (≥18 years) in whom surgical strategy was preferred due to the partial intra-articular distal radius fracture between 2012 and 2017 were evaluated from hospital medical records retrospectively. Written informed consent form was obtained from the patients.

Exclusion criteria included any chronic or acute rheumatologic condition; osteoporotic, open, or pathological fracture that occurred secondary to poly-trauma or high-impact trauma; known hypersensitivity to PR or local anesthetics, failed IB, not having regular clinical records or one-year follow up. One hundred twenty two of 194 patients met the inclusion criteria and were divided into two groups. Group IB received brachial block with a standard postoperative analgesia regimen and group PR received brachial block plus standard protocol and oral PR.

All patients underwent standard ultrasound-guided infraclavicular brachial plexus block (SonoSite M-Turbo; SonoSite, Bothell, WA, USA) by the anesthesiologist, as described in the literature (Figure 1) (9,10). After establishing infraclavicular blockade, the

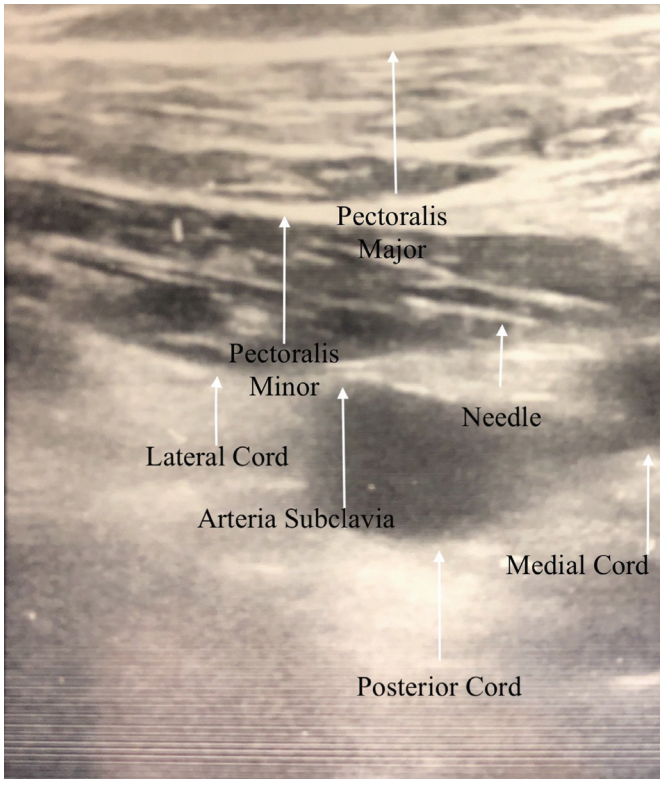

Figure 1. Section view of ultrasound-guided infraclavicular block

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orthopedic surgeon performed an open reduction and internal fixation with a volar locking plate (Acumed, Andover, UK).

The standard postoperative analgesia in both groups consisted of paracetamol 15 mg/kg IV 4 times a day. In case of severe pain [a score >3 on a visual analog scale (VAS)], intravenous tramadol 2 mg/kg was added. Nonsteroidal anti-inflammatory drugs were avoided due to their union-delaying effects. Group PR was initially administered oral PR 300 mg 1 hour before the surgery and were then maintained on oral PR 25 mg BID (two times a day) for two weeks in addition to standard analgesia protocol.

Each patient wore a splint for 2 weeks after surgery to ensure proper wound healing. The splint was removed for therapy and put back on after the treatment. Wrist motion and strength exercises were started as soon as the sutures and splint were removed (11).

The disability of the arm shoulder and hand (DASH), Mayo wrist score (MWS) and VAS scores were used to assess wrist functions and pain severity at 3-, 6- and 12-month visits. CPSP was evaluated by douleur neuropathique 4 (DN4) and the Self-completed Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) pain scales at 6- and 12- month visits. The DN4 questionnaire consists of 10 items used to identify pain of predominantly neuropathic origin based on the patient's current symptoms and signs and patients with score ≥ are considered to have neuropathic pain (12).

The S-LANSS scale consists of 7 items and patients with score ≥12 is considered to have neuropathic pain (13). Tramadol consumption of patients during hospital stay (TCHS) was also evaluated from the medical records.

