Effects of a Single-Dose of Pre-Emptive Pregabalin on Postoperative Pain and Opioid Consumption After Double-Jaw Surgery: A Randomized Controlled Trial

Ali Ahiskalioglu, MD, [*] *İlker İnce, MD,* [†] *Mehmet Aksoy, MD,* [‡] *Ertan Yalcin, DDS, PhD,* [§] *Elif Oral Ahiskalioglu, MD,* [‖] *and Adnan Kilinc, DDS, PhD* [¶]

Purpose: The effect of a single-dose of pre-emptive pregabalin is still unknown, although it is used as an adjuvant in controlling acute postoperative pain. The purpose of this study was to evaluate the effects of pre-emptive single-dose pregabalin on postoperative acute pain and 24-hour opioid consumption in patients who underwent double-jaw surgery.

Patients and Methods: Forty patients (18 to 45 yr old; American Society of Anesthesiologists status I to II) for whom elective double-jaw surgery was planned under general anesthesia were included in this study, which had been planned as a prospective, randomized, and double-blinded study. Patients were randomly divided into 2 groups: the pregabalin group (n = 20) was given pregabalin 150 mg orally 1 hour before general anesthesia and the placebo group (n = 20) was given an oral placebo capsule. The groups were administered the routine general anesthesia protocol. Postoperative analgesia was performed intravenously in the 2 groups twice a day with dexketoprofen trometamol 50 mg and patient-controlled analgesia with fentanyl. Postoperative analgesia was evaluated using the visual analog scale (VAS). Fentanyl consumption, additional analgesia requirement, and side-effects were recorded during the first 24 hours after surgery. Descriptive and bivariate statistics were computed, and significance was set at a P value less than .05.

Results: Compared with placebo, the VAS score was statistically lower in the pregabalin group during the early postoperative period ($P < .05$). The 24-hour opioid consumption was significantly higher in the placebo group compared with the pregabalin group (509.40 $\pm$ 261.56 vs 260.10 $\pm$ 246.53 μq, respectively; $P = .004$). In addition, the analgesia requirement was statistically lower in the pregabalin group ($P < .05$). Nausea or vomiting was observed more often in the placebo group, whereas other side-effects were similar for the 2 groups.

Conclusion: A single 150-mg dose of pre-emptive pregabalin decreased postoperative opioid consumption in the first 24 hours after double-jaw surgery. Multimodal analgesia techniques that contain pre-emptive analgesia can be used successfully in preventing postoperative pain caused by orthognathic surgery.

J Oral Maxillofac Surg 74:53.e1-53.e7, 2016

[*]Assistant Professor, Department of Anesthesiology and Reanimation, Ataturk University School of Medicine, Erzurum, Turkey.

[†]Assistant Professor, Department of Anesthesiology and Reanimation, Ataturk University School of Medicine, Erzurum, Turkey.

[‡]Assistant Professor, Department of Anesthesiology and Reanimation, Ataturk University School of Medicine, Erzurum, Turkey.

[§]Assistant Professor, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Ataturk University, Erzurum, Turkey.

[‖]Anesthetist, Department of Anesthesiology, Regional Training and Research Hospital, Erzurum, Turkey.

[¶]Assistant Professor, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Ataturk University, Erzurum, Turkey.

Address correspondence and reprint requests to Dr Ahiskalioglu: Department of Anesthesiology and Reanimation, Ataturk University School of Medicine, Yakutiye Research Hospital, 25070, Palandöken, Erzurum, Turkey; e-mail: aliahiskalioglu@hotmail.com

Received July 27 2015

Accepted September 13 2015

0278-2391/15/01276-8

http://dx.doi.org/10.1016/j.joms.2015.09.008

Orthognathic surgery is used for correcting congenital or developmental anomalies of the maxilla and mandible and secondary deformities of trauma.[1]

Maxillary and mandibular retrusions are dentofacial deformities that most frequently require orthognathic surgery. These deformities are followed by maxillary vertical insufficiency and mandibular progeny.[2] In the treatment of these deformities, double-jaw surgery and bilateral split ramus osteotomy (BSSO) are used for mandibular surgery, whereas Le Fort I osteotomies are used for maxillary surgery. During these procedures, saws, chisels, separators, and plate-and-screw systems are used. Infections, migrations, heat sensitivity, and pain are the disadvantages of these systems. Furthermore, inferior alveolar nerve damage can cause postoperative pain.[3,4]

