Anesthetic Management With Remimazolam for Adolescent Mitochondrial Encephalomyopathy With Lactic Acidosis and Stroke-like Episodes (MELAS): A Case Report

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We successfully anesthetized a 15-year-old male dental patient with mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome using remimazolam and remifentanil. During the rapid sequence induction, we administered intravenous continuous infusions of remimazolam and remfentanil along with boluses of fentanyl and rocuronium to quickly induce general anesthesia without complications. General anesthesia was maintained during the operation with continuous infusions of remimazolam (0.8–1.0 mg/kg/h) and remifentanil (0.15–0.2 µg/kg/min) while using a SedLine monitor to help assess anesthetic depth. Except for immediately after extubation, the patient was stable postoperatively. He progressed satisfactorily and was discharged safely the following day. This experience suggests that the combination of remimazolam and remifentanil is an effective anesthetic for adolescent patients with MELAS syndrome undergoing dental procedures requiring general anesthesia.

Key Words: Remimazolam; Mitochondrial myopathy; Encephalopathy; Lactic acidosis; Stroke-like episodes; MELAS; Pediatric thoracic surgery.

Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome is a rare neurometabolic genetic disorder that impacts mitochondrial function. It is multisystemic and progressive in nature. Patients with MELAS syndrome require respiratory and cardiovascular stability, acid–base balance, and controlled temperature regulation during general anesthesia to prevent excessive strain on energy production and glycometabolism.[1] Written consent to publish the details of this case report was obtained from the patient's parents.

CASE PRESENTATION

The patient was a 15-year-old male (height, 146.5 cm; weight, 35.5 kg; BMI, 16.5 kg/m^2) who had been diagnosed with MELAS syndrome since 7 years of age and who required general anesthesia for dental treatment to prevent epileptic seizures triggered by stress. The dental plan consisted of 3 extractions, 6 dental restorations, and a dental prophylaxis. Due to his limited communication abilities, his parents acted as intermediaries. Preoperative examination revealed elevated lactate levels (13.0 mmol/L; normal range, 0.44–1.78 mmol/L) in his arterial blood sample.

Midazolam (7 mg) was administered intravenously for sedation and to reduce anxiety preoperatively approximately 20 minutes before surgery. The patient was also blindfolded when entering the operation theater to minimize light-induced stress. Rapid induction of general anesthesia was performed using IV continuous infusions of remifentanil (0.3 µg/kg/min) and remimazolam (12 mg/kg/h) along with IV boluses of fentanyl (100 µg) and rocuronium (50 mg). Nasal intubation was performed

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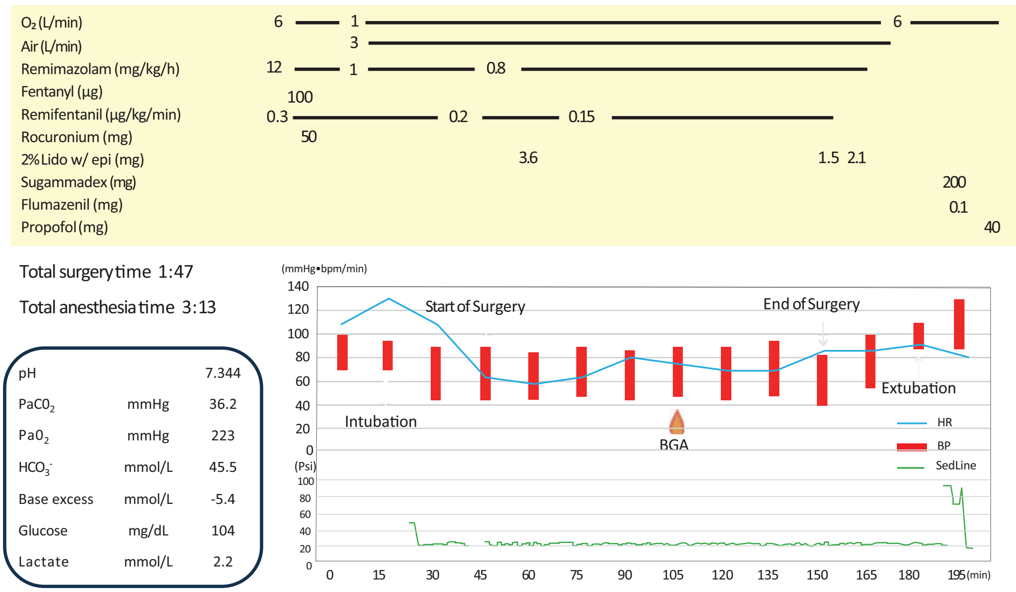
Figure. Anesthesia Record



