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# A comparison of midazolam and midazolam with remifentanil for patient-controlled sedation during operations on third molars

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**Abstract**

Our aim was to compare patients' satisfaction and cooperation, and clinical efficacy, of midazolam alone, and midazolam and remifentanil for patient-controlled sedation during removal of third molars.

Forty patients, American Society of Anesthesiologists grades I and II, admitted for extraction of impacted mandibular third molars were included in this randomised, prospective study. They were given an intravenous bolus of midazolam 0.03 mg/kg and then allowed to use patient-controlled sedation. In the midazolam group, 2 ml of 0.5 mg/ml midazolam was given automatically. In the midazolam–remifentanil group, 2 ml of 0.5 mg/ml midazolam and 12.5 μg/ml remifentanil were given in the same manner. The lockout period was 5 min. Vital signs and oxygen saturation were recorded. Patients' and surgeons' satisfaction, and the patients' degree of amnesia about the local anaesthetic, drilling, removal of the tooth, and pain during extraction were also assessed.

There were no significant differences between systolic and diastolic blood pressures during sedation, but heart rate after 30 min in the combined group was significantly lower than in the midazolam group ($p < 0.05$). Surgeons described the midazolam group as excellent in 9 and good in 11. In the combined group, satisfaction was excellent in 11, good in 7, and satisfactory or unacceptable in 1 of each.

Immediately postoperatively, 19 patients in each group ranked their satisfaction as excellent and 1 as good. Twenty-four hours later it was unchanged in the midazolam group, while 15 patients in the other group thought it was excellent, 3 good, and 2 poor.

Patient-controlled analgesia with midazolam or midazolam and remifentanil is safe and reliable during extraction of third molars.


*Keywords:* Patient-controlled sedation; Third molar surgery; Remifentanil; Midazolam

## Introduction

Dental treatment often causes fear among patients, and although local anaesthetics make dental treatment easy and painless, dental operations arouse fear and anxiety.[1,2] The use of some form of sedation is therefore common during dental operations.

Conscious sedation is a medically controlled state of depressed consciousness that allows protective reflexes to be maintained, retains the patient's ability to keep an airway patent independently and continuously, and permits appropriate responses to physical stimulation or verbal command. Patient-controlled sedation provides adequate relief for patients, and allows them to vary the degree of sedation according to the amount of stress they feel from the operation and the environment. It is often used for sedation during procedures done under regional or local anaesthesia, and is the preferred technique because the total dose can be titrated according to the patient's needs and regulated according to

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their anxiety. It also lessens the risk of overdose and inadequate sedation. Many studies have shown that this technique is safe and satisfactory.[2,3]

Sedative-hypnotics and opioid analgesics are often used together to improve comfort and provide sedative, anxiolytic, and supplemental analgesia during outpatient operations under local anaesthesia. Systemic analgesia is desirable during the initial infiltration of the local anaesthetic solution to prevent the discomfort associated with deep dissection and traction.[4]

Intravenous midazolam is a well-established sedative agent for such use, particularly in oral surgery under local anaesthesia. Its short duration of action can be counteracted with patient-controlled drugs, which are useful and safe.

Remifentanil is a new congener of the fentanyl family of opioids, the ester structure of which renders it susceptible to widespread hydrolysis, which results in rapid metabolic degradation. Remifentanil is therefore the first ultrashort-acting opioid.[5] Clinically, these properties translate into rapid achievement of a steady-state concentration both in the plasma and at the site of the effect, which produces results quicker but with less accumulation of drug than other opioids, irrespective of the duration of the infusion.

The aim of this study was to compare patients' satisfaction and cooperation, and the clinical efficacy using midazolam alone or a combination of midazolam and remifentanil for patient-controlled sedation for extraction of third molars.

## Patients and methods

Forty patients between the ages of 17 and 37years, American Society of Anesthesiologists grades I and II, who were listed for extraction of impacted mandibular third molars were included in the study; only one extraction was made from each patient. The exclusion criteria were systemic disease, inability to use the handset, history of drug addiction or current use of opioids, and allergy to the experimental drugs.

The study was both randomised and prospective. Both the patient and the surgeon were unaware of which patient was in which group. The patients were randomly divided into the two groups using sealed envelopes.

All patients were instructed to fast for 6 h before operation, and were advised to have someone to take them home. The patients were trained to use the anaesthesia device (APM II Ambulatory Pump ABBOTT Laboratories, San Diego, CA, USA) on the day before the operation. They were also invited to complete two psychological scales (The Amsterdam Preoperative Anxiety and Information Scale [APAIS] and Spielberger's State-Trait Anxiety Inventory [STAI]), and a sociodemographic questionnaire, preoperatively.

The dental chair was placed semi-supine, and patients remained in this position during the procedure. The blood pressure, pulse rate, respiratory rate, and oxygen saturation were recorded before drugs were given and at 10-min intervals during the operation. The same surgeon did all the operations.

An intravenous cannula was inserted into a vein in the dorsal side of the hand, and a continuous, free flow infusion of 0.9% sodium chloride was started. After the injection of the initial dose of 0.03 mg/kg midazolam (Dormicum; Roche, Switzerland), the patients in both groups were given the demand button for the analgesia pump and were allowed to press it until they felt adequately sedated. The pumps in the midazolam group and midazolam–remifentanil group were programmed to deliver bolus volumes of 2 ml. In the midazolam group, the bolus dose of midazolam was set at 0.5 mg/ml with each successful attempt, and the lockout interval was set at 5 min. The maximum dose was set at 12 mg of midazolam/h. In the other group, the bolus dose of the combination of midazolam–remifentanil was set to deliver 0.5 mg/ml midazolam and 12.5 μg/ml remifentanil (Ultiva$^{TM}$) with each successful attempt, and the lockout interval was also set at 5 min. The maximum dose was set at 12 mg of midazolam and 300 μg/h of remifentanil.

After the intravenous sedation, local anaesthetic (2 ml of 40 mg/ml articaine hydrochloride with 0.012 mg/ml adrenaline hydrochloride; Ultracain® D-S Forte, Aventis) was given. The efficacy of the local anaesthetic was assessed by verbal contact and by gently probing the buccal and lingual surfaces of the third molar.

The minimum oxygen saturation ($SpO_2$) value during the procedure was also recorded. Oxygen was not given routinely, but in cases of persistent desaturation ($SpO_2 < 95$) it was given through a nasal cannula at a rate of 3 l/min. Drugs were stopped after the last suture had been placed. The dose of the drug (which was measured based on the delivered volume, the total number of attempts, and the number of successful attempts) was recorded using the data saved by the analgesia device.

At the end of the operation, patients were accompanied to the recovery room where a nurse collected the postoperative data, Alderete score,[4] and Ramsey sedation score.[3] When the Alderete score reached 9, patients were discharged. The assessment of amnesia was evaluated in two stages: immediately after the operation and 24 h later. The assessment of amnesia concentrated on the recall of clinical events such as local anaesthetic injections, use of the surgical handpiece, and removal of the tooth. All the side effects that occurred during sedation and the 24-h postoperative period were recorded.

The patients were asked immediately after the operation if they were happy with the sedation they had received, if they would like to have the same sedation again, and about their overall satisfaction with the procedure. These questions were repeated 24 h later. Patients assessed the experience of sedation by assigning a score from 1 to 5, which corresponded with unacceptable, poor, satisfactory, good, and excellent.

At the end of the operation, the surgeon evaluated the degree of sedation and the operating conditions during the procedure similarly by assigning a score from 1 to 5.