Postoperative pain is an acute pain that is accompanied by an inflammatory process that occurs as a result of surgical trauma and gradually decreases with tissue recovery. However, it differs from other acute pain because its etiology is known beforehand and therefore expected.[5]

Experimental studies have shown that analgesic administration preceding surgical injury can lessen post-traumatic sensitivity and secondary hyperalgesia in the spinal cord.[6] If analgesic treatment is begun after a painful stimulant, peripheral hypersensitivity and central nervous system hyperexcitability can develop, and challenges can be encountered in the postoperative pain treatment of such cases.[7]

Different explanations have been made for preemptive analgesia. The analgesic prevents the establishment of central sensitization from incisional injury (only during the surgical period) and prevents the establishment of central sensitization from incisional and inflammatory injury (during the surgical and early postoperative periods).[8]

Pregabalin is a structural γ-aminobutyric acid analog. The mechanism of pregabalin is not completely known.[9] Pregabalin also decreases the release of many neurotransmitters, including glutamate, noradrenalin, substance P, and calcitonin gene-related peptide.[10] Recent studies have reported that pregabalin, which is used in the treatment of persistent pain, also can be used for the treatment of acute postoperative pain.[11-13]

The primary purpose of this study was to research the effects of a single 150-mg pre-emptive dose of pregabalin on postoperative analgesia and opioid consumption in patients who underwent double-jaw surgery.

Patients and Methods

Forty patients 18 to 45 years old with American Society of Anesthesiologists (ASA) status I to II undergoing elective orthognathic surgery were included in the study. This study was approved by the institutional review board of Ataturk University Hospital (Erzurum, Turkey) and all participants signed an informed consent agreement. The study was planned as a prospective, randomized, and double-blinded study.

Included were patients 18 to 45 years old with ASA status I to II who were undergoing elective double-jaw surgery. Excluded were patients who had an ASA status of at least III, were allergic to the active substance pregabalin, were using antiepileptic medications, had severe hepatic and renal insufficiency (liver enzyme levels, >3-fold of normal values; creatinine levels, >1.5 mg/dL), were pregnant or breastfeeding, refused to participate, reported long-term use of nonsteroidal anti-inflammatory and opioid analgesics, had diabetes, had other neuropathic diseases, and were unable to use the patient-controlled analgesia (PCA) device.

The patients were informed about the study protocol, the pain scale of the visual analog scale (VAS), and the PCA device that was to be used postoperatively for analgesia. Patients were divided randomly into 2 groups by a computer program; the pregabalin group (n = 20) was given pregabalin (Alyse; Abdi Ibrahim, Istanbul, Turkey) 150 mg orally 1 hour before anesthesia induction, and the placebo group (n = 20) was given an oral placebo capsule. The placebo capsule, which was prepared by a pharmacist, contained lactose powder and had the same size, taste, and color as the study drug.

Patients were administered midazolam 1 mg for premedication purposes. Vascular access was obtained with a 20-gauge intravenous catheter and a crystalloid (6 mL/kg) was infused. All patients were observed by standard electrocardiography, peripheral oxygen saturation, and noninvasive blood pressure monitoring.

Anesthesia was administered in the 2 groups using propofol (Fresenius Kabi, Bad Homburg, Germany) 2 mg/kg intravenously and rocuronium (Esmeron; GlaxoSmithKline, Brentford, UK) 0.6 mg/kg intravenously for muscle relaxation. After applying nasal intubation, rocuronium 0.1 mg/kg was administered for muscle relaxation during the operation whenever necessary. Maintenance of anesthesia was provided by 1.5% sevoflurane (Sevorane; Abbott Laboratories, Abbott Park, IL) and fentanyl 50 μg/hour, 50% N_2O in oxygen, and 50% O_2 in air (tidal volume, 6 to 8 mL/kg; frequency, 10/minute). During the operation, fentanyl 1 μg/kg was administered when an additional analgesic dose of anesthesia did not reverse the sudden increase in heart rate and mean arterial pressure values and the 50% increase in gas concentration.

For each patient, the inferior alveolar, buccal, and lingual nerves were infiltrated with 2% articaine 80 mg in addition to 1:200,000 epinephrine (Ultracain