

## Anesthetic management using total intravenous anesthesia with remifentanyl in a child with osteogenesis imperfecta

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### Abstract

In patients with osteogenesis imperfecta (OI), general anesthetic management should be carefully implemented in consideration of difficult intubation and the potential risks of cervical or mandibular fracture associated with tracheal intubation, bone fracture during postural changes, and respiratory dysfunction due to thoracic deformity. To prevent temperature elevation, moreover, many reports have recommended anesthetic management using total intravenous anesthesia (TIVA) rather than inhalation anesthetics, which contribute to temperature elevation. In an 8-year-old boy with type II (fatal type) OI (height, 81 cm; body weight, 12.4 kg), we performed general TIVA with remifentanyl and propofol, using a laryngeal mask airway for airway management. All possible intra- and postoperative complications were effectively prevented, and the remifentanyl requirement was high, as shown by a mean dose of  $0.36 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ .

**Key words** Osteogenesis imperfecta · Remifentanyl · TIVA · Laryngeal mask airway · Malignant hyperthermia

### Introduction

In patients with osteogenesis imperfecta (OI), general anesthetic management should be carefully implemented in consideration of the potential risks of malignant hyperthermia (MH) [1] and mandibular bone fracture associated with tracheal intubation [2,3]. To prevent intraoperative temperature elevation from occurring through a mechanism different from that involved in MH, moreover, many reports have recommended total intravenous anesthesia (TIVA) [1,3]. While there have been some case reports that children require a higher remifentanyl dose than adults during TIVA [4], no optimal dose has been established. We

report TIVA with continuous infusion of remifentanyl in a child with type II OI.

### Case report

Our patient was an 8-year-old boy with a height of 81 cm and a body weight of 12.4 kg. This boy, who had had multiple fractures during the fetal and perinatal period, was diagnosed with OI, which was genetically diagnosed as type II according to the Sillence classification. He frequently suffered bone fractures easily, even after infancy. However, after treatment with bisphosphonates, which resulted in successful management of the fragile bones, he became ambulatory in daily life. When he underwent open reduction of a femoral fracture at the age of 7 years, he did not develop MH after 40-min general anesthesia with inhalation anesthetics under a mask.

For the present admission, he was scheduled for open reduction of a left femoral fracture and right femoral osteotomy.

On admission, physical findings included deformity of the limbs due to multiple bone fractures, large head and short neck, without micrognathia or limited mouth opening. He had no hearing loss, but had blue sclera. He had no congenital heart disease, but had thoracic deformity due to lateral curvature and pectus excavatum. Hematologically, he had a normal serum creatinine kinase (CPK) level of  $65 \text{ IU l}^{-1}$ , and no abnormality in the time to achieve hemostasis.

He was orally pretreated with midazolam syrup at a dose of 6 mg. After a peripheral intravenous line was placed, general anesthesia was rapidly induced with propofol ( $2 \text{ mg}\cdot\text{kg}^{-1}$ ), remifentanyl ( $0.3 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ), and vecuronium ( $0.1 \text{ mg}\cdot\text{kg}^{-1}$ ) to insert a size-2 ProSeal laryngeal mask airway (ProSeal LMA; Laryngeal Mask Company, Henley on Thames, UK) cautiously so as not to damage the lower jaw or teeth. After the stomach

contents were removed via a gastric tube, a temperature probe was placed in the esophagus via an LMA drain tube to monitor esophageal temperature, while rectal temperature was monitored as well. We performed invasive arterial blood pressure monitoring and monitored the depth of hypnosis, using the Bispectral Index (BIS; Aspect Medical Systems, Natick, MA, USA). Surgery was performed under TIVA with propofol and remifentanyl. We adjusted the propofol infusion rate so that the BIS values could be set at 40–60, and the remifentanyl infusion rate so that the change in arterial blood pressure would be  $\pm 20\%$  of the baseline. Propofol was given at a rate of 4.2 to 7.5 mg·kg<sup>-1</sup>·h<sup>-1</sup> (mean, 6.7 mg·kg<sup>-1</sup>·h<sup>-1</sup>; total, 422 mg), and remifentanyl was given at a rate of 0.1 to 0.45  $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  (mean, 0.36  $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ; total, 1196  $\mu\text{g}$ ).

