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The effects of adding tramadol to ropivacaine on axillary brachial plexus blockade in uremic patients*

Aim: To evaluate the effect of tramadol added to ropivacaine on quality of anesthesia, onset of sensory and motor blockade, duration of sensory and motor blockade, and first analgesic request time for axillary brachial plexus block in uremic patients.

Materials and methods: After institutional approval and informed consent had been obtained, 45 ASA III uremic patients (age range 30-80) scheduled for arteriovenous fistula surgery were included in the study. Patients were randomly allocated into 2 groups. Axillary block was performed with a peripheral nerve stimulator by multiple injection technique. Patients in Group R (n = 23) received 38 mL of ropivacaine (3.75 mg/mL) and 2 mL of normal saline, and patients in group RT (n = 22) received 38 mL of ropivacaine (3.75 mg/mL) and 2 mL of tramadol (50 mg/mL). The onset and duration of sensory and motor block in the distribution of the radial, median, and ulnar nerves; the duration of analgesia; the time to first requirement of analgesic; hemodynamics; and side effects were recorded.

Results: Demographic data, onset of sensory and motor block, duration of sensory and motor block, quality of anesthesia, and first analgesic requirement times were similar between the groups. In addition, hemodynamic parameters and side effects did not differ between the groups.

Conclusion: The addition of 100 mg of tramadol to 3.75 mg/mL of ropivacaine does not have any beneficial effect on the nerve block characteristics of axillary brachial plexus anesthesia for arteriovenous fistula surgery in uremic patients.

Key words: Axillary brachial plexus block, ropivacaine, tramadol, chronic renal failure

Üremik hastalarda aksiller brakial pleksus bloğunda ropikaine eklenen tramadolün etkisi

Amaç: Bu çalışma; üremik hastalarda aksiler brakial pleksus bloğunda ropivakaine tramadol eklenmesinin anestezi kalitesi, duyusal ve motor blok süresi ve ilk analjezik gereksinim üzerine etkisini değerlendirmek için tasarlanmıştır.

Yöntem ve gereçler: Etik kurul onayı ve bilgilendirimiş hasta oluru alındıktan sonra arteriovenöz fistül operasyonu düşünülen kırkbeş ASA III üremik hasta (30-80 yaş arası) rastgele iki gruba ayrıldı. Aksiller blok sinir stimülatörü kullanılarak multiple enjeksiyon tekniği ile yapıldı. Grup R'deki hastalara (n = 23) 38 mL ropivakain (3,75 mg/mL) ve 2 mL serum fizyolojik ve Grup RT'deki hastalara (n = 23) 38 mL ropivakain (3,75 mg/mL) ve 2 mL tramadol (50 mg/mL) uygulandı. Radial, median ve ulnar sinirlere ait duyusal ve motor blok başlama zamanı ve süreleri, analjezi süresi, ilk analjezik gereksinim zamanı, hemodinami ve yan etkiler kaydedildi.

Bulgular: Demografik data, duyusal ve motor blok başlama zamanı ve duyusal ve motor blok başlama süreleri, analjezi süresi, anestezi kalitesi ve ilk analjezik gereksinim zamanı açısından her iki grup arasında benzerdi. Bununla birlikte, hemodinamik parametreler ve yan etkiler açısından da fark yoktu.

Sonuç: Üremik hastalarda, arteriovenöz fistül operasyonu için aksiler brakiyal pleksus anestezisinde 3,75 mg/mL ropivakaine 100 mg tramadol eklenmesi, sinir blok karakteristikleri üzerine yararlı etki göstermemiştir.