Statistical Analysis

The statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS 24.0, SPSS Inc, Chicago, IL, USA). The Kolmogorov-Smirnov test was performed to assess the distribution of the data. Case numbers and percentages were used for demographic variables. Quantitative data were analyzed using independent sample t-test, and Pearson chi-square test was performed to compare the qualitative data. A p-value <0.05 was considered statistically significant.

Table 1. Descriptive analyse of type and side of fracture, sex of patients

		n	%
Groups	Group A	62	50.8
	Group B	60	49.2
AO class	B1	90	73.8
	B3	32	26.2
Side	Dominant	72	59
	Non-dominant	50	41
Sex	Male	78	63.9
	Female	44	36.1

RESULTS

Out of 194 patients with distal radius fractures, 122 patients who had regular follow-up were analyzed in the study, consisting of 62 patients in group IB and 60 patients in group PR. The mean age was 39.4±11.6 years (range: 23-58 years), and there were 78 women and 44 men. There was no significant difference regarding average follow-up between two groups (group IB 15.13±3.85, group PR 14.85±3.88; p=0.58). Ninety patients had B1 fractures, and 32 patients had B3 fractures according to the AO classification. While dominant side was affected in 72 patients, non-dominant side was affected in 50 patients (Table 1).

The incidence of TCHS, nausea and vomiting in Group PR were significantly lower than group IB (group PR=8.3%, Group IB=22.6%, p=0.030 for TCHS; group PR=1.7%, group IB=11.3%, p=0.032).

Group PR had statistically significantly lower VAS and DASH scores and higher MWS score than Group B at months 3, 6, and 12 months (VAS scores, p=0.002, p=0.007, and p=0.02; DASH scores p=0.001, p=0.001, and p=0.001; MWS p<0.001, p<0.001, p=0.010) respectively (Table 2).

The incidence of patients with CPSP regarding to DN4 and S-LANSS scales was significantly lower in group PR than group IB at 6 and 12 months (p=0.021 and p=0.023 for DN4; p=0.034 and p=0.038 for S-LANSS respectively) (Table 3).

DISCUSSION

The principal finding of the study was that adding PR to IB with distal radius surgery reduced the risk of CPSP and improved wrist functions. Only a few trials were carried out to evaluate the efficacy of PR in conjunction with IB for postoperative multimodal analgesia in upper extremity surgery. The prospective randomized trial performed by Cegin et al. (13) reported that administration of 150 mg PR before infraclavicular nerve block reduced postoperative anxiety and increased the block quality in patients who underwent upper extremity bone surgery. In another

Table 2. Evaluation of 3rd, 6th and 12th months DASH, VAS, and Mayo wrist scores

		Group B	Group P	p-value
		Mean ± SD	Mean ± SD	
DASH score (month)	3rd	21.04±3.36	15.73±2.16	0.001
	6th	16.07±2.13	11.12±1.86	0.001
	12th	9.78±1.89	5.52±1.72	0.001
VAS score (month)	3rd	2.87±0.95	2.03±1.09	0.002
	6th	1.74±0.72	1.16±0.87	0.007
	12th	0.94±0.57	0.56±0.62	0.02
Mayo wrist score (month)	3rd	25.48±2.82	31.13±4.45	0.001
	6th	66.06±3.87	77.48±3.43	0.001
	12th	90.37±4.73	92.43±3.86	0.010

DASH: disabilities of the arm, shoulder and hand, VAS: visual analogue scale, SD: standard deviation

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study, Egol et al. (14) evaluated 187 patients who underwent open reduction volar plate fixation for distal radius fractures and compared general anesthesia and IB retrospectively. The IB had significantly more favorable effects on VAS and DASH scores within the first 6 months compared to that of general anesthesia (15). At 12 months, pain and DASH scores were similar between the two groups. The difference could be attributed to the fact that postoperative addition of PR might increase the efficacy of the block, prolong its duration of action, and increase the analgesic activity.

