Perioperative Anaesthetic Management in Pediatric Patients with Osteogenesis Imperfecta (OI) At Tertiary Referral Hospital

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Introduction

Osteogenesis Imperfecta (OI), a condition also known as brittle bone disease, is marked by decreased bone mass and easily fractured bones. It is a genetic disorder of connective tissue caused by mutations in one of two genes, COL1A1 or COL1A2, which produce type one collagen. This abnormality affects mainly bones, cartilage and the soft tissues. These patients often undergo surgery due to their susceptibility to bone fractures. Anaesthesia poses numerous challenges including those concerning the airway, respiratory and cardiovascular systems, positioning and potential bleeding. The prevalence of OI globally depends on the molecular genetic classification, race and geographical location. Osteogenesis Imperfecta is of clinical importance in South Africa as a severe form (type III), which is described as ‘progressively deforming’. A relatively high frequency is found in the indigenous black Southern african population, where mutations in the FKBP10 gene have been implicated. There is a paucity of literature addressing the anaesthetic management of OI patients in the perioperative period, especially in low-to-middle income countries such as South Africa. A 2020 retrospective chart review by Mohammad at el. in South Africa, recruited 39 patients and reviewed 93 anaesthetic operations, the majority of whom were black Africans with OI type III.

Aim
1. To describe anaesthetic complications related to OI
2. To make recommendations on how perioperative complications can be prevented
3. To present the findings of my own study: A retrospective chart review describing and evaluating the perioperative management of OI paediatric patients presenting for surgery at Inkosi Albert Luthuli Central Hospital (IALCH).

Classification
Classifying OI helps us to identify the severity and prognosis of disease. The most common classification was created by Sillence and colleagues in 1979, which focusses on clinical and radiological findings and reflects the mode of inheritance. This is reflected in the table below.

<table>
<thead>
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<th>Type</th>
<th>Genetic Pattern</th>
<th>Clinical presentations</th>
<th>Severity</th>
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<tr>
<td>I</td>
<td>Autosomal Dominant (AD)</td>
<td>Blue sclera, short stature with or without dentinogenesis imperfecta (DI)</td>
<td>Mild</td>
</tr>
<tr>
<td>II</td>
<td>Autosomal Recessive (AR)</td>
<td>Dark sclera, multiple ribs and long bone deformities and large skull</td>
<td>Lethal perinatally</td>
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### Diagnosis of OI

The diagnosis of OI can be made on the basis of a positive family history and/or clinical presentation, as evidenced by blue sclera, hyper-laxity of the joints and skin, late hearing loss and radiological features of multiple fractures, osteopenia and Wormian bones. Clinical features are often present in early childhood. DNA studies on white blood cells and dermal fibroblasts show genetic mutation in 90% of cases. A negative DNA test for genetic mutation therefore does not exclude the diagnosis of OI. Provided below are images of types III and II of OI.

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<tr>
<td>III</td>
<td>AR</td>
<td>DI , Progressive deformity, short stature, severe scoliosis and normal sclera</td>
<td>Severe</td>
</tr>
<tr>
<td>IV</td>
<td>AD</td>
<td>Moderate form of type III</td>
<td>Moderate</td>
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**OI type III shows**

Sever kyphoscoliosis and bowing deformity of upper and Lower limbs

**Skeletal radiograph of type II OI at 35 weeks of gestation with multiple rib and long bone fractures**
Management
OI is not a curable disease but it is managed supportively and symptomatically.

Medical treatment
- Oral or intravenous bisphosphonate has been shown to decrease pain and increase bone density but it is uncertain if it decreases the risk of fracture.³
- Growth hormones, parathyroid hormones⁶ and vitamin D are described for short stature in type III and IV³

Surgical treatment
OI is well known to the orthopedic surgeon due to frequent fracture management. The main indications for surgery include pain management, fracture fixation and realignment of long bone deformity⁸ and correction of scoliosis. The majority of cases needing surgery are the severe types (III and IV) and less commonly, mild OI type I.³

Physiotherapy and Rehabilitation
It is essential to improve pain, reduce drug requirements, increase muscle strength, and decrease length of hospital stay. Rehabilitation measures focus on correct positioning, head support and chest and perioperative physiotherapy.¹

Perioperative complications
The perioperative anaesthetic considerations and complications are based on the type of OI the patient has. Type III has a 6 times more risk of anaesthetic complications than type I.⁹

Position
It may be challenging to position the patient for surgery due to the presence of a prominent occiput, increased head diameter, thin skin, joint hyper-laxity, chest deformity and bone fragility.¹⁰ Patients are at increased risk for skin trauma, joint dislocation, and bone fracture whilst being moved to and from the operation table. Severe kyphoscoliosis and limb deformity may also make it difficult for the patient to lie comfortably in the supine position.¹¹ In a case study by Sullivan et al, it was described how a patient sustained fractures related to handling by the theatre team.¹² Rothschild et al reported two cases involving perioperative fractures where the reason was unknown.⁹ It is also highlighted that the risk of joint dislocation may increase with using muscle relaxation.¹³ In the review by Mohammad et al, no fractures associated with positioning were reported.⁵

