

Anaesthesia in children with osteogenesis imperfecta — report of 14 general anaesthetics in three children

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ABSTRACT

Osteogenesis imperfecta is a rare, genetically inherited syndrome involving connective tissue. It results in extremely fragile bones and disorders of other organs and body systems. Children with osteogenesis imperfecta are susceptible to bone fractures and often require surgery and anaesthesia. We describe a series of 14 general anaesthetics in three patients suffering from this disease. In one of these cases, perioperative hyperthermia was observed. Anaesthetic management of osteogenesis imperfecta and a possible relationship between this syndrome and malignant and non-malignant hyperthermia are discussed.

Key words: osteogenesis imperfecta, general anaesthesia; osteogenesis imperfecta, malignant hyperthermia

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Osteogenesis imperfecta (OI) is a rare inherited syndrome. There are few reports in the literature pertaining to anaesthesia in such patients. The authors of these reports highlight the risk of iatrogenic trauma, coagulopathy, and above all, malignant hyperthermia (MH).

In this paper, we describe a series of anaesthetics in patients with OI and discuss contemporary knowledge of the relationship between OI and MH, as well as other practical issues related to anaesthetic management of these patients.

OI is a generalised disorder of connective tissue involving the bones, teeth, skin, fasciae, tendons and sclerae. The most important symptom is bone fragility. Usually, the first discerned symptoms are blue sclerae; fragile skin, excessive joint mobility and hernias are also frequent findings.

OI is clinically and genetically heterogeneous. The majority of patients have mutations of genes encoding collagen type I chains. Clinical heterogeneity results in a wide range of manifestations, from lethal forms to phenotypes with normal life expectancy and only minor depletion of bone mass [1].

There are four main types of OI described in the literature.

Type I is inherited in an autosomal dominant fashion and is characterised by blue sclerae, fragile bones, hyperextensible joints, progressive hearing loss and dentinogenesis

imperfecta. It is the most common form of OI. There is variability in expression, but most patients sustain fractures during childhood. Fractures are less common in adulthood. These patients may have aortic root dilatation, aortic insufficiency, or mitral valve prolapse; rarely, they may develop cor pulmonale from severe kyphoscoliosis.

Type II OI is lethal either in utero or in the perinatal period. It is characterised by blue sclerae; growth retardation; short, deformed limbs with multiple fractures; and severe thoracic abnormalities. If not stillborn, most patients die in the perinatal period of respiratory insufficiency. Inheritance may be either autosomal recessive or dominant.

Type III OI is inherited in an autosomal dominant fashion and is characterised by blue sclerae at birth that normalise thereafter, as well as multiple fractures and progressive bone deformities. Patients usually die during childhood or adolescence as a consequence of cardiopulmonary complications.

Type IV OI is inherited in an autosomal dominant fashion and is characterised by bone fragility and multiple fractures without the ocular, audiological, and dental abnormalities of type I OI. As in type I OI, there is improvement after puberty, and fractures are uncommon in adults [2].

Due to the frequency of bone fractures and deformities, these patients often need surgical interventions; therefore, they also require anaesthesia.

CASE SERIES

PATIENT J.S.

At the age of 21 months, this boy was scheduled to undergo intramedullary nailing of the tibia due to a fracture. Apart from the fractured extremity, physical examination was normal. The child weighed 10 kg and was premedicated intravenously with 2 mg of midazolam; then, general anaesthesia was induced with intravenous fentanyl 50 µg, thiopental 50 mg, atropine 0.1 mg, and cisatracurium 1 mg. The patient was intubated with a size 4.5 endotracheal tube. Anaesthesia was maintained with sevoflurane and nitrous oxide. Surgery was uneventful; we did not observe excessive blood loss, and the patient was stable with a heart rate of approximately 110 min⁻¹. In the final stage of the procedure, tachycardia to a rate of almost 170 min⁻¹ was noted, but other parameters (SpO₂, ETCO₂) remained normal. The tachycardia subsided soon after emergence from anaesthesia.

Three months later, the same patient underwent a closed reduction of a fractured femur. The boy was intravenously administered 1 mg of midazolam, 0.1 mg of atropine, and 50 mg of thiopental; anaesthesia was maintained with nitrous oxide and sevoflurane, with spontaneous ventilation. After 20 minutes of anaesthesia, the heart rate rose once again from an initial 110 min⁻¹ to 160–170 min⁻¹, while other parameters (SpO₂, ETCO₂) remained unchanged. After emergence from anaesthesia, tachycardia persisted for approximately 30 min, with a concomitant elevation of body temperature to 38.8°C. Physical cooling, along with an intravenous infusion of paracetamol, were promptly implemented, and the temperature returned to normal. In the following days, no further rise in body temperature was noted.

