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Sedative-analgesic activity of remifentanil and effects of preoperative anxiety on perceived pain in outpatient mandibular third molar surgery

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Abstract. The aim of this study was to assess the sedative-analgesic activity of different doses of remifentanil and effects of preoperative anxiety on intraoperative pain levels in patients attending a dental clinic. The patients ($n = 60$) were divided into two groups according to the remifentanil infusion dose given: group R_1: 0.05 μg/kg/min; group R_2: 0.1 μg/kg/min. The following were evaluated: haemodynamic parameters, State-Trait Anxiety Inventory (STAI) TX-I score, pain level due to local anaesthesia injection, time to reach a Ramsay Sedation Scale (RSS) score of 3, amount of bolus dose, total drug consumption, recovery period, patient and surgeon satisfaction, and complications. The patient satisfaction score on a visual analogue scale (VAS) was 90 in group R_1 and 100 in group R_2 ($P = 0.008$); the surgeon satisfaction score was 80 in group R_1 and 90 in group R_2 ($P = 0.004$). The time to reach an RSS score of 3 and the amount of bolus dose were significantly lower in group R_2 than in group R_1. High levels of anxiety did not affect intraoperative pain levels. In conclusion, high doses of remifentanil can safely be used for various same-day dental surgery interventions.

Key words: outpatient anaesthesia; remifentanil; preoperative anxiety; third molar surgery.

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The use of outpatient anaesthesia procedures has increased in dentistry, especially among patients considering maxillofacial surgery. Sedative-analgesia is needed in maxillofacial surgery because of the sensation of pain caused by local and regional anaesthesia applied prior to the procedure, the sensation of pressure during the procedure, and high levels of anxiety due to the fear of dental treatment.

Outpatient anaesthesia is an easy procedure associated with high patient and operator satisfaction. It is performed in many clinics, particularly for painful interventions that cause patient discomfort.[1,2]

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The required level of anaesthesia depends on the targeted level of consciousness, severity of pain, and other negative stimuli. Several studies have examined the optimum anaesthetic drug combinations and dosages in various procedures.[3,4] They have also investigated the sedative-analgesic activity of different anaesthetics, including remifentanil, fentanyl, dexmedetomidine, midazolam, and their combinations, in various dental interventions.[1,5,6] Midazolam and opioids are the most commonly used anaesthetic drugs.

Although midazolam provides a good quality of sedation, it does not have analgesic activity and has an extended hypnotic effect at high doses.[1,7] Therefore, there are concerns about single usage of this drug. Hence, midazolam is frequently combined with opioids. Opioids are preferred because they provide haemodynamic stability, even at high concentrations. They also have analgesic activity and reduce the need for hypnotics. However, opioids may cause intraoperative or postoperative problems, such as respiratory depression, nausea, and vomiting. They can also have an extended time of action.[7] In contrast, remifentanil has a short duration of action due to its pharmacokinetic profile, which differs from that of other opioids.

The pharmacokinetic profile of remifentanil decreases the aforementioned side effects of opioids.[7] As a result, remifentanil has become the preferred agent for the treatment of anxiety during many surgical procedures.[2,4]

In dentistry, fear and anxiety are common symptoms observed in patients in the preoperative period.[8] Preoperative anxiety arises from the patient not knowing what they will encounter during the procedure and concerns about the pain they might feel. Many negative side effects of patient anxiety have been reported,[9] and many studies have reported a correlation between anxiety and the sensation of pain.[10,11] However, few studies have been performed on the pain felt in the intraoperative period.[12,13]

This study aimed to investigate the optimum dose of remifentanil during mandibular third molar surgery to ensure surgeon and patient satisfaction and a speedy recovery. A second aim was to evaluate the effect of preoperative anxiety in patients scheduled to undergo mandibular third molar surgery on the perceived level of pain during the intraoperative period.

