Effective anesthetic management with remimazolam and ketamine without muscle relaxants for parotidectomy in a patient with myotonic dystrophy
A case report

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Abstract
Rationale: Patients with myotonic dystrophy (DM) are highly sensitive to anesthetics, muscle relaxants, and opioids, necessitating appropriate anesthetic management. Recently, remimazolam, an ultra-short-acting benzodiazepine, has been approved for use as a general anesthetic in Japan, and patients with DM have reportedly been treated with remimazolam. However, to the best of our knowledge, no study has reported on endotracheal intubation without the use of muscle relaxants under anesthetic management with remimazolam, nor on the combination of remimazolam and ketamine.

Patient concerns: A 23-year-old man was referred to our hospital for right parotidectomy and diagnosed with DM just before surgery. At the surgeon’s discretion, he was scheduled to undergo nerve monitoring to preserve the facial nerve.

Diagnosis: Myotonic dystrophy.

Interventions: We planned total intravenous anesthesia without muscle relaxants and selected remimazolam for anesthesia. Our aim was to prevent the intraoperative or postoperative complications associated with propofol and inhalational anesthetics. Additionally, we selected multimodal analgesia, including ketamine, to avoid opioid use. General anesthesia was induced with ketamine 30 mg, remifentanil 0.72 μg/kg/min, and remimazolam 12 + 6 mg. Endotracheal intubation was performed under videolaryngoscopy without the use of muscle relaxants. For postoperative analgesia, we administered additional doses of ketamine 20 mg and acetaminophen 1000 mg, and the surgeons infiltrated 8 mL of xylocaine 0.5% with epinephrine into the skin incision before starting the surgery. Intraoperative anesthesia was maintained with remimazolam 0.9 to 1.0 mg/kg/h and remifentanil 0.26 to 0.50 μg/kg/min. Flumazenil was administered for rapid awakening and safe extubation. All vitals, including the bispectral index, were stable during surgery.

Outcomes: The patient did not develop facial nerve paralysis, sore throat, or hoarseness, nor did he have any memory of the surgery. Good postoperative analgesia was achieved.

Lessons: We achieved effective anesthetic management using remimazolam without muscle relaxants in a patient with DM. Furthermore, the combination of remimazolam and ketamine provided good sedation and postoperative analgesia.

Abbreviations: ASA-PS = American Society of Anesthesiologists-physical status, BIS = bispectral index, DM = myotonic dystrophy, LOC = loss of consciousness, TIVA = total intravenous anesthesia.

Keywords: bispectral index, flumazenil, ketamine, muscle relaxant, myotonic dystrophy, opioid, remimazolam

1. Introduction
Myotonic dystrophy (DM) is an inherited disorder characterized by myotonia and extramuscular features, including cardiac conduction abnormalities and dysphagia.1,2 The increased sensitivity of patients with DM to anesthetics, muscle relaxants, and opioids may pose serious problems during anesthetic management.3 Anesthesia-induced postoperative respiratory failure was observed in a patient with DM.4 Remimazolam, a novel and ultra-short-acting benzodiazepine, was recently approved for use as a general anesthetic in Japan.5 Studies have reported that remimazolam can be used for the anesthetic management of patients with DM.6,7 However, to the best of our knowledge, no study has reported endotracheal intubation without muscle relaxants in a patient with DM under anesthetic management with remimazolam and ketamine.
intubation under anesthetic management with remimazolam without the use of muscle relaxants. Moreover, no study has reported on the combination of remimazolam and ketamine. Herein, we report effective anesthetic management with remimazolam and ketamine without the use of muscle relaxants for parotidectomy in a patient with DM. The patient provided written consent for the publication of this case report.

2. Case presentation

The patient was a 23-year-old man (height, 178.4 cm; weight, 57.8 kg), who was referred to our hospital for right parotidectomy. He was diagnosed with DM just before surgery based on the following episodes and various test results.

He became aware of weakness in grip strength in junior high school and gradually encountered problems in getting up. The family history was notable since his father and uncle had similar symptoms but had not been formally diagnosed with DM. Physical examination revealed distal extremity weakness beyond the wrist joint, grip and percussion myotonia, masseter muscle atrophy, and slight limitation in tongue movements. The serum creatine phosphokinase level was 919 U/L (reference range, 59–248 U/L). Electromyography revealed myotonic discharge. Electrocardiography showed a first-degree atrioventricular block and sinus rhythm at 61 beats per min. There were no abnormal findings on echocardiography or pulmonary function testing.

