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Comparison of tramadol/acetaminophen fixed-dose combination, tramadol, and acetaminophen in patients undergoing ambulatory arthroscopic meniscectomy

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ABSTRACT

Objectives: Preemptive analgesia is a technique in which analgesics are administered before a surgery to provide better postoperative pain relief with fewer side effects. In this study, we aimed to compare the preemptive efficacy of tramadol/acetaminophen fixed-dose combination, tramadol, and acetaminophen in patients undergoing ambulatory arthroscopic partial meniscectomy.

Methods: We evaluated the patient records of 75 patients who underwent ambulatory arthroscopic partial meniscectomy. We divided the patients into three groups consisting of 20 patients each to equalize the groups. Group A comprised patients who were administered 37.5 mg tramadol/325 mg acetaminophen fixed-dose combination, Group B comprised patients who were administered 50 mg tramadol, and Group C comprised patients who were administered 500 mg acetaminophen. Premedication was not used in any group.

Results: There were no significant differences between the groups in terms of age, sex, BMI, and duration of surgery and anesthesia. All patients in Group B and Group C and 17 patients in Group A required rescue analgesics in the first 6 h. Visual analog scale (VAS) was 4.75 ± 3.05 in Group B at time 0 and was 6.10 ± 1.86 in Group C in the first hour and was higher than the other groups with a statistically significance ($p = 0.030$ and 0.020, respectively). VAS at 24 h postoperatively was ≤3 (1.60 ± 1.63, 1.55 ± 1.84 and 1.70 ± 0.65 respectively in each group), and none of the patients in any group required rescue analgesics. No major side effects, except for slight nausea in one patient requiring no medication, were noted in any group.

Conclusion: The fixed-dose combination of tramadol/acetaminophen or tramadol alone is better than acetaminophen alone as a preemptive analgesic in patients undergoing ambulatory arthroscopic meniscectomy.

Level of evidence: Level III, therapeutic study.

Introduction

Knee is the most common joint subjected to arthroscopy. Arthroscopic meniscectomy is associated with moderate to severe postoperative pain due to insertion of arthroscopic instruments into the joint, soft tissue dissection, and distension caused by irrigation of the joint.[1–3] Inadequate management of postoperative pain results in increased morbidity, delayed discharge, and decreased patient satisfaction after surgery.[4,5] Preemptive analgesia is a new technique that has been applied over the last two decades. In this technique, analgesics are administered before the painful stimuli to prevent amplification of postoperative pain,

Abbreviations: PACU, post-anesthesia care unit; NNT, number needed to treat; BMI, body mass index.

This study was carried on Süleyman Demirel University School of Medicine Orthopedics and Traumatology and Anaesthesiology and Reanimation Departments after the approval of the ethical committee (2017/115).

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resulting in better postoperative pain relief with fewer side effects, shorter hospital stay, faster recovery, and lesser social burden.[6–10] Among the medications used are local anesthetics, non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen, opioid, gabapentinoids and magnesium sulfate alone or in combination with local anesthetics.[11–13] In preemptive analgesia, the agents can be used either alone or in combination to increase the analgesic effect via different mechanisms and to reduce the incidence of side effects.[8,14] This approach increases postoperative patient satisfaction, while minimizing systemic narcotic use and reducing the undesirable side effects of narcotics, such as nausea, vomiting, sedation, and respiratory depression.[5,15] Although NSAIDs are mostly used for preemptive analgesia, they are associated with major side effects such as irritation of the gastrointestinal mucosa and inhibition of platelet activation. In addition, they are not an ideal choice as preemptive analgesic in orthopedic surgery owing to perioperative bleeding via cyclooxygenase (COX)-1 isoenzyme.[5,12,16]

Considering the side effects of NSAIDs via COX-1 isoenzyme, selective COX-2 inhibition seems to be a good choice for postoperative pain management.[5] Acetaminophen is the most widely used non-opioid analgesic. It acts centrally, and its pharmacological profile is similar to that of selective COX-2 inhibitors in that it increases pain threshold through nitric oxide system and does not inhibit prostaglandin synthesis or irritate the gastrointestinal mucosa.[17,18]

Orthopedic postoperative patients who have a high incidence of severe pain are responsive to the combination of acetaminophen and opioids as an alternative to NSAIDs.[19] It was reported that almost all patients who underwent arthroscopic meniscectomy were required to be hospitalized for relieving unbearable pain with the help of high-dose opioids. However, many of these patients complained from side effects of opioids, such as sedation and respiratory depression[3,5,15] Considering the side effects and addiction of opioids, tramadol, an inhibitor of both mild μ-opioid receptor binding and norepinephrine and serotonin (5-HT) reuptake, seems to be a good alternative.[19] Furthermore, combining tramadol with acetaminophen provides a unique example of the potential benefits of combination therapy[16,20] The combination of tramadol and acetaminophen results in synergistic analgesia, faster onset, and longer duration of action than either component alone, particularly in orthopedic surgery.[16,19,21]

To the best of our knowledge, no study has so far compared the preemptive analgesic efficacy of tramadol, acetaminophen, and tramadol/acetaminophen fixed-dose combination in the management of postoperative pain within the first 24 h of ambulatory arthroscopic partial meniscectomy. Considering the side effects of opioids and NSAIDs used for pain management after arthroscopic meniscectomy we aimed to compare the preemptive efficacy of opioids and NSAIDs in patients who underwent ambulatory arthroscopic partial meniscectomy as they have fewer side effects in these patients.