Anahtar sözcükler: Aksiller brakiyal pleksus blok, ropivakain, tramadol, kronik böbrek yetmezliği

* This study was presented at Euroanesthesia meeting 2007 in Munich, Germany

Introduction

Patients with chronic renal failure (CRF) most commonly present to the operating room for creation or revision of an arteriovenous fistula under local or general anesthesia (1). Many anesthesiologists prefer brachial plexus block as a suitable anesthesia technique for this procedure (2,3). The resulting analgesia and sympathetic blockade provide optimal surgical conditions, and subsequently adequate duration of postoperative block prevents arterial spasm and graft thrombosis. In the early postoperative period, the arteriovenous fistula blood flow was shown to be significantly increased in patients having brachial plexus blockade when compared to those having halothane or isoflurane anesthesia (4). It is reported that the local anesthetics were absorbed faster from the axillary region into circulation and due to reduced clearance of them their plasma concentrations were higher in CRF patients (5). Moreover, the hyperdynamic cardiovascular system and metabolic acidosis secondary to chronic anemia increase the elimination rate of local anesthetics, resulting in a shorter duration of the axillary block compared to those with normal renal function (2,6).

Ropivacaine was used for axillary block with high efficacy and safety (7-9). Since the metabolites of ropivacaine are excreted in urine, the potentially toxic metabolites may accumulate in chronic renal failure patients (10). This is why lower concentrations of ropivacaine are recommended in patients with chronic renal failure when large doses are planned to be used (5). However, it is reported that brachial plexus block was performed with a smaller ropivacaine concentration in patients with chronic renal failure; the duration of analgesia was shorter than the higher ropivacaine concentration in patients with normal renal function (11). The addition of tramadol to local anesthetics significantly prolonged the duration of brachial plexus block in patients with normal renal function (12-14). Tramadol is one of the least problematic opioids for patients with chronic renal failure (15). Tramadol seems to be a good alternative for additionally providing the above mentioned.

On the basis of these data we aimed to evaluate the effects of tramadol as an adjuvant to ropivacaine on the onset and duration of sensory and motor blockade, quality of anesthesia, and first analgesic request time for axillary brachial plexus blockade in CRF patients.

Materials and methods

After approval from the hospital's Ethics Committee and written informed patient consent were obtained, 45 patients with chronic end-stage renal disease that were scheduled for creation of an arteriovenous fistula were included in the study. The ages of the patients ranged between 30 and 80 years and all were ASA physical status III. The exclusion criteria were a body weight more than 130 kg, height less than 140 cm, or a history of neurological, neuromuscular, psychiatric, hepatic, respiratory, or cardiac disorders.

The patients received premedication with midazolam 1-2 mg IV at the discretion of the anesthesiologist. Three-lead electrocardiogram, noninvasive oscillotonometric arterial blood pressure, and pulse oxymetry (ADU S/5 Datex-Ohmeda, Finland) were used for monitoring. An IV infusion of normal saline 250 mL/h was started before anesthesia. The randomization was performed from a list of random numbers; instructions for randomization were prepared in a sealed envelope for each patient. The patients were allocated into 1 of the 2 groups for axillary brachial plexus block.

The patient was placed in a supine position with the arm abducted 90° and the elbow flexed 90° to identify the pulse of the axillary artery. The area was prepared with povidone-iodine solution and multiple injections were performed to obtain a perivascular axillary brachial plexus block. Each nerve was identified with a short, beveled electrical stimulation needle (Stimuplex, B. Braun Melsungen AG, Melsungen, Germany) connected to a nerve stimulator using low currents. Fourteen milliliters of the study solution was injected near each nerve with intermittent aspiration, after the nerves were identified by obtaining a peripheral motor response with a current near or below 0.5 mA. The study solution consisted of 40 mL of ropivacaine (Naropin, AstraZeneca, Sweden) 3.75 mg/mL and 2 mL of saline in Group R, whereas it contained 40 mL of

ropivacaine 3.75 mg/mL and 2 mL of tramadol 100 mg in Group RT. The patients were informed about the signs of local anesthetic toxicity before the injections and the verbal contact was maintained until the end of the injection period. Firm digital pressure was maintained during the injection and 3 min thereafter immediately distal to the injection site to prevent flow of the solutions distally. Following injection, the arm was kept adducted with the hand resting on the chest. Sensory block was assessed in the innervation areas of the median, radial, and ulnar nerves by pinprick testing. Pinprick testing was performed using a blunt-ended 27-gauge dental needle at 0, 2, 5, 10, 20, and 30 min and then every 15 min during the procedure. The patients assessed the pinprick sensation as sharp (normal sensation), blunt (analgesia), or no sensation of touch (anesthesia). The motor block was assessed by thumb abduction (radial nerve), thumb adduction (ulnar nerve), and thumb opposition (median nerve) on a 3-point scale for motor function (0 = normal motor function, 1 = reduced motor strength but able to move finger, 2 = complete motor block) with the same intervals as the pinprick.

