Manuscript template: The effects of pregabalin and adductor canal block on postoperative pain in arthroscopic anterior cruciate ligament reconstruction

Abstract

Background/aim: To determine the effectiveness of pregabalin and adductor canal block on opioid consumption, postoperative pain and fast-tracking.

Materials and methods: A total of 51 ASA I-II patients aged 18-70 years who were scheduled to undergo elective anterior cruciate ligament reconstruction were included in the study. Patients were randomized into groups P, A and C. Patients in group P (n=16), received preoperative 150 mg oral pregabalin, patients in Group A (n=17) received postoperative adductor canal blockade, and patients in group C (n=18) received neither adductor canal block nor pregabalin. Surgeries were performed under spinal anesthesia with hyperbaric bupivacaine following monitorization. Demographic data along with block features, hemodynamic data, mean opioid consumption, numerical rating scale score, White’s fast-track score, and postoperative adverse effects were recorded.

Results: Fifty-seven patients were enrolled in the study and 6 patients were excluded from the study and data of 51 patients were included in the final analyses of the study. Demographic characteristics and hemodynamic data were similar between the three groups. Postoperative opioid consumption was significantly lower in Group A and P compared with Group C (Group P=178.75 mg, Group C=318.61 mg, Group A=236.47 mg, p<0.05). The regression of sensory block was significantly slower in Group P (p<0.05). The first analgesic requirement was earlier in Group C than Group P and A (p<0.05). Patients in Group P had higher fast-track scores at 8 and 12 hours compared with Group C (p<0.05) but Group A fast-track scores were similar to the other two groups (p>0.05). The rate of postoperative adverse effects was similar between the groups (p>0.05).
Conclusion: Preoperative 150 mg pregabalin reduced postoperative opioid consumption as much as adductor canal block in patients undergoing anterior cruciate ligament reconstruction. The first analgesic requirement was earlier in Group C than Group P and A. In addition, pregabalin can provide prolong the spinal sensory block duration as well as shorter time to achieve high fast-tracking scores. We recommend that both methods can be preferred as part of multimodal analgesia.

Keywords: pregabalin, adductor canal block, postoperative pain
1. Introduction

Repair of the anterior cruciate ligament is one of the most commonly performed outpatient arthroscopic procedures [1, 2]. Optimal analgesia facilitates early rehabilitation and mobilization, improves functional recovery, reduces postoperative morbidity and increases patient satisfaction after anterior cruciate ligament reconstruction (ACLR) [1, 3]. Multimodal analgesia using opioids and a variety of other analgesics is, therefore, recommended in the management of acute pain after knee surgery [4].

Pregabalin is a structural analog of γ -aminobutyric acid (GABA) acting on the α2δ subunit of voltage-dependent calcium channels. Pregabalin is frequently being used as a part of neuropathic and postoperative pain management [4]. Previous studies demonstrated that preoperative pregabalin reduced opioid consumption during the 24-hour postoperative period in patients who received spinal or general anesthesia [5-11].

The adductor canal block (ACB) has recently gained popularity as an alternative to femoral nerve blockade due to reduced incidence of quadriceps muscle weakness [2, 12]. Several neural structures traverse the canal including the saphenous nerve and its infrapatellar branch, the nerve to the vastus medialis, the posterior branch of the obturator nerve, and in some cases, the medial cutaneous nerve and the anterior branch of the obturator nerve. With the exception of the nerve to the vastus medialis, these branches provide sensory innervation of the anterior and medial knee. ACB combined with local anesthetic infusion within the canal not only provides efficient analgesia but also contributes to maintaining lower extremity motor functions following knee surgery [12].

The primary objective of the current study was to evaluate the effectiveness of a single dose of oral pregabalin and ACB on opioid consumption in patients undergoing arthroscopic ACLR. The secondary objectives were to compare its effectiveness on postoperative pain, spinal block characteristics and fast-tracking. We hypothesized that would reduce
postoperative opioid consumption of oral pregabalin and ACB when compared with a control

group.

