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Comparison of dexmedetomidine/fentanyl with midazolam/fentanyl combination for sedation and analgesia during tooth extraction

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Abstract. Dexmedetomidine is an α2-adrenergic receptor agonist that causes minimal respiratory depression compared with alternative drugs. This study investigated whether combined dexmedetomidine/fentanyl offered better sedation and analgesia than midazolam/fentanyl in dental surgery. Sixty patients scheduled for unilateral impacted tooth extraction were randomly assigned to receive either dexmedetomidine and fentanyl (D/F) or midazolam and fentanyl (M/F). Recorded variables were patient preoperative anxiety scores, vital signs, visual analogue scale (VAS) pain scores, Observer's Assessment of Alertness/Sedation Scale (OAAS) scores after drug administration, surgeon and patient degree of satisfaction, and the duration of analgesia after surgery. The OAAS scores were significantly lower for patients administered D/F compared to those who received M/F. The duration of analgesia after the surgical procedure was significantly longer in patients who received D/F (5.3 h) than in those who received M/F (4.1 h; $P = 0.017$). The number of surgeons satisfied with the level of sedation/analgesia provided by D/F was significantly higher than for M/F ($P = 0.001$). Therefore, dexmedetomidine/fentanyl appears to provide better sedation, stable haemodynamics, surgeon satisfaction, and postoperative analgesia than midazolam/fentanyl during office-based unilateral impacted tooth extraction.

Keywords: dexmedetomidine; midazolam; fentanyl; dental surgery; day surgery; analgesia.

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Nitrous oxide/oxygen inhalation is the preferred sedation technique for the management of dental patients, due to its analgesic and anxiolytic properties, rapid onset, and recovery time.[1] However, nitrous oxide/oxygen inhalation is not suitable for extremely anxious patients who require painless techniques, such as general anaesthesia. In these cases, the most widely used form of sedation is the combination of a benzodiazepine with an opioid. The benzodiazepine has amnesic, anxiolytic, and sedative properties, while the opioid provides analgesia and amnesia, and sedation with benzodiazepines is synergistic.[2] However, these sedatives frequently cause significant oxygen desaturation and, occasionally, cardiopulmonary complications.[3]

Dexmedetomidine (DEX) is an α2-adrenergic receptor agonist that, in addition to providing sedation, analgesia, and anxiolysis,[4] is known to have minimal effects on respiratory physiology.[5] Furthermore, it has neuroprotective properties and reduces neurocognitive dysfunction (delirium, restlessness) during anesthesia.[6] However, the real value of DEX lies in the way it induces a unique pattern of sleep that closely resembles that of normal physiological sleep, whilst enabling easy arousal even by verbal stimuli.[7,8] When awoken, the patient cooperates well with the doctor and sleeps soon after the stimulus is removed. DEX is particularly suitable for patients during dental surgery who are required to cooperate with the surgeon during the surgical procedure.[9–11] During outpatient shockwave lithotripsy, recovery from sedation and analgesia was significantly higher with DEX when compared with combined midazolam and fentanyl.[12]

In the present study we compared the efficacy and safety of combined DEX/fentanyl with combined midazolam/fentanyl as sedatives during dental outpatient procedures. We hypothesized that DEX/fentanyl would provide better sedation and analgesia than midazolam/fentanyl.

Materials and methods

Subjects and study protocol

This study was conducted from January 2012 to March 2013. Sixty patients were enrolled who had previously used or had no known allergy to DEX, midazolam, paracetamol, and other non-steroidal anti-inflammatory drugs. All provided written informed consent. The patients were American Society of Anesthesiology (ASA) physical status I or II, between 19 and 60 years old, and had unilateral impacted teeth for which they were scheduled to undergo extraction under local anaesthesia. Patients were excluded if they had a clinical history or electrocardiographic evidence of heart block, ischaemic heart disease, asthma, sleep apnea syndrome, impaired liver or renal function, known psychiatric illness, or chronic use of sedative or analgesic drugs or opioids. Also excluded were those who consumed alcohol in excess of 800 ml per week, refused to participate, were pregnant, or presented with preoperative inflammation at the site of surgery.

