Osteogenesis Imperfecta: A Literature Review and Case Study

November 13, 2012
Abstract

Osteogenesis imperfecta is a connective tissue disorder resulting in brittle bones that fracture easily. There are different classifications that range in severity. There are many complications and abnormalities associated with this disorder. When performing medical procedures, extra care must be taken to prevent further injuries. Some treatments include physical and occupational therapies, the administration of biphosphates, and surgical stabilization.
Introduction

Osteogenesis Imperfecta (OI) is a genetic connective tissue disorder affecting males and females equally, and is found in all races and ethnic groups. OI means imperfect bone formation. Individuals with OI have brittle bones most often as a result of mutations affecting collagen type I, which is the most prevalent protein in bone, skin and other connective tissues. These mutations can lead to different levels of skeletal deformities and in some cases frequent multiple fractures. OI has different classifications that range in severity and affect patients differently. Some have brittle bone without fractures; others, severe bone abnormalities, while many die shortly after birth.

There are many complications involved for patients living with OI. They often have frequent multiple fractures. Many OI patients experience further injuries during surgery as a result of their brittle bones. Hearing loss is a common problem associated with OI. Additionally, spinal and thoracic cage deformities cause breathing difficulties.

Literature Review

OI was formerly referred to as Lobstein’s disease, named after the first to correctly identify the pathophysiology of the disease. Oakley and Reece (2010) state OI is one of the most prevalent skeletal dysplasias and that it occurs in approximately 1 in every 20,000 births. Mutations in genes responsible for making the proteins that are used in type I collagen account for 90% of OI cases.

OI consists of 8 different phenotypes which vary in their severity, with the first 4 being more prevalent. Rabiee and Etemadi (2011) describe type I as the most common and mild form. Individuals with this type have blue sclera and the majority of their fractures occur prior to puberty. Blue sclera is a result of an abnormal scleral collagen which alters light reflectance.
Mild forms of scoliosis can occur due to vertebral fractures. Type II is lethal and individuals with this form typically die in utero or shortly after birth. Type III is the most severe non-lethal form. Typical characteristics include multiple fractures, normal sclera, progressive long bones, spine deformities and short stature. OI type IV is a more moderate form and has normal sclera. Cundy (2012) describes some additional clinical features of OI. One feature is dentinogenesis imperfecta, which is an abnormality of the dentin in the teeth. Abnormal collagen in dental pulp will lead to enamel breakage. The lower teeth are commonly more severely affected than the upper teeth. Another clinical characteristic of OI is hypermobility due to tendon and ligament involvement. (See Figure 1)

Borland and Gaffey (2012) describe how fractures in individuals with OI heal at a normal rate; however they have a poor quality callus. Reoccurring fractures typically lead to progressive deformity, both shortening and angulation. This is due to the poor quality callus being easily deformed by weight-bearing forces.

**Common Complications**

Hearing Loss ranging from mild to profound is a significant characteristic of OI in many patients. “In national surveys of hearing loss in OI, prevalence rates of hearing loss of 46% have been reported” (Pillion, Vernick, & Shapiro, 2011, p. 2). Abnormal collagen in the ear affects both hard and soft tissues of the auditory structures, which leads to early-onset hearing loss. Depending on the type of OI the individual has, hearing loss will vary.

LoMauro et al. (2012) discuss a study where rib cage deformities due to OI can lead to respiratory difficulties. Patients with severe forms of OI and moderate forms of OI were monitored in separate groups. A group of healthy patients were also monitored as a control group. This test used standard spirometry, which is a pulmonary function test measuring lung
function. It measures the volume and flow of air that can be inhaled and exhaled. Additionally, rib cage geometry, breathing pattern, and regional chest wall volume changes at rest, in seated, and in supine positions were assessed. This was done using opto-electric plethysmography. The system uses 8 special infrared video cameras that work at a sampling rate of 60Hz to compute the 3D coordinates of retro-reflective markers placed on specific anatomic points from the clavicles to the pubis. Patients were analyzed during 3 minutes of spontaneous quite breathing while awake in seated positions first followed by supine positions. This study showed that the respiratory difficulties correlated to the severity of the disease and to the sternal deformities. It also shows functional assessment and treatment of OI should be differentiated in the various forms of the disease.

Surgery presents additional challenges for patients with OI. Positioning of the patient is essential step for all operating room staff members and care should be taken to avoid fractures. The simple act of moving a patient to the operating table from a stretcher can result in a fracture. The table should be padded paying close attention to pressure points. When possible, molding mattresses are ideal due to the patient’s inability to lay flat and supine. The pressure from automated blood pressure cuffs can cause fractures in patients with OI. Arterial lines may be placed to avoid this issue.

Another problem posed during surgery with OI patients is securing an airway. Overextension of the cervical spine may cause odonto-axial dislocation or even fractures. If the patient has dentinogenesis imperfecta or a fragile mandible, a broken jaw or easily chipped or dislodged teeth can occur. Extra care must be used to avoid these complications.

Other complications individuals with OI face are spinal and thoracic cage deformities. Kyphoscoliosis and thoracic cage deformities are both common in OI populations.
Kyphoscoliosis is an abnormal curvature in both the coronal and sagittal planes. Oakley and Reece (2012) found scoliosis was found in patients under the age of 5 in 26% of the cases. This percentage increased to 82% in older children. “Respiratory complications secondary to chest deformity and scoliosis lead to limitations in thoracic function and make it the principle cause of death in most patients with OI.” (p. 49)

When the thoracic spine curvature is less than 35 degrees, respiratory function during exercise is impaired. If the curvature is over 50 degrees, there will be a decrease in vital capacity at rest. When the curvature is greater than 80 degrees, there is a dramatic increase in morbidity and mortality. Lung expansion and thoracic movements can be limited by deformities in the thoracic spine and abnormal positioned ribs. The severity of these limitations will increase due to rib fractures and respiratory weakness.