2. Materials and methods

The trial was approved by the Ethical Committee of the Ministry of Health Diskapi Yildirim
Beyazit Training and Research Hospital in Ankara, Turkey (Ethical Committee 29.01.2018
No: 45/17). The study was conducted at University of Health Sciences Diskapi Yildirim
Beyazit Training and Research Hospital, between June 2018 and August 2018.

A single-center, prospective, randomized, patient and assessor-blinded, placebo-controlled
study was performed. All patients were informed and written informed consent were obtained
from the patients.

Patients who were listed to undergo elective unilateral ACLR were screened for inclusion in
the study. The inclusion criteria were as follows: elective unilateral arthroscopic
reconstruction of the anterior cruciate ligament; age 18–70 years; and American Society of
Anesthesiologists (ASA) classification I to II. The exclusion criteria were as follows: refusal
to participate; incapacity to provide informed consent; contraindication to ACB (local
infection, local anaesthetic allergy, coagulopathy); contraindication to neuraxial anesthesia
(patient refusal, coagulopathy or bleeding diathesis, skin infection at the lumbar area,
increased intracranial pressure and allergy to local anesthetics); peripheral neurologic
dysfunction or neuropathy; surgery under general anaesthesia; body mass index (BMI) greater
than 45 kg/m²; known allergy to any medicine; history of drug or alcohol abuse; use of
opioids or sedative medications; history of psychiatric conditions; and pregnancy or lactation.

Preoperative visits were conducted for all of the patients by an anesthesiologist, and the
patients were instructed in the use of the Numeric Rating Scale (NRS) for pain assessment (0
= no pain; 10 = worst pain imaginable) and a system for patient-controlled analgesia (PCA).
Patients were randomly divided into three groups after recruitment using a computer-generated list. The patient blinded to the treatment, and all records were recorded by an anesthesiologist blinded to group allocation (Figure 1).

One hour before anesthesia induction, 150 mg pregabalin capsules (Lyrica 150 mg capsule, Pfizer, Istanbul, Turkey) were administered to Group P patients. During the same period, capsules containing placebo were administered to Group C and Group A patients. Placebo capsules were prepared by the pharmacy and were identical to the relevant trial drugs in size, shape, color, weight and were tasteless. Premedication was not applied to any patients. The electrocardiogram, blood pressure, and peripheral oxygen saturation were monitored upon the patient's entry into the operating room and subsequently every five minutes. Intravenous access was established using a 20-G intravenous cannula, and each patient was preloaded with Ringer's lactate solution 15 mL/kg. Spinal anesthesia was administered in the sitting position in the L4-L5 space with 2.5 mL of 0.5% hyperbaric bupivacaine using a midline approach with a 25-G Quincke needle. Oxygen was administered to all patients via facemask at 2–4 L/min. If the patient experienced either a decrease in systolic blood pressure <30% from the baseline value or a mean arterial blood pressure <60 mm Hg, repeated doses of intravenous ephedrine 10 mg were administered. Routine intraoperative sedation was not provided. The sensory block was evaluated every two minutes by loss-of-pinprick discrimination, and the motor block was evaluated with the Bromage scale [13]. Onset times for sensory and motor blocks were recorded. Surgical intervention was initiated when the block reached the T10 level. The onset time of sensory block at the L1-T10 level, the highest level of sensory block, duration of sensory block, time for two segment regression of sensory block and time for regression to Bromage 2 were recorded.