Chronic pain, unlike acute pain, is a compel-to-manage condition with a low likelihood of being adapted to it (16). Its underlying pathology is thought to involve disturbances in several mechanisms of the central and peripheral nervous systems such as neuroplasticity, pain modulation, and central sensitization (17). Acute pain after surgery is estimated to progress to chronic pain in 10-50% of patients, which makes prevention of transition to chronicity very critical (17). PR acts as a potent ligand for alpha 2-delta subunits of the voltage-gated calcium channels in the nervous system. Such action results in a reduction in the depolarization-induced influx of calcium, hence a reduction in the release of excitatory neurotransmitters including glutamate, noradrenaline, dopamine, and serotonin. The reduction of these neurotransmitters is suggested to lead to central desensitization (18). Owing to this effect on acute pain, perioperative use of PR may inhibit the evolution of acute pain to chronic pain (19). Several studies involving cases of distal radius fracture surgery reported the prevalence of chronic pain as high as 16-30% (20,21). In the current study, the incidence of one-year chronic pain assessed by the DN4 and S-LANSS scales were 21% and 19.4% in group IB, respectively, which were similar to the literature. However, the incidence of chronic pain according to DN4 and S-LANSS scales scores in group PR (DN4, 6.7%; S-LANNS, 6.7%) was significantly lower than group IB (p=0.038). This also suggests that PR administration for 2 weeks after IB is effective for reducing CPSP.

In orthopedic practice, the efficacy of PR has been studied in elective surgical procedures such as knee, hip arthroplasty, and carpal tunnel release. While these have suggested that PR reduce the need for opioids and thereby decrease the rates of side effects like nausea and vomiting, its efficacy for acute and chronic postoperative pain and function remains controversial. Buvanendran et al. (6) reported diminished postoperative chronic pain in patients who underwent total knee prosthesis surgical and received 300 mg PR in the preoperative period, followed by a 14-day course of 50-150 mg PR twice daily. On the other hand, YaDeau et al. (22) administered 50 to 150 mg PR twice daily starting just before surgery until the first postoperative day in patients undergoing total knee arthroplasty and reported no effect on postsurgical acute or chronic pain, opioid use, or adverse effects of analgesics such as increased sedation and patient dissatisfaction. While these two contradictory studies both used combined epidural regional anesthesia and postoperative patient-controlled epidural analgesia as a standard approach, Buvanendran et al. (6) administered infiltrative anesthesia for establishing multimodal analgesia as compared with femoral blockade used in the latter study (7-22). The different outcomes of these studies might be explained by the distinctive multimodal analgesia regimens, dosages, and duration of administration.

Table 3. Incidence of CPSP assessed by S-LANSS and DN4 scores at 6th and 12th month's visit

S-LANSS	CPSP	Group IB		Group PR		p-value
		n	%	n	%	
6th month	-	45	58	50	83	0.031
	+	17	42	10	17	
12th month	-	46	74	56	93	0.044
	+	16	26	4	7	
DN4						
6th month	-	43	69.4	52	86.7	0.021
	+	19	30.6	8	3.3	
12th month	-	49	79	56	93.3	0.023
	+	13	21	4	6.7	

CPSP: chronic post-surgical pain, S-LANSS: Self-completed Leeds Assessment of Neuropathic Symptoms and Signs Pain scale, DN4: douleur neuropathique four

The effects of PR administration or type of anesthesia on opioid consumption and related side effects are controversial. For instance, Hadzic et al. (23) investigated the effects of IB vs general anesthesia added on perioperative infiltrative local analgesia in both groups who underwent hand and wrist surgery. Acetaminophen, IV Morphine and codeine were used for postoperative analgesia protocol. The rates of opioid consumption, nausea and vomiting were reported significantly higher in general anesthesia group (23). On the other hand, Rundgren et al. (24) and O'Neil et al. (25) also compared the anesthesia methods in the patients who underwent distal radius surgery and noted that the anesthesia method (regional or general) was not effective on total opioid consumption. In current study, we found that perioperative low dose PR addition to IB reduced the incidence of in-hospital opioid consumption, nausea, and vomiting. This combination seemed to be effective to lower opioid consumption and related side effects. Different results may depend on choosing different anesthesia techniques and multimodal analgesia methods.

Study Limitations

Our study had some limitations, including involvement of only a single center, having a retrospective design, and a lack of opioid doses and long-term outcomes.

CONCLUSION

Low dose PR administration for 2 weeks after IB reduced the incidence and severity of chronic pain and improved functional outcomes in patients who underwent open reduction and plate fixation for distal radius fracture. Thus, addition of PR to regional anesthesia seems to be an efficacious alternative for successful postoperative pain management following distal radius surgery.

Ethics Committee Approval: Ethical approval was obtained from the University of Health Sciences Turkey, Okmeydanı Training and Research Hospital Clinical Research Ethics Committee (decision no: 807, date: 09.01.2018).

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