Type I collagen comprises approximately 85% of cardiac muscle. In addition, it provides rigidity to the ventricular wall. Deficiencies in the collagen can lead to major changes in the structure and function of the myocardium. Oakley and Reece (2012) discuss the importance of perform echocardiography to rule out cardiac abnormalities in high risk OI patients prior to performing any surgical procedure. They found that the most commonly reported cardiac anomaly for OI patients is mitral valve prolapsed. Unfortunately, this is also one of the most common anomalies in humans making it difficult to say if it is a result of the OI. The most common cardiac abnormality specific to OI was reported to be aortic root dilatation.

**Treatments**

Treatment of OI consists of rehabilitation including physical and occupational therapy to promote gross motor development and maximize functional independence, and surgery to stabilize bones and correct deformities. Biphosphates are often used in children with OI to
reduce the occurrence of fractures. Biphosphates are drugs that prevent the loss of bone mass. They inhibit the digestion of bone by encouraging osteoclasts to undergo apoptosis, or cell death, thereby slowing bone loss. Suresh and Thomas (2010) found this to be beneficial in moderate to severe cases of OI in reducing the rate of fractures and deformities.

When biphosphates are used, it typically results in sclerotic bands which have a band-like appearance at the metaphysis of long bones which can be visualized on radiographs. There is increased bone mineralization due to the decrease in osteoclasts activity during these treatments. These lines are usually perpendicular to the axis of growth spanning the width of the bone. “The bands are the result of the failure of remodeling of the primary spongiosa into the secondary spongiosa in the physis. Further growth of the physis results in the appearance of normal bone, which results in the bands” (Suresh and Thomas, 2010, p. 43). The number of lines correlate to the number of treatments the child received. The lines will be closer together the more frequent the treatments and can be seen as early as 2 months following the first treatment. The bands cease appearing following physeal closure.

Fractures are more common in the long bones of the lower extremities. Because of this, the more severely affected OI patients are limited in their potential in achieving independent walking. Surgical stabilization can serve to reduce the fracture rate for lower limbs up to adolescence. Nicolaou, Bowe, Wilkinsin, Fernandes, and Bell (2011) discuss splinting of the long bones with the use of intramedullary implants in order to prevent recurrent fractures and allow correction of deformities. There are concerns when inserting these across a physis. Rod entry across the knee and ankle joints may lead to later complications due to breaching of the joint and insertion into the articular cartilage.
The Sheffield system was developed in the 1980s and is comprised of a male and female component, with a fixed, notched T-piece designed to anchor the rod within the epiphysis to prevent migration. (See Figure 4) The rods are manufactured from stainless steel and are available in different diameters and lengths. These rods are associated with low complication rates. The number of fractures following initial instrumentation is reduced by the use of telescope rods, resulting in high patient satisfaction.

**Case Study**

An infant with history of OI was seen 4 times in a 1 year period. Each time she presented with similar symptoms. She was in apparent pain, not feeling well, and showed a history of OI. Various x-rays were obtained including images of her pelvis, lower extremities, and a bone survey. On each of the visits, each of the x-rays demonstrated fractures in the lower extremities. Also present were multiple sclerotic bands on the femur, tibia, and fibula. (See Figures 2 and 3)

The bone survey showed bowing of the proximal femora bilaterally which is consistent with OI. It also showed an irregularity of the proximal femora bilaterally consistent with prior fractures. It demonstrated thin sclerotic bands at the metaphysis of the long bones bilaterally and symmetrically. The radiologist stated that this is most likely related to therapy. No fractures were identified during the bone survey.

**Discussion**

Osteogenesis imperfecta is a connective tissue disorder that affects a lot of individuals. There are different classifications that range in their severity. Patients with this disorder suffer from brittle bones that may lead to frequent recurrent fractures. Special care must be used in caring for these individuals to avoid injuries. Certain complications arise when performing
medical procedures on these patients depending on the severity of their condition. A simple blood pressure cuff can result in fracture as well as other complications.

Treatment of OI can include both physical and occupational therapies to aid in gross motor development. It can also help increase functional independence. Biphosphates can be used to aid in reducing fracture rates by increasing bone mineralization. The use of these will result in sclera bands that can be visualized on radiographs. Surgical stabilization can also be used to prevent fractures or correct deformities. These are beneficial to the patient, but they also have concerns that need to be considered.
Figures

**Figure 1.** Clinical features of OI in adults. **a.** Blue sclerae shown in a mother and daughter with a mild form of OI. **b.** Dentinogenesis imperfecta in an adult patient with a mild form of OI. **c.** Hypermobility in an adult patient with a moderate-to-severe form of OI. **d.** OI presenting as postpartum osteoporosis. Multiple vertebral compression fractures are shown.

Figure 2. Ap view of the femur of a 1 year 9 month old female infant showing an acute transverse fracture involving the proximal femoral diaphysis with approximately 90 degrees of varus angulation at the fracture site. Multiple growth arrest lines are present within the metaphyses of the femur.

Note: Image printed with permission

Figure 3. Lateral view of the tibia and fibula of same patient. The tibia and fibula also show multiple growth arrest lines.

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**Figure 4.** Photographs showing the male and female components of the Sheffield intramedullary rod before and after mating.

References