Materials and methods

Study design

This was a double-blind, prospective, randomized clinical study. Sixty patients aged 18–60 years who were scheduled to undergo impacted mandibular third molar surgery (class IIB, Pell and Gregory classification) and had an ASA score of I or II (American Society of Anesthesiology) were included in the study.[14] Third molars without pathological lesions such as cysts, tumours, and pericoronitis were included in the study. The number of patients was determined on the basis of a power analysis (according to an independent two-sample *t*-test). All of the patients were informed about the procedure. Exclusion criteria were severe systemic disease, pregnancy, and an allergy to the anaesthetics to be used in the procedure. Patients were also excluded if they were taking benzodiazepines, antidepressants, or any other psychotropic medications. In addition, patients who did not reach the level of sedation required (a Ramsay Sedation Scale (RSS) score of 3) and in whom anaesthesia could not be achieved in the surgical area after a local anaesthesia injection were excluded from the study, and their dental treatment was re-scheduled.

After surgery, the patient's vital signs were monitored closely and they were discharged 1 h later. Patients were discharged with a companion and asked not to drive an automobile for 12 h. The same surgical team performed all of the surgical procedures. The patients, surgeons, and assistant medical personnel were blinded to the remifentanil doses that were administered. The surgeon did not enter the surgical suite until the patient had been sedated by the anaesthetist. The patients in the study were randomized by the anaesthesiologist in accordance with a permuted block randomization technique. None of the patients received premedication.

All patients were asked to complete the State-Trait Anxiety Inventory (STAI) TX-I questionnaire form before the procedure.[15] An infusion of 0.9% sodium chloride was started after the patient was placed on the operating table, and vascular access was established with a 20-gauge cannula. The patients were monitored by electrocardiography, and their systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, heart rate, and peripheral oxygen saturation were measured and recorded every 5 min.

A 0.03-mg/kg dose of midazolam (Dormicum 5 mg/5 ml; Roche) and 0.05-μg/kg dose of remifentanil (Ultiva 2 mg; GlaxoSmithKline) were slowly administered intravenously to all patients, followed by an infusion of remifentanil. The patients were divided into two groups according to the remifentanil infusion dose: 0.05 μg/kg/min of remifentanil was administered to group R_1 and 0.1 μg/kg/min was administered to group R_2. The surgeon was asked to apply local anaesthesia with articaine (Ultracaine DS Forte, 1/100 000 2 ml; Sanofi Aventis) 2 min after the infusion had started. After the injection of local anaesthetic, the time to achieve an RSS score of 3 was recorded. The surgeon started the operation after the patient had achieved an RSS score of 3. The RSS score was recorded every 5 min.

In both groups, 0.05 μg/kg of remifentanil was administered intravenously to patients who felt pain or had not reached an intraoperative RSS score of 3. All the bolus doses were recorded. Adverse effects were noted, including nausea, vomiting, respiratory depression (a respiratory rate of <8 breaths per min, or peripheral oxygen saturation <95%), bradycardia (a heart rate of <45 beats per min), and hypotension (when systolic arterial blood pressure decreased more than 20% according to the baseline level, or was below 80 mmHg). The anaesthetic infusion was suspended in these circumstances. Bradycardia was treated with 0.5 mg of atropine; hypotension was treated with 0.1 mg/kg of ephedrine. The infusion was stopped at the end of the procedure, and the patients were transferred to the post anaesthesia care unit. The recovery time was recorded as the duration between the end of the operation and the achievement of a modified Aldrete score of 9. After recovery, the patients were asked to evaluate their pain due to the local anaesthetic injection on a visual analogue scale (VAS; 0 = no pain, 100 = unbearable pain); the results were recorded. In addition, the patients and surgeon were asked to evaluate their satisfaction using a VAS (0 = completely dissatisfied, 100 = completely satisfied). The total drug consumption was calculated and recorded.

STAI

State anxiety refers to various emotions, such as fear, nervousness, and discomfort, which result in the arousal of the autonomic nervous system following exposure to situations perceived as dangerous. State anxiety is temporary and refers to how a person feels at the time of a perceived threat.[15] The STAI consists of a set of questions designed to assess different types of anxiety.[15] There are 20 items in the STAI TX-I. Each of these 20 items is scored from 1 to 4, with 1 denoting 'almost

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