



ORTHOPAEDIC MANAGEMENT OF CHILDREN WITH OSTEOGENESIS IMPERFECTA. (Experience of Republican children's orthopaedic center)

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Abstract:

Limitation of movement and fear from multiple fractures in children with Osteogenesis Imperfecta (OI) lead to decrease of comfort in normal daily life. Correction of deformation and proper medical treatment facilitates to achieve better functional results.

In this paper, we present sixty-four patients with clinically diagnosed OI had been treated in Republican children's orthopaedic center. There were 42 male and 22 female OI affected patients. Diagnosis was made according to clinical presentation and radiographic examination. 41 patients treated with intravenous third generation bisphosphonates – Zometa, every 4-6 months. 36 operations were done in 25 patients with lower limb deformation as described Sofield and Millar. All operations were performed in purpose of lower limb bone deformity correction. Fixation of lower leg bones after correction of deformation made by using different intramedullary nails and pins. Fassier Duval (FD) telescopic nail used in 19 patients (femur - 11, tibiae - 13). In 3 patients with older age (15, 16 and 18 years old) fixation was made by Slim nails (femora – 3, tibia - 5). Ilizarov pins were used to fixate 4 tibiae in 3 patients, due to difficulty of using FD nail.

No complication was detected except prolonged swelling in 4 adolescent patients after operation of tibiae which subsided without complications.

Purpose of this paper to present management of patients with OI in Republican center of children's orthopaedics in the Republic of Uzbekistan.

Keywords: Osteogenesis imperfecta, Sofield operation, Fassier Duval telescopic nail.

INTRODUCTION.

Osteogenesis imperfecta (OI) is a rare congenital skeletal bone disease characterized multiple skeletal fractures due to extreme bone fragility. Up to eleven different forms, characterized by over 280 gene mutations have been described. The incidence of occurrence is 1 to 20,000 live birth [1-4]. More than 70% of OI cases are associated with autosomal dominant mutations in collagen chains (COL1A1, COL1A2). [5,6]. Orthopaedic manifestations of OI are multiple fractures leading to progressive skeletal deformations, short stature and spinal deformations. Triangular face, blue sclera and dentinogenesis imperfecta are common clinical symptoms which helps to make diagnosis.

Deformations of upper and mostly lower extremity in patients with Osteogenesis imperfecta, occurs due to multiple fractures of long bones and cause limitation of range of motion in joints. Most of

the time fractures treated by casting of affected limb in deformed position. Also, muscle imbalance plays a role in healing of bones in bowed position.

The current medical treatment with bisphosphonates (BP), in particular, pamidronate and Zoledronic acid, has been shown to increase bone density, reduce the occurrence of fracture and pain, as well as functional improvement, including ambulation in children with OI [7].

Medical approach to the treatment of OI is different from fractures in children without underlying diseases. Casting and using plates, flexible nails as a fixators showed its ineffectiveness of preventing deformations. Intramedullary (IM) rodding of these long bones is the current orthopedic approach. The goals of orthopedic surgery are: correct long bone deformity and reduce the incidence of fractures. Correction of deformity combined with bone stabilization has been used for many years. Sofield and



Millar [8] reported their technique of bone fragmentation and subsequent fixation with solid small-diameter rods in 1959. Fixation of bone fragments with Fassier Duval telescopic intramedullary nail facilitates stability during growth of long bones in pediatric patients.

Purpose of this paper to present management of patients with OI in Republican center of children's orthopaedics in the Republic of Uzbekistan.

MATERIALS AND METHODS.

Since 2020, sixty-four patients with clinically diagnosed OI had been treated in Republican children's orthopaedic center. There were 42 males and 22 females. Diagnosis was made according to clinical presentation and radiographic examination. Mostly, patients had characteristic triangular face (58 cases), blue sclera (48) and dentinogenesis imperfecta (53). Generalized ligament laxity evaluated in all patients. Patients with multiple fractures of upper and lower extremity had affected segment deformation. Character of deformation of femur was varus (20) with procurvatum (9). However, tibia and fibula were in procurvatum (24) position combined with valgus (11) deformation. In 15 patient's parents, mostly mothers (10 cases) had blue sclera and upper or lower limb fractures (one or two times) in their life.

Table 1. Distribution of patients according to their clinical manifestation.

Gender	Blue sclera	DI*	Skeletal deformations				
			Humeral bone	forearm	femur	Tibia and fibula	Vertebral deformity
Male	31	34	6	3	18	21	8
female	17	19	3	2	11	14	4
Total	48	53	9	5	29	35	12

*DI – dentinogenesis imperfecta

CONSERVATIVE TREATMENT.