The duration of anesthesia was defined as the time interval between the onset of analgesia and the recovery of sensation of touch. The duration of motor block was defined as the time interval between the onset of the motor block and the recovery from the motor block. The surgery started when pinprick anesthesia was achieved in the regions of the median, radial, and ulnar nerves. The surgeon injected 1% prilocaine into the surgical site if the block was not achieved in this site after 45 min. Fentanyl 0.05-0.1 mg was administered IV if the patient experienced pain despite the block. The patients with anxiety were administered IV midazolam 1-2 mg.

A visual analog scale (VAS) was used to assess pain at 0, 1, 2, 4, 8, 12, and 24 h postoperatively. Heart rate, blood pressure, oxygen saturation, respiratory rate, and sedation scores were recorded at the same time points. Nausea and vomiting were recorded if present. The duration of anesthesia was defined as the time between the local anesthetic injection and the time that the first analgesic was required.

The data were analyzed using SPSS 13.0 for Windows (SPSS Inc., Chicago, IL, USA). Patient characteristics and times were analyzed for normality and the 2 groups were compared using Student's t-test. Categorical data were analyzed using the chi-squared test. Data were expressed as the mean ± SD and patient numbers as appropriate. A P value of less than 0.05 was considered statistically significant.

Results

Five of the 45 patients originally included in the study were subsequently excluded because the anesthesia could not be achieved in 3 patients in Group R after 45 min and the radial nerve could not be identified in 2 patients in Group RT.

The demographic data, ASA physical status, and surgical characteristics were similar between the 2 groups (Table 1, P > 0.05).

Table 1. Demographic data and surgical characteristics (mean ± SD).

	Group R (n = 20)	Group RT (n = 20)	P
Age (years)	55.1 ± 14.5	61.5 ± 10.9	0.229
Body weight (kg)	60.7 ± 10.4	67.7 ± 12.9	0.312
Height (cm)	162.1 ± 10.7	164.8 ± 6.7	0.385
Gender (M/F)	5/15	6/14	1.000
Surgery start (min)	20.4 ± 11.9	22.6 ± 6.8	0.229
Duration of surgery (min)	51.6 ± 15.2	50.9 ± 14.3	0.693

R, ropivacaine only; RT, ropivacaine+tramadol. Values are mean ± standard deviation or n

Time to onset for the sensory block and the duration of the sensory block showed no differences between the groups (Table 2, P > 0.05). The groups also did not differ in terms of the time to onset for the motor block or its duration (Table 3, P > 0.05).

Average time to first requirement of analgesic was 218.9 ± 39.0 min in Group R and 233.7 ± 22.2 min for Group RT with no differences between the groups (P = 0.176). VAS scores were similar between the groups (P > 0.05) except for at 2 h postoperatively (P = 0.042).

The groups were similar in terms of the need for an analgesic supplement or sedation during the procedure (P > 0.05). It was noted that the patients in Group R needed sedation more frequently, but the difference between the groups was not significant (P > 0.05).

There were no significant differences between the groups in terms of the sedation scores, or respiratory or hemodynamic parameters (P > 0.05). Side effects, such as hypotension and bradycardia, were not observed in either group during the study period. Three patients in Group RT and 1 patient in Group R experienced nausea/vomiting, but there were no statistically significant differences between the groups.

Discussion

In this study, we achieved a sufficient and good-quality axillary plexus block with 40 mL of 3.75 mg/mL ropivacaine (150 mg) for creation of an arteriovenous fistula in patients with chronic renal failure. Although these parameters were not statistically significant adding tramadol to ropivacaine

Table 2. Onset time and duration of sensory block for analgesia (mean ± SD).