Monitors
There have been multiple reports of patient with OI sustaining fractures while using non-invasive blood pressure (NIBP) cuffs and tourniquets. Some recommend to avoid the use of tourniquets when inserting intravenous lines.¹¹ The use of invasive blood pressure (IBP) monitoring is
controversial. Sullivan et al recommended the use of NIBP cuff monitoring to reduce the cost and complications associated with IBP. On the other hand, Bhandari et al recommended the use of manual sphygmomanometer instead of an automated blood pressure cuff to reduce the risk of fracture. Despite these concerns, Mohmmad et al did not find any complications related to the use of blood pressure cuffs or tourniquets, which were used in the majority of cases of the study population.

Airway management
It has been highlighted in the literature that patients with OI are at risk of being a “difficult airway”. This is reportedly due to the features associated with a difficult airway such as a prominent occiput, protruding mandible, cleft palate, large tongue, short neck, laxity of cervical spine joints, risk of airway bleeding, Pigeon chest and fragile mandibles. Despite this claim Hall et al, Rothschild et al and Mohmmad et al have reported a low number of patients presenting with a “difficult airway” for anaesthesia. In our study, all patients under went general anaesthesia where the majority had a SGAD inserted and very few were intubated; Airway complications were found to be low (3.22%). An explanation for this may be related to the use of supraglottic airway devices (SGAD) by expert hands. The Proseal LMA has been used in patients with OI successfully and has been recommended in a study by Santos et al. Video-assessed laryngoscopy has been shown to reduce the risk of airway trauma, rate of failure of intubation and dislocation of cervical spine.

Basilar Invagination
It is a rare but serious complication occurring in OI and often leads to death if not recognised early. It is the movement and infolding of occipital bones into the skull and upward displacement of the cervical bone causing obstruction of cerebrospinal fluid drainage and blood supply of the brain, as well as compression of the brain stem. Patients may complain of headache, upper limb weakness, nystagmus and instability of the head and neck. It is therefore important to exclude and document exclude any neurological deficit prior to anaesthesia, use imaging for confirmation. The cautious use of a SGAD or flexible fibre-optic laryngoscopy for airway management may limit neurological injury in this manner.

Difficult intra-venous line insertion
The presence of thin skin, fragile vessels and limited tourniquet use (in case of fracture), may make intravenous access difficult. Rothschild et al study reported very few cases had difficult line insertion and half of them type III.

Hyperthermia
Most of the literature describes no correlation between malignant hyperthermia (MH) and OI, but the exact answer is not yet known. Patients with OI may present with hyperthermia under anaesthesia as a result of increased metabolic rate due to increased thyroid hormone levels, which is especially seen with type III, or due to dysregulation of the temperature centres.
review in 1992, Hall et al recruited 266 OI patients, and reported that these patients may have an increased metabolism and a tendency to pyrexia. They however refuted the concept that OI is associated with malignant hyperthermia. 14 Mohmmad at el showed that 55.9% of their study population had an insignificant increase in body temperature under anaesthesia.5

**Anaemia and Blood Transfusion (BT)**
Anaemia is very common, especially in the severe types of OI (III and IV). This may be due to chronic illness, bleeding tendency and multiple surgeries, but the exact mechanism is unknown. Mohmmad at el found that more than 65% of their study population were anaemic. This was diagnosed preoperatively where 50% were diagnosed by haemoglobin point-of-care testing and the laboratory testing. Despite this finding, only a few patients required blood transfusion perioperatively.5 Possible approaches to reduce blood transfusion and complications are preoperatively diagnosing anaemia, and appropriately correcting it using measures such as iron and folate supplementation and the use erythropoietin. 17

**Bleeding tendency**
Patient with OI have an increased bleeding tendency due to anaemia, thrombocytopenia, abnormal capillaries, reduced levels of factor VIII and abnormal or low collagen, which is important for platelet aggregation. 11,18 Rothschild at el reported that 17% of their study population had significant blood loss perioperatively, most of whom were of the III and VI types.9 Mohmmad at el mentioned that more than 24% of population presented with abnormal platelet counts and few of them needed BT.5

**Cardiac anomalies**
Collagen forms an integral part of cardiac and vascular development. More than two thirds of cardiac muscle consist of collagen type I, which is important for cardiac tensile stiffness. OI presents with a variety of cardiac abnormalities related to the abnormality in collagen. These include aortic dissection, ventricular rupture, mitral valve prolapse or aortic or mitral valve regurgitations 11,19 Interestingly, cardiac lesions do not correlate with the clinical form severity of OI.20 Mohmmad et al showed that 3.2% of their study population had electrocardiogram (ECG) and echocardiography (echo) studies performed, all of which were unremarkable. Clinical judgement guided decision making when requesting an ECHO or ECG.