PATIENT K.K.

During the years this girl was under our care, she also consulted a metabolic disorders clinic (due to OI) and a cardiology clinic (due to mitral insufficiency). Between the ages of 13 and 15 years, she underwent four surgical procedures in our hospital: two for stabilisation of femoral fractures, one for a knee arthroscopy, and one for removal of osteosynthetic implant. During these procedures, midazolam, thiopental, etomidate, atropine, fentanyl, vecuronium, neostigmine, nitrous oxide, and sevoflurane were used. All procedures were uneventful; no tachycardia, hyperpyrexia or hypercarbia was observed.

PATIENT P.C.

This girl had been under the care of our institution since the age of two years. Between the ages of two and five years, she underwent eight operations to treat femoral and ulnar fractures. During these procedures, midazolam, thiopental, ketamine, morphine, fentanyl, neostigmine, nitrous oxide,

and sevoflurane were used. Use of these anaesthetics was uneventful; no tachycardia, hypercarbia or pyrexia was observed.

All anaesthetics are presented in Table 1.

DISCUSSION

A patient with OI can present substantial challenges to the anaesthesia team.

Due to the extreme fragility of bones, excessive neck extension may lead to a fracture, whereas overly vigorous laryngoscopy may cause mandibular injury. Even muscle fasciculation after succinylcholine may cause fractures. Positioning before surgery must be undertaken with caution [2].

Fractures have also been reported as a result of inflation of the cuff during blood pressure measurement; thus, in severe cases of OI, it is advisable to opt for invasive blood pressure monitoring. Kyphoscoliosis or limited mobility of the neck may result in a difficult airway [2]. Successful use of laryngeal and intubating laryngeal masks has been described in the literature [3–5]. Patients with concomitant dentinogenesis imperfecta are also at a greater risk of dental injury during the perioperative period than the general population [2].

Some patients with OI are at risk of excessive perioperative haemorrhage due to thrombocytes dysfunction; successful treatment with desmopressin has been described [2, 6].

A Caesarean section is often necessary in parturients with OI due to cephalopelvic disproportion and the risk of pelvic fractures. Successful epidural and spinal blocks in OI parturients have been reported, but potential coagulopathy should be taken into consideration. Selection of the dose of local anaesthetic may be difficult in patients with scoliosis or a short stature; some authors have suggested a continuous epidural block with slow titration of the local anaesthetic [2, 6–9].

The relationship between OI and MH has been widely discussed in the literature. In the perioperative period, some patients with OI develop a hypermetabolic state with a fever (such symptoms were observed in our patient, J.S.). Hyperthermia associated with physical exercise, decreased heat tolerance, and hyperhydrosis have also been described in OI [10].

Earlier publications presented OI as a condition predisposing to MH, as deaths related to anaesthesia were reported [11]. More recent publications suggest that the hypermetabolic state and hyperthermia observed in OI during the perioperative period are not MH because they are self-limiting, muscle rigidity is not seen, and normocarbia is maintained. It is more likely that this phenomenon is a disorder of central thermoregulation, which can be triggered by various factors [2, 9, 12].

The following question remains: what is the safest method of general anaesthesia in OI patients?