	Group R (n = 20)	Group RT (n = 20)	P
Onset time of radial nerve sensory block	6.01 ± 1.4	5.2 ± 1.1	0.093
Duration of radial nerve sensory block	197.9 ± 32.6	220.1 ± 22.7	0.806
Onset time of median nerve sensory block	6.5 ± 1.5	5.9 ± 1.4	0.322
Duration of median nerve sensory block	201.4 ± 29.3	222 ± 23.2	0.045
Onset time of ulnar nerve sensory block	6.71 ± 1.4	5.7 ± 1.3	0.092
Duration of ulnar nerve sensory block	205.7 ± 29.8	221.3 ± 22.6	0.122

R, ropivacaine only; RT, ropivacaine+tramadol. Values are mean ± standard deviation or n

Table 3. Onset time and duration of motor block (mean ± SD).

	Group R (n = 20)	Group RT (n = 20)	P
Onset time of radial nerve motor block	8.7 ± 2.3	8 ± 1.9	0.876
Duration of radial nerve motor block	195.7 ± 37.1	192 ± 26.9	0.965
Onset time of median nerve motor block	8.1 ± 1.6	8.5 ± 1.7	0.282
Duration of median nerve motor block	198.6 ± 35.2	192 ± 27.4	0.743
Onset time of ulnar nerve motor block	8.1 ± 1.4	8.1 ± 1.9	0.912
Duration of ulnar nerve motor block	197.9 ± 36.8	192.7 ± 26.8	0.759

R, ropivacaine only; RT, ropivacaine+tramadol. Values are mean ± standard deviation or n

clinically shortened the time to onset for the sensory block and increased the duration of it minimally without changing the block characteristics. The time to requirement for an analgesic was relatively delayed when tramadol was added to ropivacaine.

Bupivacaine is a frequently used local anesthetic and has the clinical advantages of long duration of action and favorable ratio of sensory to motor neural block. Ropivacaine may potentially provide better success rates for axillary brachial plexus block than bupivacaine, because it enables larger doses to be used owing to its low cardiotoxicity (7,8). It was reported that 0.25% ropivacaine is similar in quality to 0.25% bupivacaine in most aspects for brachial plexus block. As both of them are frequently associated with inadequate sensory and/or motor block, Hickey et al. (16) recommended 0.5% concentration for both. Vainnionpaa et al. (17) reported that both bupivacaine and ropivacaine were equally effective for an axillary brachial plexus block at a concentration of 0.5%. This result was confirmed by McGlade et al. (18) and Bertini et al. (19), who reported that ropivacaine was better suited for axillary brachial plexus block than bupivacaine, and increasing the ropivacaine concentration increased the risk of systemic toxicity without any clinical advantages.

Pere et al. used 7.5 mg/mL ropivacaine (total 300 mg) for axillary block in uremic and non-uremic patients. Pharmacokinetic data in the study with ropivacaine showed that faster absorption into circulation and increased binding α_1-acid glycoprotein, reducing liver extraction, led to significantly higher plasma concentrations of ropivacaine and its metabolites in uremic patients. However, the quality of sensory and motor block was similar between the uremic and non-uremic patients. No toxic symptoms occurred despite occasional large plasma concentrations soon after the injection of ropivacaine (20).

Ropivacaine is not excreted through the kidneys and therefore impairment of renal function does not impair its elimination. However, because renal function is important for elimination of 2,6 pipecoloxylide (PPX) and 3-OH-ropivacaine, renal insufficiency may cause accumulation of those compounds. Large concentrations of PPX may unexpectedly develop (20). The free plasma concentrations of PPX (80%-90% of the total) may reach the toxic level although PPX is clearly less toxic than ropivacaine (11).