All patients subsequently underwent arthroscopically assisted ACL reconstructions with bone-tendon-bone (BTB) autograft. Patients were blocked under ultrasound guidance after
surgery. Surgical bandages were applied before surgical closure and were positioned with mild external rotation of the surgical limb. Under sterile conditions, the femoral artery, vein and accompanying nerve branches were located using ultrasound (HFL 38X/13–6 MHz; SonoSite M turbo ultrasound machine; SonoSite Inc., Bothell, WA, USA) halfway between the anterior superior iliac spine and the patella. The patient ultrasound monitor and block were isolated in a way that the application area was not seen. In group A, after local anaesthesia, an 18-G 10 cm 50 mm stimulator needle (Echoplex®, Vygon, Ecouen, France) was inserted under ultrasound guidance in the plane 30° off of a short-axis view until it was visualized next to the nerve(s) and artery under the fascia of the sartorius muscle [14]. It was used 10 mL of 0.25% bupivacaine with 5 μg/mL epinephrine in fractionated doses via ultrasound guidance by the same anesthesiologist [12]. Group P and Group C patients were placed in similar positions and simulated adductor blocks were performed with an ultrasound probe. A sham subcutaneous injection of 0.5 ml sterile normal saline in Group P and Group C, was subsequently performed at the ACB site using ultrasound guidance with transducer pressure intended to simulate a real block procedure. Standard surgical bandages were then applied to the operated knees of all patients including the puncture part of the needle. Upon discharge from the postanesthesia care unit, all patients received a standard postoperative multimodal regimen of dexketoprofen trometamol 50 mg every 12 hours and a tramadol intravenous PCA (10 mg bolus with a 10 minute lockout period) device (CADD-Legacy® PCA pump, Smiths Medical, USA) for 24 hours. Postoperative pain was assessed by the patient using the NRS and WFTSS [15] (Appendix 1) at 1, 4, 8, 12 and 24 hours after surgery and was recorded by a blinded researcher. Patients with a NRS score of 4 or more received 50 mg tramadol intravenously. The times of the first request for postoperative analgesia, the number of injections, the total amount of tramadol consumed by PCA device
after 24 hours and patient demand were recorded. All assessments were recorded by a blinded researcher.

The incidence of opioid-related side-effects, nausea, and vomiting, dry mouth, urinary retention, pruritus, pregabalin-related side-effects, confusion, headache, diplopia and dizziness were defined as present when at least one episode was noted during the first 24 hours after surgery.

G*Power version 3.1.9.2 (© Franz Faul, Edgar Erdfelder, Albert-Georg Lang, and Axel Buchner, 2006, 2009) was used to perform a priori sample size calculation based on pilot data on postoperative 24 h tramadol consumption [16]. In the preliminary study which was included 10 patients, tramadol consumption (mean ± SD) was showed 180±59.31 in the pregabalin group and 246±74.12 in the adductor group. 25% decrease in tramadol consumption in group P was been detected compared to group A. Accordingly, the number of patients required in each group was determined as α-error = 0.05 at 85% power, at least 16 patients per group. In this study, 19 patients were included in each group for analysis due to dropout.

Data were analyzed using Statistical analysis was performed with the Statistical Package for Social Sciences (SPSS) software version 24 (SPSS, Inc., Chicago, IL, USA). The normality of the distribution of continuous variables was evaluated using the one sample Shapiro-Wilk test. Patient demographics and characteristics were expressed as number and percentage, median (interquartile range, IQR) and mean (standard deviation, SD), and were analyzed using the chi-square test for categorical variables and the independent t-test for normally distributed continuous variables. Mann–Whitney U-test and Kruskal Wallis were applied for comparisons of non-parametric and non-normally distributed data. Nominal data were analyzed by Pearson chi-square or Fisher’s exact test where appropriate. The corrected
Bonferroni test was used for multiple comparisons. P values < 0.05 were considered statistically significant in each test.

3. Results

Fifty-seven patients were enrolled in the study. Patients were randomly assigned to one of three groups. Five patients had a surgical method change, and one patient received general anesthesia due to failed spinal anesthesia. Consequently, 51 patients (Group P n = 16, Group C n = 18, Group A n=17) were included in the study (Figure 1).

Age, sex, BMI, ASA status, duration of surgery (min), duration of anesthesia (min), intraoperative ephedrine and atropine consumption were similar between the groups (p>0.05) (Table 1). The three groups were similar in terms of mean heart rate and mean arterial blood pressure (p>0.05) (Figure 2 and 3). T10 sensory block, time to Bromage 3 block, mean maximal sensory level, time to regression to Bromage 2, time to resolution of motor blockade were similar between the groups (p>0.05) (Table 2). Time to 2-segment regression of sensory block was longer in patients who received pregabalin compared with Group A and C (p<0.05), as shown in Table 2.