In purpose of strengthen the bone tissue, to reduce frequency of fracture and to improve ambulatory or mobility status third - generation of bisphosphonates – Zoledronic acid administered to 41 OI patients. Zometa (4mg/5ml, NOVARTIS PHARMA STEIN, AG, Switzerland) was a medicine of choice and administered intravenously (IV). Dosage calculation was performed according to the age and weight of patients. 0.025 mg/kg /dose for patients <3 years and 0.05 mg/kg/dose for >3 years old. Blood analysis for vitamin D and calcium level were necessary before IV

intake (Vitamin D level is above 50nmol/l and blood calcium level 2.5 millimol/L).

OPERATIVE TREATMENT.

36 operations were done in 25 patients with lower limb deformation as described Sofield and Millar [8]. All operations were done in purpose of lower limb bone deformity correction. Fixation of lower leg bones after correction of deformation made by using different intramedullary nails and pins. Fassier Duval (FD) telescopic nail used in 19 patients (Figure 1) (femur - 11, tibias - 13). In 3 patients with older age (15, 16 and 18 years old) fixation was made by Slim nails (Figure 2) (femora – 3, tibia - 5). Ilizarov pins were used to fixate 4 tibias in 3 patients, due to difficulty of using FD nail. Difficulties consisted of extremely bone fragility and clogged bone marrow cavity due to callus formation.

All fixators cannot maintain rotational stability. To provide healing in proper position we applied cast immobilization for 3 weeks after surgery. Hip spica cast for femoral osteosynthesis and long leg cast with derotator after operation on tibia and fibula bones were applied. Cast immobilization removed as soon as confirmation of callus formation on plain radiographs.

RESULTS.

41 patients had IV Bisphosphonate (Zometa) treatment every 4-6 months. Total number of intakes ranged from 3 to 6 times. Better feeling, improvement in range of motion and decreased number of fractures were noticed in all patients. No remarkable complications were detected. In 34 patients body temperature increased up to 38.5 degrees of Celsius during 4 days and decreased without complications after NSAID intake. Control radiographs of long bones showed "Zebra" (Growth line block) lines. All patients started feeling better in terms of ambulation and extremity movement. According to parents' report, patients became more confident in daily activity. Patients who planned to be operated, IV BPs administered at least 15 days before surgery.

Sofield - Millar procedure [8] performed in 25 patients to corrects deformities of lower limb. 14 femora and 22 tibias deformations corrected and fixated with various intramedullary fixators according to bone fragility and age of patients. Fassier-Duval interlocking pins were used in 11 femora and 13 tibias. Patients age ranged from 5 to 12years old. In severely affected 3 patients (4 tibias) with extreme bone fragility and medullary cavity narrowing Ilizarov (diameter 1.8 mm) pins were used as a fixator. In one patient (13 years old boy) Ilizarov pin was replaced to



FD fixator after 6 months when radiographic image of tibia showed well developed medullary canal. In older Patients with higher bone density, Slim IM nails used to fixate bone fragments. Osteotomy for correction of deformity performed at 1 to 3 levels and length of shortening osteotomy were from 0 to 5 cm both in femoral and tibia segment for all patients. All patients' recovery after surgery proceeded uneventfully. In 2 patients swelling of calf remained during 4 days after surgery and healed without complications.

DISCUSSION.

This is the first paper dedicated to orthopaedic management of patients with Osteogenesis imperfecta in Uzbekistan. Hence, modern attitude started in 2020, short term results available. Diagnosis of OI made based on clinical and radiographic findings. Additional extra skeletal manifestations include valvular insufficiency and aortic root dilation, generalized ligamentous laxity, hernias, easy bruisability, and excessive sweating could help to make diagnosis. The bulging calvaria causes facial-cranial disproportion, which gives the face a triangular shape.

In severely affected 11 patients, the long bones are slender and smaller than normal and the cortices are extremely thin, with a paucity of medullary spongy bone. Multiple recent or/and healed fractures, with varying degrees of angular or torsional deformities were also noted.

The spine in individuals may show varying degrees of deformity, usually scoliosis, often with compression fractures and wedging of the vertebral bodies. Kyphosis may be combined with scoliosis. Scoliosis is present in 20% to 40% of patients. Scoliotic deformation of the spine noticed in 12 non-ambulatory patients. The most common type of curve is thoracic scoliosis. [9,10]

One of the common clinical finding is short stature, which is caused by deformities in the limbs from angulation and overriding of fractures, growth disturbance at the physes, and the marked kyphoscoliosis. Generalized ligamentous laxity with resultant hypermobility of joints is common. Pes valgus is a frequent physical finding. Blue sclerae are one of main features of OI [11] but, as noticed in our cases, are not present in all patients. The blueness of the sclera is caused by the thinness of its collagen layer secondary to decreased production of COL1. Normal-colored sclera in patients with OI have normal.