**Pulmonary disease**
Patients may present with restrictive lung disease and reduce total lung volumes, especially in those with severe spinal deformities.11 Pulmonary pathologies may result in adverse perioperative events such as laryngospasm, bronchospasm, poor compliance, difficulty ventilating and postoperative pulmonary complications.21 Mohmmad et al reported that although 18.2% of the patients in their study had abnormal chest x-ray findings and 6.2% had abnormal pulmonary function test (PFT) findings, very few experienced post-operative pulmonary complications 5
**General anaesthesia versus regional anaesthesia**

This topic is controversial and ultimately factors such as the presenting pathology, urgency of surgery and severity of OI all play a role.

**General anaesthesia (GA)**

General anaesthesia may be a better choice where regional anaesthesia is difficult to perform or contraindicated due to severe anatomical deformities or bleeding diathesis. In paediatric anaesthesia, a regional anaesthesia-only technique may be difficult to perform, especially in those with an intravenous line secured. In those patients with severe cardiac disease, GA may allow better haemodynamic control. Karabiyik et al. described using an intubating LMA and total intravenous anaesthesia in patients with OI as a GA technique associated with less airway trauma and cervical spine movements. They also recommended avoiding the use of succinylcholine as fasciculation-induced fractures and fatal hyperkalemia (from prolonged immobility) may occur. In the study by Mohmmad et al, all patients had general anaesthesia for surgery, of which only 12% had a sole GA technique without regional anesthesia.

**Regional anaesthesia (RA)**

Regional anaesthesia includes both neuraxial and peripheral nerve local anaesthesia and should be used provided there is no contra-indication such as a bleeding diathesis. This technique avoids the need to instrument the airway, pulmonary complications and unwanted depolarising muscle relaxant side effects. The rate of a successful block may be better where the anatomy is clear and where ultrasound guided techniques are used. A case report by Bhardwaj et al. described a 21 year old patient with OI who underwent a lower limb fracture fixation under spinal anaesthesia only without any major anaesthetic implications. Rothschild et al and Mohmmad et al had similar rates of success and few reports of difficulty reported.

**Combined GA and RA**

The combination of a GA and RA are useful in the paediatric population. A SGAD can be used to secure the airway and keep the patient immobile whilst regional anaesthesia is performed. Using a SGAD precludes the risk of intubating OI patients, who are at risk of having difficult airways. Regional anaesthesia contributes to the multimodal approach of analgesia and may also reduce opioid requirements in patients at risk for pulmonary complications, as explained earlier. Mohmmad et al described that more than two third of cases in their study had combined GA and RA with good outcomes.

**Drugs to be used with caution**

- Succinylcholine: may cause contraction-induced fracture, fatal hyperkalemia and possibly MH
- Anti-cholinergic agent: Atropine dose increase body temperature
Recommendations

1. It is the theatre team’s responsibility to avoid joint dislocation and bone fractures while positioning and moving patients. Exercise extra caution by using moulding mattresses, place padding under pressure points and avoid placing any equipment on the patient.

2. NIBP may be used in mild forms of OI with an increased time interval and reduced inflation pressure. Arterial lines should be reserved for severe cases where frequent haemodynamic monitoring and blood gas sampling is required. Exercise vigilance for hematomas and fractures.

3. Carefully assess the airways of all patients. We suggest the use of a SGAD if not contraindicated. Mask ventilate carefully to avoid jaw fractures and avoid hyper-extending the neck.


5. Monitor temperature carefully as patients are prone to hyperthermia and hypothermia.

6. Preoperative full blood count and coagulation studies are important prior to surgery or regional anaesthesia. Optimizing haemoglobin and platelet counts may be required to avoid unnecessary blood transfusions.

7. Focused CVS examination is important. An ECG and Echocardiography may be necessary to avoid missing and significant cardiac abnormalities.

8. To prevent perioperative respiratory complications we need to evaluate patient clinically and look for complications of chest or spine deformities.

9. The use of regional anaesthesia should be highlighted unless there is an absolute contraindication present. Use nerve stimulators with caution as these may cause fractures. Ultrasound use may improve success rates.

10. GA with SGAD, TIVA and RA has all been used successfully.

11. Avoid the use of atropine
CONCLUSION
In my study all of the surgeries were performed in a tertiary hospital, and it was found that most of the study patients had Osteogenesis Imperfecta Type III. Despite their severe form of disease, few complications and difficulties were described peri-operatively. We can assume from this that extra care and vigilance were employed by experts in a tertiary centre, thus preventing complications. We also found that a combined technique of general and regional anaesthesia using a SGAD was a safe technique. OI is a genetic disorder affecting multiple systems, presenting the anaesthetist with a variety of challenges. These patients require a multidisciplinary team who are familiar with the disease. This includes anaesthetists, surgeons, endocrinologists, cardiologists, pulmonologists, physiotherapists etc. The focus should be on preoperative optimization, planning and vigilant care at every step to prevent intra- and post-operative complications and prolonged hospital stays.
REFERENCES