Tramadol consumption was lower in Group P and A compared with Group C (Group P= 178.75 mg, Group C= 318.61 mg, Group A= 236.47 mg, p <0.05) and was similar between Group P and Group A (p>0.05), as shown in Table 3. The first analgesic requirement was earlier in Group C than Group P and A (p=0.001), and no obvious differences were observed between Group A and Group P (Table 3). The number of PCA demands, number of patients who required rescue analgesics and the amount used were similar between the groups (p>0.05) (Table 3). The rest NRS score at 8 hours was significantly lower in Group P and A compared with Group C (p= 0.040, p= 0.049, respectively) and the rest NRS score was similar between Group P and Group A (Figure 4). The dynamic NRS score at 8 hours was
lower in Group A than in Group C and was similar between Group P and Group A (p= 0.022) (Figure 5). The rest and dynamic NRS score were found similar in the other time interval (Figure 4 and 5).

The fast-tracking score was higher in Group P than in Group C at 8 and 12 hours and was found similar in the other time interval (p<0.005) (Figure 6). The fast-tracking score was similar between Group P and Group A in the all-time interval (p>0.05) (Figure 6). Also, the fast-tracking score was similar between Group A and Group C in the all-time interval (p>0.05) (Figure 6).

Two patients in each group developed nausea and vomiting and one patient in Group P had drowsiness. Itchiness was observed in one patient in Group A, urinary retention in three patients in Group A and in one patient in each of the Groups P and C. None of the patients reported headache, dry mouth, voiding difficulties, diplopia or confusion.
4. Discussion

In this study, patients who received pregabalin and ACB had significantly lower consumption of opioids than the control group. The first analgesic requirement was earlier in Group C than Group P and A. Also, the regression of sensory block was significantly slower in the pregabalin group. Finally, in Group P, the number of patients reaching the maximum total fast-track score at the eighth hour was higher than in the control group.

Although ACLR, compared with conventional knee surgery, is less invasive in nature, patients can still experience moderate to severe post-arthroscopic pain. Inadequate postoperative analgesia can delay discharge, increase unplanned admission and readmission after discharge, delay functional recovery, and reduce patient satisfaction with ACLR [1, 3, 12]. Although opioids have side effects, they still have an important role in postoperative pain management [6]. To reduce opioid-related side effects, multimodal analgesia, including local infiltration analgesia, NSAIDs, peripheral nerve blocks, and other adjuncts like pregabalin has been suggested [2]. Because of all these reasons, we used ACB from periferic blocks and pregabalin from adjuvant agents in the management of postoperative analgesia.

Pregabalin is an analgesic anticonvulsant with anxiolytic effects. It is frequently used in the treatment of chronic neuropathic pain but has recently been increasingly used in the treatment of acute pain [17]. As a part of multimodal analgesia, pregabalin reduces opioid consumption and relieves postoperative pain in patients undergoing knee surgery [11]. Likewise, ACB is applied to reduce postoperative pain and opioid consumption in patients undergoing knee surgery [12]. There is no proof of superiority between the methods yet. Each of the methods has adverse effects. For example, pregabalin may cause dose-dependent adverse effects, which mainly include somnolence, sedation, and dizziness [9]. Conversely, ACB can cause adverse effects such as prolonged motor block and quadriceps weakness [18].
The effectiveness of a single preoperative dose of pregabalin on postoperative analgesia has been explained by a theory using an electrical hyperalgesia model. The theory showed that pregabalin reduced central sensitization and exerted anti-hyperalgesic effects during and immediately after surgery [19]. Different doses of pregabalin (75, 150, 300, 600 mg, etc.) are preferred in acute pain, but higher doses have been associated with more adverse effects. A few studies have shown that a single preoperative oral dose of pregabalin 150 mg can reduce postoperative pain and adverse effects in patients undergoing orthopedic surgeries, as well as other surgeries [4, 10, 11]. In this study, we also used the lowest effective dose of preoperative 150 mg pregabalin, which was similarly effective with the literature.