At the surgeon’s discretion, he was scheduled to undergo nerve monitoring to preserve the facial nerve. Therefore, we suggested the provision of general anesthesia and planned total intravenous anesthesia (TIVA) without muscle relaxants in consultation with the surgeon to ensure the patient’s safety. Remimazolam was selected as the general anesthetic agent. Our aim was to prevent the intraoperative or postoperative complications associated with propofol and inhalational anesthetics. Additionally, we selected multimodal analgesia, including ketamine, to avoid opioid use.

Noninvasive blood pressure monitoring, electrocardiography, pulse oximetry, and bispectral index (BIS) determination were performed intraoperatively. First, we administered ketamine 30 mg and started continuous infusion of remifentanil 0.72 μg/kg/min for analgesia. Thereafter, we administered remimazolam 12 mg intravenously for 1 minute and started continuous infusion at 1 mg/kg/h. Since loss of consciousness (LOC) did not occur after 3 minutes, we also administered remimazolam 6 mg for 1 minute. After confirmation of LOC, we established adequate mask ventilation without the use of muscle relaxants. After laryngeal deployment using a McGrath™ MAC laryngoscope (Covidien, Medtronic Inc, Tokyo, Japan), we confirmed that the glottis was slightly open, and protectively inserted an 8.0 endotracheal tube into the trachea. Endotracheal intubation was successful, without any incidence of coughing.

Thereafter, we maintained continuous infusion of remifentanil 0.26 to 0.5 μg/kg/min and remimazolam 0.9 to 1.0 mg/kg/h for adequate analgesia and sedation. For postoperative analgesia, we administered ketamine 20 mg and acetaminophen 1000 mg, and the surgeons infiltrated 8 mL of xylcaine 0.5% with epinephrine into the skin incision before starting the surgery. We refrained from using muscle relaxants intraoperatively since the surgery was performed with nerve monitoring to preserve the facial nerve.

The duration of surgery was 63 minutes. He started weak spontaneous breathing 10 minutes after termination of remimazolam and remifentanil administration and was administered flumazenil 0.2 mg. When he achieved sufficient tidal volume and could follow instructions, we administered an additional dose of flumazenil 0.3 mg to antagonize the effect of remimazolam and removed the tracheal tube. All vital signs, including the BIS, were stable during surgery (Fig. 1).

A postoperative interview was performed on the day after the procedure. He did not develop facial nerve paralysis, sore throat, or hoarseness, nor did he have any memory of the surgery. He required only a single dose of a nonsteroidal anti-inflammatory drug after surgery.
3. Discussion

Regional anesthesia with minimal sedation should be considered whenever possible for patients with DM, and anesthesiologists should be extremely careful whenever general anesthesia is planned. Although the use of a videolaryngoscope does not prevent sore throat, hoarseness, and dysphagia after extubation.

However, Ketamine induces a greater increase in the bispectral index (BIS) value compared to midazolam in the presence of general anesthesia (ketamine 0.4–0.5 mg/kg increases the BIS value in the presence of propofol or sevoflurane anesthesia). Moreover, in our patient, we had to particularly refrain from using muscle relaxants intraoperatively since nerve monitoring was needed to preserve the facial, leading to a large dose of intraoperative remifentanil. Although a relatively large dose of intraoperative remifentanil may lead to acute opioid tolerance and hyperalgesia, studies have demonstrated that they can be prevented by ketamine and withdrawal of remifentanil infusion.

In this case, even when a total ketamine dose of 0.9 mg/kg was administered during remifentanil infusion, the BIS value was stable and maintained at a range of 40 to 60, which corresponded to the BIS value when low-risk surgical patients (ASA-PS 1–2) were administered remifentanil 0.97 to 0.99 mg/kg/h. We provided multimodal analgesia with ketamine to achieve minimal opioid usage in the perioperative period, leading to good postoperative pain control.

4. Conclusions

In summary, we achieved effective anesthetic management using remifentanil without the use of muscle relaxants in a patient with DM. Furthermore, the combination of remimazolam and ketamine provided good sedation and postoperative analgesia. Further studies are needed to assess the feasibility of combining remimazolam and ketamine for this purpose.