Intraoperatively, both the esophageal and rectal temperatures were within a range from 36°C to less than 37°C, and there was no myoglobinuria or change in urine color. Approximately 15 min before the end of surgery, single doses of fentanyl (3  $\mu\text{g}\cdot\text{kg}^{-1}$ ) and flurbiprofen (1 mg·kg<sup>-1</sup>) were intravenously administered. At the end of the surgery, treatment with remifentanyl was discontinued. Once spontaneous respiration was confirmed, the LMA was removed. Blood loss was 140 ml; fluid infusion, 596 ml; urine volume, 127 ml; and anesthesia duration, 327 min. Hematologically, the serum CPK level increased to 1351 IU·l<sup>-1</sup> postoperatively, but there was no abnormality in serum lactate. With no clinical symptoms suggestive of postoperative MH or propofol infusion syndrome, the patient steadily recovered.

## Discussion

OI is a genetic disorder associated with abnormality in type I collagen, a major component of connective tissues, with a prevalence of 1 in approximately 20000 persons [5]. It is genetically classified as types I to IV, according to the Sillence classification scheme. The disorder is currently classified into seven types (types V, VI, and VII are not associated with type I collagen gene defects) based on differences in clinical presentation and bone architecture [6]. Clinical symptoms include bone fragility, bone deformity, failure to thrive, dentinogenesis imperfecta, hearing loss, blue sclera, abnormal platelet function, and hypermetabolism. Many patients have frequently had surgeries, such as open reduction or correction of fracture, since an early age. Anesthetic management is complicated by temperature elevation occurring under general anesthesia, ventilation or intubation difficulty, cervical or mandibular fracture associated with tracheal intubation due to bone fragility, fracture during postural changes, and respiratory dys-

function due to thoracic deformity [2,3]. The mechanism of temperature elevation under general anesthesia is considered to be related to MH [1], while negative mechanisms [2,7] such as hypermetabolism, due to an increase in thyroid hormone [3], are also reported. Therefore, many reports have recommended anesthetic management using TIVA rather than inhalation anesthetics, which contribute to temperature elevation [1,3,8].

The condition in our patient with OI was classified as type II according to the Sillence classification, the most severe type, which previously resulted in perinatal death in many patients. However, advances in bisphosphonate therapy, which inhibits bone resorption by impairing the function of osteoclasts, have contributed to an increase in surviving patients, who may require general anesthetic management in coming years. As exemplified by this 8-year-old boy weighing 12.4 kg who suffered from severe failure to thrive, this type of OI requires more cautious countermeasures against intraoperative complications than other types.

Preoperatively, we discussed whether we would perform TIVA, so avoiding MH produced by inhalation anesthetics, or whether we would use volatile anesthesia, which would avoid propofol infusion syndrome. However, in this controversial situation, because we were not able to completely rule out the relationship between inhalation anesthetics and MH, we chose TIVA to avoid the fatal complication of MH. We performed TIVA with remifentanyl and propofol. High doses of remifentanyl (mean, 0.36  $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ) were required. While anesthesia with remifentanyl is widely used in children, there have been many reports that children require more remifentanyl than adults. Muñoz et al. [4] reported that children required approximately twice as much remifentanyl as adults in skin incision under TIVA (0.3 and 0.15  $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ , respectively). Park et al. [9] reported that remifentanyl reduced the propofol requirement for the insertion of LMAs in children. While the use of remifentanyl may also reduce the total dose requirement of propofol, prolonged TIVA with propofol in children requires that special attention be paid to the development of symptoms of propofol infusion syndrome, such as postoperative metabolic acidosis or rhabdomyolysis. Given a report that propofol infusion syndrome occurred in a child with OI after as short a duration as 150-min general anesthesia with propofol [10], hematological examination should be performed postoperatively to follow up serum lactate and base excess.

In surgery in the present patient, which was anticipated to be prolonged, airway management with the ProSeal LMA was selected to prevent complications due to tracheal intubation [11, 12]. Especially in patients with OI, who are more vulnerable to these complica-

tions, an LMA is useful in preventing such complications, including mandibular or cervical fracture and damage to teeth associated with tracheal intubation [1,5,8,9,12]. In addition, airway management with an LMA provides smooth extubation to prevent excitement and movement-related bone fracture, complications requiring special attention in children with OI.

We performed anesthetic management using TIVA with remifentanil in a child with Sillence type II OI. In children with OI, it is important to implement anesthetic management with due attention to possible intraoperative complications. Children may require more remifentanil than adults during TIVA with remifentanil.

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