In a study conducted on patients undergoing spinal surgery, Fujita et al. [7] found that morphine consumption and postoperative pain scores decreased in the pregabalin group. Nader et al. [12], in a study conducted on patients who underwent total knee arthroplasty and received either adductor canal blockade or saline, found that ACB effectively reduced pain and opioid requirement in the postoperative period. In this study, opioid consumption was similar between the pregabalin and adductor groups and was significantly lower in these groups compared to the control group during the 24-hour postoperative period. Rest and dynamic NRS scores were similar in all the three groups with the contribution of spinal anesthesia up to the eighth hour. Rest and dynamic NRS scores were lower in both pregabalin and ACB groups at the eighth hour compared to the control group. This may be due to the relatively long half-life of pregabalin with consequent prolongation in sensory block [20].

Studies assessing sensory and motor block characteristics following the use of a single dose of pregabalin in patients receiving regional anesthesia are limited. Cegin et al. [21] compared the pregabalin and control group in patients undergoing upper extremity bone surgery under the infraclavicular block. They found that the sensorial block termination durations were prolonged in the pregabalin group, but the duration of the motor block did not change. Park et
al. [22] compared the effectiveness of pregabalin in patients under spinal anesthesia and reported that a single dose of preoperative pregabalin significantly prolonged the duration of sensory, motor blockade, and two-segment sensory regression, and reduced the total opioid consumption compared to placebo. Kampitak et al. [23] performed postoperative single-injection ACB or local infiltration analgesia in patients undergoing total knee arthroplasty under spinal anesthesia and found no difference between the groups in terms of time to first request for analgesia. The total morphine consumption was, however, lower in the ACB group. In this study, it was found that the time to two-segment regression of sensory block was longer in patients who received pregabalin compared to the ACB and control group. The duration of motor block and time to regression of motor block was similar between the groups. This study showed that oral 150 mg pregabalin administered one hour before spinal anesthesia prolongs only sensory blocks induced by spinal bupivacaine anesthesia. The mechanisms by which pregabalin premedication prolongs sensory blocks using local anesthetics in spinal anesthesia are not clear. Evoked pain during movement is enhanced by central neuronal sensitization [22, 24], and the permanent pregabalin effects observed in our study may be thought to have been caused by preoperative pregabalin preventing central nervous system sensitization. Regarding to our opinion, although groups differed with regards to 2-segment regression of sensory block, combined peripheral nerve block in Group A may have prolonged the time to first request for analgesia reducing the total opioid consumption in this group and eventually leading to a similarity in total opioid consumption between the two groups.

The effective reduction of pain in the postoperative period in knee surgery has contributed to the rapid disappearance of undesirable motor blockade and shorter discharge time [12]. Nader et al. [12] compared the ACB and the control group and found that ACB provides better analgesia and shorter discharge time. They suggested that ACB should be part of the “fast-
track protocol” in patients undergoing total knee arthroplasty. In this study, in Group A, we did not observe superiority in fast-tracking compared to the control and pregabalin group. In Group P, however, the number of patients reaching the maximum total fast-track score at the eighth hour was higher than in the control group. In other words, patients in the pregabalin group could be ready for discharge from the eighth hour. According to the postoperative routine discharge protocol in our hospital, patients are not discharged during the first 24 hours. Therefore, we could not discharge the patients according to their fast-tracking scores.

Several studies have shown that postoperative pain could persist for two to six weeks after discharge, this could limit a patient’s participation in daily activities [4]. Additionally, poorly controlled postoperative pain may lead to chronic pain [25]. Even though studies have shown that preoperative pregabalin provides longer analgesia [26], in this study, we did not follow up on chronic pain. A potential limitation of this study is the relatively short postoperative follow-up period. Another limitation is that the volume (10 ml) used for ACB was lower than that used in clinical practice (i.e., 15mL, 20 mL vs. 25 mL). Because the higher volume used may influence the incidence of quadriceps muscle weakness. A comparison of different doses of bupivacaine may be performed in subsequent studies.