We used 3.75 mg/mL (150 mg) ropivacaine for creation of arteriovenous fistula in chronic renal failure patients because the aforementioned factors. The mean onset time of analgesia was 6.4 ± 1.4 min and the duration of anesthesia was 201.7 ± 30.6 min in different dermatomes of the brachial plexus. When used for brachial plexus block, the onset time depended on the technique used. The onset times for analgesia and anesthesia ranged from 11.2 to 20.2 min and 23.3 to 48.2 min, respectively, with a concentration of 0.25% ropivacaine for subclavian brachial plexus block (19). Analgesia in different brachial plexus dermatomes was achieved in 5-20 min and anesthesia in 12-45 min with a concentration of 0.5% ropivacaine for axillary plexus block (17). The mean duration of analgesia and anesthesia ranged from 9.2 to 13 h and 5 to 10.2 h, respectively, with the concentration of 0.25% ropivacaine for subclavian brachial plexus block (16). The duration of anesthesia produced by 0.5% ropivacaine via axillary block ranged from 3.7 to 8.7 h. The duration of anesthesia in CRF patients was relatively short in our study and this may have been due to acidosis and hyperdynamic circulatory status, which increase the elimination rate of local anesthetics, resulting in a shorter duration of the axillary block compared to those with normal renal function.

Tramadol is an analgesic that acts at central and peripheral μ-opioid and monoaminergic receptors (21). It also exhibits local anesthetic properties (22). There have been few studies on adjunctive tramadol for peripheral nerve blocks. Büyükakıllı et al. examined the interaction of tramadol plus bupivacaine on compound nerve action potential in an isolated frog sciatic nerve (23). They reported that the addition of tramadol to bupivacaine did not enhance local anesthetic nerve block. Antonucci et al. reported that the effects of tramadol 100 mg combined with ropivacaine 0.75% prolonged analgesia and anesthesia of brachial plexus block with less adverse effects than clonidine and sufentanil (13). The investigators used tramadol added at a lower dose and volume (150 mg, 20 mL) of injectate at 0.75%

concentration of ropivacaine under axillary block for patients with normal renal function undergoing carpal tunnel release. However, Kesimci et al. (24) demonstrated that the addition of 100 mg of tramadol to 7.5 mg/mL of ropivacaine, for axillary brachial plexus block, did not prolong the duration of motor and sensory block and analgesia. Similarly, Mannion et al. did not demonstrate a clinically important local anesthetic or peripheral analgesic effect of tramadol as an adjunct to psoas compartment block with levobupivacaine 0.5% (25). Our results were consistent with the experience of Kesimci et al. Although it is difficult to compare these contradictory results due to differences in dose and concentration of local anesthetic and technique of block, the patients with CRF in our study had metabolic acidosis and hyperdynamic circulatory status, which may mask the effect of additional tramadol on axillary brachial plexus block with ropivacaine (0.375%, 40 mL).

Kapral et al. demonstrated that adding tramadol 100 mg to mepivacaine 1% prolonged the duration of both motor and sensory blocks in axillary brachial plexus block (12). Wakhlo et al. reported that tramadol was a good agent for quickening the onset and prolonging of sensory and motor block, while butorphanol was a suitable agent for prolonged postoperative analgesia (26). Although Robaux et al. demonstrated that the onset time for median and ulnar nerve blockade was shorter and the duration of sensory and motor blockade was longer in tramadol combined with mepivacaine 1.5% for brachial plexus block, they reported that these differences were not significant (14). In addition, tramadol significantly increased the duration of postoperative analgesia in a dose-dependent manner in this study. Kapral (12), Robaux (14), and Wakhlo et al. (26) added tramadol to short acting local anesthetics mepivacaine (1%, 1.5%) and lignocaine (2%) respectively in patients with normal renal function. The lack of analgesic effect of additional tramadol (100 mg) in our study could be related to the choice of a long acting local anesthetic (ropivacaine) at a dose (40 mL; 3.75 mg/mL) that provides long duration analgesia. This may obscure any potential peripheral analgesic effect of tramadol, and its administration into a compartment versus into the brachial plexus sheath may have been affected by the type, dose, and concentration of local anesthetics.

In conclusion, a sufficient-quality axillary brachial plexus block was achieved in both groups (3.75 mg/mL ropivacaine and 100 mg tramadol added 3.75 mg/mL in 40 mL) for creation of arteriovenous fistula in patients with chronic renal failure. Further studies with lower ropivacaine concentrations may offer further clarification on the influence of tramadol on axillary brachial plexus block characteristics.

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