Anesthesia record details drug administration (above), intraoperative vital signs (lower right), and intraoperative arterial blood gas analysis results (lower left). Abbreviations: BGA, blood gas analysis; BP, blood pressure; HR, heart rate; SedLine, patient sedation index via SedLine monitor.

after a train of four (TOF) ratio count of 0 was confirmed. Maintenance of general anesthesia utilized continuous infusions of remifentanil (0.15–0.2 µg/kg/min) and remimazolam (0.8–1.0 mg/kg/h) as well as electroencephalogram monitoring with a SedLine device to help assess depth of anesthesia. A total volume of 7.2 mL of 2% lidocaine with 1:80,000 epinephrine (lidocaine 144 mg; epinephrine 0.09 mg) was administered via infiltration for local anesthesia (Figure).

An arterial blood sample taken 1 hour into the surgery revealed a reduced lactate level (2.2 mmol/L) compared with the preoperative value. After completion of the dental treatment (1 h, 47 min), sugammadex (200 mg) was administered and the patient was extubated awake after return of spontaneous breathing and confirmation of recovered neuromuscular function (ie, a TOF ratio >0.9). Extubation was performed once the patient could open his eyes upon command, but he was too drowsy to expectorate sputum and oral secretions. To help avoid risks of aspiration and asphyxia, we administered IV flumazenil (0.1 mg). However, the patient was then determined to be at increased risk of falling out of bed due to excitement and excessive body movements, necessitating prompt resedation. A nonbenzodiazepine was needed due to the flumazenil, so IV boluses of propofol (40 mg total via 4 divided doses spaced over 10 min) were given. The operation and anesthesia lasted 107 and 193 minutes, respectively, with a total infusion volume of 200 mL. The patient was safely discharged the next day without any adverse events.

DISCUSSION

Selecting the appropriate general anesthetic management for patients with mitochondrial diseases, including MELAS syndrome, can be difficult. Inhaled anesthetics may increase the risk of malignant hyperthermia.[2] Although total IV anesthesia (TIVA) may be indicated, it often employs propofol. The risk of propofol-related infusion syndrome is reportedly high in patients with mitochondrial disease,[3] which may be a concern prompting the use of TIVA with propofol alternatives. However, anesthetic management using a combination of IV midazolam and dexmedetomidine failed to result in complete immobilization per a previous report.[4]

Remimazolam is like other benzodiazepines in that it offers dose-dependent central nervous system depression, hemodynamic stability, and has a specific antagonist but differs with its exceptional pharmacokinetic profile. Similar to remifentanil, remimazolam undergoes ultra-rapid esterase-based metabolism. There are prior reports of its use in adult patients with MELAS syndrome[5] but not in adolescents. Midazolam can be used as a premedication, but its interaction with remimazolam in humans has not yet been determined. In the present case, midazolam premedication was not a major problem during general anesthesia induction or maintenance. However, considering the dosing and half-lives of the midazolam[6] and fentanyl[7] given in this case, it cannot be ruled out that either or both may have negatively influenced the patient's arousal status postextubation despite the use of remimazolam and remifentanil. The epinephrine doses used in the local anesthetic did not elevate lactate levels, and intraoperative management proceeded smoothly.

Although flumazenil was used due to the potential risk for excessive sedation and airway obstruction during emergence and recovery, spontaneous awakening is generally preferable. Propofol was chosen postflumazenil due to its quick resedation capabilities and seizure control, and the small doses of propofol administered were unlikely to trigger propofol-related infusion syndrome.

CONCLUSION

This case describes the successful anesthetic management of an adolescent dental patient with MELAS syndrome using remimazolam and remifentanil for induction and maintenance.

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