Conclusion

Preoperative pregabalin provides postoperative analgesia as effective as ACB. In addition, pregabalin can provide a shorter time to achieve high fast-tracking scores in patients with ACLR. Pregabalin group was found to be superior in terms of sensory block duration compared to ACB and control group. However, we observed that this advantage did not differ between pregabalin and ACB groups in terms of postoperative total opioid consumption. We recommend that both methods should be adopted as part of multimodal analgesia.
Ethics Committee Approval: Ethical Committee of the Ministry of Health Diskapi Yıldırım Beyazit Training and Research Hospital in Ankara, Turkey (Ethical Committee 29.01.2018 No: 45/17)

Informed Consent: Consent form was filled out by all participants.

Peer-review: External and internal peer-reviewed.

Authorship Contributions


Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.
Appendix 1. White's Fast Track Scoring System

I. Level of consciousness

Awake and oriented – 2
Arousable with minimal stimulation – 1
Responsive only to tactile stimulation – 0

II. Physical activity

Able to move all extremities on command – 2
Some weakness in movement of extremities – 1
Unable to voluntarily move extremities – 0

III. Hemodynamic stability

Blood pressure of 15% of baseline – 2
Blood pressure of 30% of baseline – 1
Blood pressure of 50% of baseline – 0

IV. Respiratory stability

Respiratory rate 10–20 breaths/min, able to breathe deeply – 2
Tachypnea with good cough – 1
Dyspneic with weak cough – 0

V. Oxygen saturation status

Maintains value 90% while breathing room air – 2
Requires supplemental oxygen to maintain saturation of 90% – 1
Saturation <90% with supplemental oxygen – 0

VI. Postoperative pain assessment

No or mild discomfort – 2
Moderate-to-severe pain controlled with intravenous analgesics – 1
Persistent moderate-to-severe pain – 0

VII. Postoperative emetic symptoms

No or mild nausea with no active vomiting – 2

Transient vomiting or retching controlled with intravenous antiemetics – 1

Persistent moderate-to-severe nausea and vomiting – 0

References


Figure 1. Flow Chart
Figure 2. Mean Blood Pressure.

Data were expressed as mean ± SD. Min=minute, hr=hour, postop=postoperative.

Figure 3. Heart rate.

Data were expressed as mean ± SD. Min=minute, hr=hour, postop=postoperative.
Figure 4. Rest NRS Score

These box plots display the median and 25th and 75th percentiles of Numeric Rating Scale (pain at rest) rating at different time points, asterisk extreme outliers, open circles slight outliers.

* Significant compared to the control group (p = 0.040)

& Significant compared to the control group (p = 0.049)
Figure 5. Dynamic NRS score

These box plots display the median and 25th and 75th percentiles of Numeric Rating Scale rating at different time points, asterisk extreme outliers, open circles slight outliers.

& Significant compared to the control group (p:0.022)
Figure 6. These box plots display the median and 25th and 75th percentiles of White Fast Track Scores rating at different time points, asterisk extreme outliers, open circles slight outliers.