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References

[1] Mangla C, Bais K, Yarmush J. Myotonic dystrophy and anesthetic challenges: a case report and review. Case Rep Anesthesiol. 2019;2019:4282305.
[2] Morimoto Y, Mii M, Hirata T, et al. Target-controlled infusion of propofol for a patient with myotonic dystrophy. J Anesth. 2005;19:336–8.
[3] Koyama Y, Kohno M, Tsuzaki K, et al. Bilevel positive airway pressure therapy in a patient with myotonic dystrophy and postoperative respiratory failure: a case report. Saudi J Anaesth. 2020;14:241–3.
[4] Masu K. Remimazolam besilate, a benzodiazepine, has been approved for general anesthesia!!!. J Anesth. 2020;34:479–82.
[5] Morimoto Y, Yoshimatsu A, Yoshimura M. Anesthetic management for a patient with myotonic dystrophy with remimazolam. J Anesth. 2021;7:10.
[6] Fukuda M, Tachibana S, Nishihara N, et al. Remimazolam for a patient with myotonic dystrophy. J Anesth. 2005;19:336–8.
[7] Yoo SW, Baek SJ, Kim DC, et al. A case report of malignant hyperthermia in a patient with myotonic dystrophy type I: a CARE-compliant article. Medicine (Baltimore). 2021;100:e25859.
[8] Boyd A, Nathan N, Feiss P. Propofol in myotonic dystrophy. Anaesthesia. 1991;46:705.
[9] Kinney MA, Harrison BA. Propofol-induced myotonia in myotonic dystrophy. Anesth Analg. 1996;83:665–6.
[10] Tzabar Y, Marshall R. Myotonic dystrophy and target-controlled propofol infusions. Br J Anaesth. 1995;74:108–9.

[11] Dos M, Morita K, Takeda J, et al. Efficacy and safety of remimazolam versus propofol for general anesthesia: a multicenter, single-blind, randomized, parallel-group, phase IIIb/III trial. J Anesth. 2020;34:543–53.

[12] Brodsky MB, Akst LM, Jellinek E, et al. Laryngeal injury and upper airway symptoms after endotracheal intubation during surgery: a systematic review and meta-analysis. Anesth Analg. 2021;132:1023–32.

[13] Lewis SR, Butler AR, Parker J, et al. Videolaryngoscopy versus direct laryngoscopy for adult patients requiring tracheal intubation: a Cochrane Systematic Review. Br J Anaesth. 2017;119:369–83.

[14] Bouvet L, Stoian A, Jacquot-Laperrière S, et al. Laryngeal injuries and intubating conditions with or without muscular relaxation: an equivalence study. Can J Anaesth. 2008;55:674–84.

[15] Kim CS, Park JM, Park D, et al. Opioid use may be associated with postoperative complications in myotonic dystrophy type 1 with high-grade muscular impairment. Sci Rep. 2021;11:6.

[16] Brinck EC, Tiippana E, Heesen M, et al. Perioperative intravenous ketamine for acute postoperative pain in adults. Cochrane Database Syst Rev. 2018;12:CD012033.

[17] Brown EN, Lydic R, Schiff ND. General anesthesia, sleep, and coma. N Engl J Med. 2010;363:2638–50.

[18] Matsushita S, Oda S, Otaki K, et al. Change in auditory evoked potential index and bispectral index during induction of anesthesia with anesthetic drugs. J Clin Monit Comput. 2015;29:621–6.

[19] Vereecke HE, Vanluchene AL, Mortier EP, et al. The effects of ketamine and rocuronium on the A-Line auditory evoked potential index, Bispectral Index, and spectral entropy monitor during steady state propofol and remifentanil anesthesia. Anesthesiology. 2006;105:1122–34.

[20] Hans P, Dewandre PY, Brichant JF, et al. Comparative effects of ketamine on Bispectral Index and spectral entropy of the electroencephalogram under sevoflurane anaesthesia. Br J Anaesth. 2005;94:336–40.

[21] Vereecke HE, Struys MM, Mortier EP. A comparison of bispectral index and ARX-derived auditory evoked potential index in measuring the clinical interaction between ketamine and propofol anaesthesia. Anaesthesia. 2003;58:957–61.

[22] Wu JX, Assel M, Vickers A, et al. Impact of intraoperative remifentanil on postoperative pain and opioid use in thyroid surgery. J Surg Oncol. 2019;120:1456–61.

[23] Yalcin N, Uzun ST, Reisi R, et al. A comparison of ketamine and paracetamol for preventing remifentanil induced hyperalgesia in patients undergoing total abdominal hysterectomy. Int J Med Sci. 2012;9:327–33.

[24] Joly V, Richebe P, Guignard B, et al. Remifentanil-induced postoperative hyperalgesia and its prevention with small-dose ketamine. Anesthesiology. 2005;103:147–55.

[25] Saxena S, Gosotte K, Terram W, et al. Gradual withdrawal of remifentanil delays initial post-operative analgesic demand after thyroid surgery; double-blinded, randomized controlled trial. BMC Anesthesiol. 2019;19:60.

[26] Han SS, Do SH, Kim TH, et al. Stepwise tapering of remifentanil at the end of surgery decreased postoperative pain and the need of rescue analgesics after thyroidectomy. BMC Anesthesiol. 2015;15:46.