The administration of sex hormones, [12] sodium fluoride [13], calcitonin [14], calcium, growth hormone [15], magnesium oxide, and vitamins D and C were all attempted in the past, and results were

mixed or absent. Administration of bisphosphonates showed considerable results in children with OI. The indication for BP therapy remains to be "medical center" specific, based on scientific evidence and clinical experience. In our center, Zoledronic acid is widely used for medical treatment. Dietary consult is beneficial to optimize calcium, phosphate, and vitamin D intake. We ensure that calcium, phosphorus, and 25(OH) vitamin D are within normal range prior to the initiation of BP therapy. Bisphosphonates found to inhibit osteoclastic resorption of bone, which appears to be increased in patients with OI. Aminohydroxypropylidene (pamidronate) has been studied extensively and used widely among worldwide orthopaedic surgeons. However, third generation medicine – Zometa became popular in recent days. Transient fever is not common complication after BP and subsides after NSAID intake. Metaphyseal bands of increased density are seen in radiographs after BP treatment. [16]

The goal of orthopaedic treatment is to maximize the affected patient's function, prevent deformity and disability resulting from fractures, correct deformities that have developed, and monitor for potential complicating conditions associated with OI. Worldwide accepted choice of operative treatment is Sofield - Millar procedure described in 1959, consists of multiple diaphyseal osteotomies (fragmentation) with intramedullary fixation. [14] The indications for fragmentation and rodding are a long bone deformity that interferes with fitting of orthoses and impairs function and repeated fractures. These indications are much more frequent in the lower than in the upper extremity.

In general, reports are favorable in that deformity is corrected and mobility maintained or achieved. Complications of the procedure include nonunion, infection, and rod migration. We did not observe complications in our case series.

Fixation of bone fragment is challenging. Plates and external fixators are not advisable due to decreased bone density. Sofield and Millar used a fixed intramedullary rod (a straight, round steel rod, Rush rod, or Küntscher rod) for internal fixation. [17] Others have used Rush rods [18,19] or Williams rods. [20, 21] Intramedullary rods cannot maintain fixation during growth of long bones. In 1963, Bailey and Dubow introduced an extensible intramedullary fixation rod to reduce the need for reoperation because of bone overgrowing the rod. [22]

In 1989, Stockley and associates described a modified version of the original device, now commonly referred to as the Sheffield rod. [23] Experience with



the Sheffield rod over a 10-year period has shown significant reduction in the frequency of fractures and improvement in ambulatory status. [24] The newest telescoping device, the Fassier-Duval rod, was introduced in 2003 in Canada. Advantages of FD rod is the single proximal entry point and threaded epiphyseal portion that allows screw-in fixation. It is implanted through small incisions, showed good stability and function of the implants. [25] There is a paper results of improver functional outcomes (ambulation, gross motor function, self-care, and mobility) at 1-year follow-up in 60 children treated with Fassier-Duval rodding of the femur and bisphosphonate administration. [26]

Slim IM nails useful to fixate bone fragment in older patients whose longitudinal growth slowed or ceased. Slim intramedullary nail is long stable and has threaded end at the bottom. It provides stability in sagittal and coronal planes. However, steady stability in rotational profile is insufficient which is assisted by cast immobilization.

In conclusion, orthopaedic management of patients with OI is challenging and maintaining high bone density and limb alignment are main goal. We believe, medical and operative treatment based on the modern technologies with extensive rehabilitation will improve general and ambulatory status of children with OI.

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Figure 1 (a). 11 years old female patients with severe antecurvatum deformation of both tibias.



Figure 1 (b). Same patient after surgical treatment on both lower leg and fixated with FD telescopic IM nail.

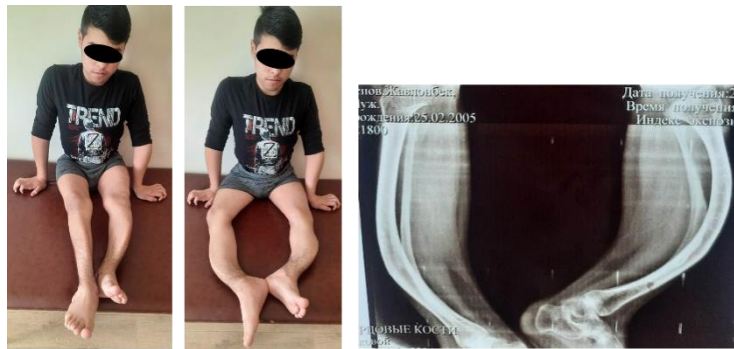


Figure 2 (a). 17 years old male patient with antecurvatum deformation of both tibias.



Figure 2 (b). Clinical and radiographic images of same patient after surgical treatment on tibias. Slim IM nails used as a fixator.