Table 1. Characteristics of all anaesthetics in described individuals

Age, body weight	Orthopaedic diagnosis, procedure	Anaesthetic medication	Airways, breathing	Complications
Patient J.S.				
21 months, 10 kg	Shaft fractures of both shin bones, intramedullary nailing of bilateral tibial fractures	Midazolam, fentanyl, thiopental, atropine, cisatracurium, N ₂ O, sevoflurane	Tracheal intubation, controlled ventilation	Tachycardia up to 170 min ⁻¹ in the end stage of the procedure
2 years, 10 kg	Femoral shaft fracture — closed reduction	Midazolam, fentanyl, atropine, thiopental, N ₂ O, sevoflurane	Facial mask, spontaneous ventilation	Tachycardia up to 170 min ⁻¹ starting at the end of the procedure, persisting for approximately 30 min; body temperature rising up to 38.8°C
Patient K.K., concomitant disorder: mitral insufficiency				
13 years, 37 kg	Femoral fracture — Ender nail removal, stabilisation with a plate	Midazolam, atropine, fentanyl, thiopental, vecuronium, neostigmine	Tracheal intubation, controlled ventilation	None
15 years, 48 kg	Removal of stabilisation material from femur	Midazolam, fentanyl, thiopental, vecuronium, neostigmine	Tracheal intubation, controlled ventilation	None
15 years, 50 kg	Stabilisation of pseudoarthrosis of femur by means of the IVOSS system and a plate	Midazolam, fentanyl, thiopental, vecuronium, N ₂ O, sevoflurane	Tracheal intubation, controlled ventilation	None
15 years, 50 kg	Knee arthroscopy	Midazolam, fentanyl, atropine, etomidate, N ₂ O, sevoflurane	Facial mask, spontaneous ventilation	None
Patient P.C.				
2 years, 10 kg	Right femoral shaft fracture — stabilisation with a micro plate	Atropine, thiopental, morphine, vecuronium, neostigmine, N ₂ O, sevoflurane	Tracheal intubation, controlled ventilation	None
2 years, 10 kg	Ulnar and radial shaft fractures — stabilisation with Kirschner wires	Midazolam, fentanyl, thiopental, vecuronium, N ₂ O	Tracheal intubation, controlled ventilation	None
3 years, 13 kg	Left femoral shaft fracture — stabilisation with a plate	Midazolam, fentanyl, thiopental, vecuronium, N ₂ O	Tracheal intubation, controlled ventilation	None
3 years, 13 kg	Removal of stabilisation material from both femurs	Fentanyl, thiopental, vecuronium, N ₂ O	Tracheal intubation, controlled ventilation	None
4 years, 15 kg	Right femoral fracture — stabilisation with a plate	Midazolam, fentanyl, thiopental, vecuronium, atropine, neostigmine, N ₂ O	Tracheal intubation, controlled ventilation	None
4 years, 15 kg	Right femoral fracture — intramedullary nailing	Midazolam, fentanyl, atropine, thiopental, vecuronium, neostigmine	Tracheal intubation, controlled ventilation	None
4 years, 15 kg	Left femoral fracture — intramedullary nailing	Midazolam, atropine, fentanyl, vecuronium, thiopental, N ₂ O	Tracheal intubation, controlled ventilation	None
5 years, 17 kg	Intramedullary nail removal from left femur	Midazolam, thiopental, ketamine	Facial mask, spontaneous ventilation	None

Fuerderer et al. [12] reported 45 anaesthetics in 22 children with OI. In 27 procedures, balanced anaesthesia was administered using fentanyl and enflurane, while in 18 procedures, total intravenous anaesthesia (TIVA) was administered using propofol and alfentanil. In the TIVA group, a slight decrease of the body temperature was noted intraoperatively, while in the enflurane/fentanyl group, intra- and postoperative elevation of body temperature was observed.

One child in the enflurane/fentanyl group died (the authors did not report the cause of death). On the basis of these observations, the authors assumed that TIVA is a safer technique in children with OI [12].

Lactic acidosis during TIVA with propofol in a child with OI has been reported [13]. However, acidosis has also been reported in a patient with OI after the use of halothane [14].

In a recent review, Benca and Hogan describe OI as a condition with a weak association with MH [15]. They state that there have not been any documented cases of MH in patients with any form of OI after a brief exposure to known potent triggering agents such as sevoflurane and enflurane (for example, the time it takes for inhalational induction of anaesthesia and placement of an intravenous catheter). These newer potent inhaled anaesthetics are well recognised as triggers of MH when caused by mutations in the *RYR1* genes encoding skeletal muscle calcium channels.

In patients with these rare disorders for which the association with MH is weak, the authors advise that, with due care in consultation, communication, monitoring, and preparation, it is reasonable to perform an inhalational induction to secure intravenous access and then to change to a non-triggering technique for the maintenance of anaesthesia [15]. This method may be especially useful when a difficult airway is anticipated.

CONCLUSIONS

Because of the rarity and heterogeneity of OI and the inherent difficulties of conducting studies on this population, we cannot unequivocally state the safest anaesthetic technique in this disorder. TIVA, with the option of sevoflurane induction (especially when a difficult airway or difficult vascular access is anticipated), seems most appropriate. The metabolic disturbances associated with OI require further research.

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