Patients and methods

The medical records of 94 patients, who underwent ambulatory arthroscopic partial meniscectomy under general anesthesia and had preemptive analgesia in 2016, were retrospectively evaluated after obtaining the approval of the local ethics committee (year: 2017, no: 115). The inclusion criteria were as follows: age 18–50 years old; underwent ambulatory arthroscopic partial meniscectomy; operation time <1 h, chondral lesions ≤ grade 2, having an American Society of Anesthesiologists (ASA) score ≤ 3, and preoperative visual analog scale (VAS) score < 3 or no pain at rest. The patients with knee instability due to cruciate or collateral ligament injuries or both, cartilage damage requiring surgical interventions, lower extremity mal-alignment due to congenital, acquired, or traumatic lower extremity deformities, missing informed consent, lack of cooperation capability, cancer co-morbidity, osteoarthritis or rheumatoid arthritis, alcohol or drug abuse, previous major surgery on the affected joint, neurologic or psychiatric disease, allergy to any of the drugs, known heart, kidney, liver, or hematological diseases, history of gastrointestinal bleeding, chronic pain, routine use of analgesics, or those who had taken analgesic agents within the last 48 h were excluded from the study.

Seventy-five of the 94 patients who fulfilled the inclusion criteria were included in the study. The evaluation of patient records of these 75 patients showed that preemptive analgesia with 37.5 mg tramadol + 325 mg acetaminophen was administered in 26 patients, 50 mg tramadol in 29 patients, and 500 mg acetaminophen in 20 patients. Based on the results of a previous study[22] and the assumption that a difference of 20 units in postoperative pain scores in VAS is clinically relevant, the effect size was defined as 2, with an estimated standard deviation of ±2. By setting $\alpha = 0.05$ and power to 0.9, we calculated a minimum sample size of 18 patients/group, and the patients were divided into three groups of 20 patients each to equalize the groups.

Group A comprised patients who were administered 37.5 mg tramadol/325 mg acetaminophen fixed-dose combination (Zaldiar® 37.5 mg/325 mg film-coated tablet; Abdi İbrahim, İlaç San. ve Tic. A.Ş., İstanbul/Turkey), Group B comprised patients who were administered 50 mg tramadol (Contramal® 50 mg; Abdi İbrahim), and Group C comprised patients who were administered 500 mg acetaminophen (Parol® 500 mg tablet, Atabay Kimya San. ve Tic. A.Ş., Turkey). Premedication was not used in any group. Preemptive agents were orally administered 1 h before surgery owing to onset of analgesic efficacy.[23]

Anesthesia and surgical procedure

All surgical procedures were performed under general anesthesia after monitoring through standard anteromedial and anterolateral arthroscopic portals under a tourniquet pressure of 300 mm Hg by the same surgical team. After monitoring, 2–3 mg/kg propofol and 3–4 μg/kg remifentanil were administered intravenously for induction. After tracheal intubation, the patients received mechanical ventilation, and the remainder of anesthesia was performed using 1–1.2% isoflurane and a mixture of N_2O and O_2 in equal proportions. Once the operation ended, muscle relaxation was reversed by 0.04 mg/kg neostigmine and atropine intravenously. Postoperative parameters, namely, electrocardiography, non-invasive systolic and diastolic blood pressure, and the duration of anesthesia and surgery were recorded.

Following surgery, the patients were transferred to post-anesthesia care unit (PACU). After the patients regained full consciousness in PACU (time = 0) and at 1, 2, 6, 12, and 24 h after surgery, a VAS assessment was performed by an anesthesiologist. As a rescue analgesic, 8 mg of intravenous lornoxicam (XEFO, Abdi İbrahim, Turkey) at maximum daily doses (2 × 1) were administered to patients with a VAS > 3. All patients were discharged 24 h postoperatively. An anesthetist performed postoperative pain assessment before discharge.

The primary outcomes in the postoperative period (first 24 h) were pain intensity measured by VAS score and time of rescue analgesic consumption. The secondary outcome was side effects of the agents administered in different groups.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences v. 15.0 (SPSS Inc., Chicago, IL, USA). Data were

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