The 60 patients were divided equally into two treatment groups using a computer-generated random list and sealed envelope technique. Patients in the first group were given an infusion of combined midazolam and fentanyl (group M/F) and patients in the second group an infusion of combined DEX and fentanyl (group D/F). Each patient had an intravenous cannula inserted. Investigators who were not directly involved in the care of the patient prepared the infusions, while the dental surgeon, anaesthetist, and the patients were blinded to the group allocation and drugs given.

Patients in group D/F received DEX (0.5 μg/kg) and fentanyl (1 μg/kg) in 20 ml of normal saline for 10 min, and then a continuous infusion of DEX (0.5 μg/kg/h) until the end of the surgery. Patients in group M/F received midazolam (0.05 mg/kg) and fentanyl (1 μg/kg) in 20 ml of normal saline for 10 min, followed by a continuous infusion of midazolam (0.05 mg/kg/h) until the end of the surgery. Ten minutes after the start of the loading dose, local anaesthesia was provided with 2% lidocaine given by qualified dental surgeons. Three surgeons then performed the standard surgical procedure during which patients were provided with a mouth prop to help keep the mouth open when required. At the end of the operation, patients were kept in the recovery area. A modified Aldrete score of 10 was the hospital discharge criterion.[13] Patients were prescribed one analgesic tablet containing 500 mg of paracetamol. The patients were advised to take the pain medication prescribed if the postoperative visual analogue scale (VAS) pain score was more than 3.

Outcome measures

All indices were recorded before initiating sedation (i.e., baseline), and then at 10-min intervals until 2 h after the start of drug infusion. Systolic blood pressure (SBP), heart rate (HR), and saturation of pulse oxygen (SpO_2) were recorded at 10-min intervals until 2 h after the start of drug infusion. Sedation levels were assessed using the Observer's Assessment of Alertness/Sedation Scale (OAAS).[14] The patients evaluated their level of pain subjectively using a VAS ruler, with zero representing no pain and 10 the worst pain the patient had ever experienced. Similarly, patients scored preoperative anxiety on a scale of 0–10 (0 being no anxiety and 10 being very anxious). Surgeon and patient satisfaction levels were also rated on scales of 0–10 (0 being very poor and 10 being very good). Patients were asked to rate their satisfaction with the levels of sedation and analgesia they had received and the time taken for the analgesia to wear off after they were sent home. The total time taken for the analgesic effect was calculated by taking into account the number of hours the VAS pain score of the patient remained below 3 after the end of the procedure.

Statistical analyses

All variables were tested for normal distribution using the Shapiro–Wilk test (results not shown). The data are expressed as the mean ± standard deviation (SD), median and interquartile range (IQR), or number and percentage. The preoperative anxiety score, surgeon satisfaction score, OAAS, and VAS scores were analyzed using the Kruskal–Wallis test. SpO_2, HR, and SBP values, age, weight, duration of surgery, and time taken until analgesic medication was required were analyzed using the two-sample *t*-test. Gender was analyzed using the χ^2 test. Statistical analyses were performed using the commercial software SAS 8.01 (SAS Institute, Cary, NC, USA). *P*-values of <0.05 were considered statistically significant.

In a preliminary study, with stable haemodynamics as the primary outcome, we determined that after 120 min of continuous infusion, a SBP of 140 ± 23 mmHg dropping to110 mmHg was of clinical importance ($\alpha = 0.05$, power = 0.9). The analysis showed that 15 subjects per group would be sufficient to detect a difference between the two groups. Assuming a 10% drop-out rate, the final sample size was set at a minimum of 17 patients per group.

Results

There were no significant differences in age, weight, gender, preoperative anxiety