* Significant compared to the control group (p<0.05).
Table 1. Demographic data

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group P (n=16)</th>
<th>Group C (n=18)</th>
<th>Group A (n=17)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>29.50±9.49</td>
<td>33.27±14.06</td>
<td>28.76±8.26</td>
<td>0.434</td>
</tr>
<tr>
<td>Body mass index (kg/m(^2))</td>
<td>27.59±3.90</td>
<td>27.45±5.69</td>
<td>26.09±2.89</td>
<td>0.549</td>
</tr>
<tr>
<td>Sex (female/male) (n)</td>
<td>2/14</td>
<td>3/15</td>
<td>3/14</td>
<td>0.690</td>
</tr>
<tr>
<td>ASA status (I/II) (n)</td>
<td>9/7</td>
<td>9/9</td>
<td>10/7</td>
<td>0.864</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>80.25±35.20</td>
<td>75.50±26.94</td>
<td>80.76±24.13</td>
<td>0.839</td>
</tr>
<tr>
<td>Duration of anesthesia (min)</td>
<td>90.68±33.80</td>
<td>84.94±26.71</td>
<td>90.05±23.94</td>
<td>0.807</td>
</tr>
<tr>
<td>Intraoperative ephedrine (mg)</td>
<td>0 (0-20)</td>
<td>0 (0-20)</td>
<td>0 (0-10)</td>
<td>0.632</td>
</tr>
<tr>
<td>Intraoperative atropine (mg)</td>
<td>0 (0-0.5)</td>
<td>0 (0-0.5)</td>
<td>0</td>
<td>0.391</td>
</tr>
</tbody>
</table>

The data are presented as mean ± SD, median (IQR).

Table 2. Onset time and duration of sensory and motor blocks.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group P (n=16)</th>
<th>Group C (n=18)</th>
<th>Group A (n=17)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to T10 sensory block (min)</td>
<td>6.43±3.61</td>
<td>5.44±1.94</td>
<td>5.29±1.86</td>
<td>0.388</td>
</tr>
<tr>
<td>Time to Bromage 3 block (min)</td>
<td>9.37±4.44</td>
<td>9.33±3.80</td>
<td>9.17±3.28</td>
<td>0.980</td>
</tr>
<tr>
<td>Mean of the maximal sensory level (dermatome)</td>
<td>8 (6-10)</td>
<td>6 (6-10)</td>
<td>6 (5-10)</td>
<td>0.537</td>
</tr>
<tr>
<td>Time for two segment regression of sensory block (min)</td>
<td>70 (60-112.5)(^a)</td>
<td>47.5 (45-63.75)</td>
<td>50 (45-60)</td>
<td>0.008</td>
</tr>
<tr>
<td>Time for regression to Bromage 2 (min)</td>
<td>120 (75-180)</td>
<td>120 (120-180)</td>
<td>120 (120-130)</td>
<td>0.686</td>
</tr>
<tr>
<td>Time to resolution of the motor blockade (min)</td>
<td>240 (180-292.5)</td>
<td>235 (207.5-255)</td>
<td>240 (200-290)</td>
<td>0.824</td>
</tr>
</tbody>
</table>

The data are presented as mean ± SD, median (IQR).

\(^a\) According to the Bonferroni correction Group P was different than Group C and A (p=0.020, p=0.039 respectively).
Table 3. Postoperative Features

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group P (n=16)</th>
<th>Group C (n=18)</th>
<th>Group A (n=17)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tramadol consumption 24 hour (mg)</td>
<td>178.75±65.40(^a)</td>
<td>318.61±127.89(^a)</td>
<td>236.47±80.69(^a)</td>
<td>0.001</td>
</tr>
<tr>
<td>Number of PCA demand (n)</td>
<td>27 (17-51)</td>
<td>51 (38-84)</td>
<td>40 (23-65)</td>
<td>0.220</td>
</tr>
<tr>
<td>Total rescue analgesic consumption (mg)</td>
<td>0 (0-50)</td>
<td>25 (0-100)</td>
<td>0 (0-50)</td>
<td>0.174</td>
</tr>
<tr>
<td>Number of rescue analgesics (n)</td>
<td>6</td>
<td>9</td>
<td>5</td>
<td>0.469</td>
</tr>
<tr>
<td>Time of first analgesia requirement (min)</td>
<td>386.25±47.59</td>
<td>272.77±45.21(^c)</td>
<td>343.52±66.51</td>
<td>0.001</td>
</tr>
</tbody>
</table>

The data are presented as mean ± SD, median (IQR).

\(^a\) According to the Bonferroni correction, Group C was different than Group P and A (p=0.001, p=0.046 respectively).

\(^b\) According to the Bonferroni correction, Group P was similar to Group A (p=0.277).

\(^c\) According to the Bonferroni correction, Group C was different than Group P and A (p=0.001, p=0.002 respectively).