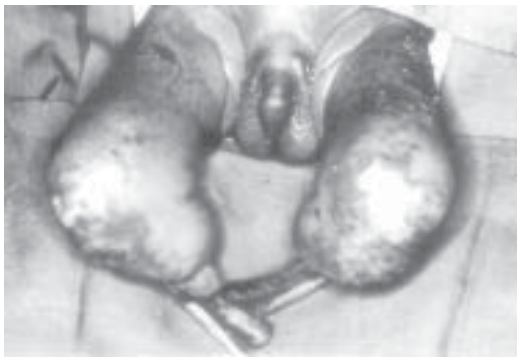

Fig. 1. Photograph showing neonate with loss of soft tissue of both lower limbs with exposed bones.

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Oral Alendronate in Osteogenesis Imperfecta

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We report a case of Osteogenesis Imperfecta (OI) in an eight-year-old boy who was admitted with complaints of recurrent long bone fractures. With oral alendronate treatment significant increment occurred in the bone mineral density and the number of fractures decreased. The usage of oral bisphosphonates is inexpensive and easy to administer in selected cases of OI. This case report supports the usage of oral alendronate treatment as an alternative treatment in OI.

Keywords: *Alendronate, Osteogenesis imperfecta.*

Osteogenesis imperfecta (OI) is a heritable disorder characterized by either a reduction in the production of normal type I collagen or the synthesis of abnormal collagen as a result of mutations in the type I collagen genes. Affected patients tend to have fragility fractures from the mildest trauma. Other common symptoms are progressive skeletal deformities, varying degrees of short stature, blue sclerae, dentinogenesis imperfecta, joint laxity and the onset of deafness in adulthood(1,2).

There is no effective medical treatment for OIs. Bisphosphonates are synthetic analogues of pyrophosphate that inhibit bone resorption by their action on osteoclasts. In recent years, bisphosphonates have been used in children for treatment of a growing number of disorders associated primarily with generalized or

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localized osteoporosis, metabolic bone diseases, heterotopic calcification in soft tissues and for resistant hypercalcemia. Recently, beneficial effects of intravenous pamidronate treatment are also reported in OI(2,4,5). No data are available regarding oral alendronate treatment alone in children with OI. We report a case of OI in an eight-year-old boy who responded favourably to oral alendronate.

Case Report

A 8-year-old boy presented with history of repeated (eight in all) fractures following minor trauma; first fracture was noticed at birth. The child had blue sclera. Serum concentrations of calcium, phosphorus and $1,25(OH)_2$-vitamin D_3 were normal; serum alkaline phosphates (ALP) level was high (854 IU/L). Dual Energy *X*-ray Absorptiometry (DEXA) scan of the lumbar spine showed low bone mineral density (BMD) with BMD of lumbar spine found as 0.251 g/cm^2. BMD z score was calculated as –4.77 according to Turkish children standards (data in press). Taking into account that DEXA could be influenced by delayed skeletal maturity, BMD z score was calculated according to the bone age (Greulich-Pyle atlas) which was 3 years below chronological age(6). Type I OI was considered according to Sillence classification(7). He was treated with oral alendronate at a dose of 5 mg per day. The patient was administered pills 30 minutes before the breakfast and asked to stay in upright position for an hour after the dose. At the end of the 36 months of treatment, his chronological age was 11 and bone age was 8. According to Tanner stage, his puberty was stage I and height SDS was –1.69 after treatment as compared to –1.78 before therapy. Only one fracture occurred during the 36 months of the treatment.

DEXA scan was repeated after 12 and 36 months of alendronate treatment. BMD at lumbar spine was significantly increased 0.403 g/cm^2 Z score –1.97). At the end of the treatment, BMD increase was calculated to be 20.1% per year. The treatment was tolerated well and no side effects were reported.

Discussion

Bisphosphonates are synthetic analogues of pyrophosphate that inhibit bone resorption by their action on osteoclasts. Bone mineral density and fracture rates in children with osteogenesis imperfecta improve with intravenous bisphosphonates(8). The efficacy of oral bisphosphonates has not been studied extensively. Nitrogen-containing bisphosphonate like alendronate is generally accepted as a safe, effective, and well-tolerated treatment for postmenopausal osteoporosis; it increases the lumbar and femoral neck BMD and prevents new bone fractures. Alendronate preferentially binds hydroxyapatite and inhibits osteoclast-mediated bone resorption by suppressing the recruitment and activity of osteoclasts and shortening their life span but there is few experience about alendronate use in children and adolescents(2,8).

Concerning the use of bisphosphonates in children, there have been fears that interference with the rapid remodeling process, which is necessary in growing bones, might result in bone deformity or serious disruption of the normal mineralization process. The studies have shown that the linear growth of children, who were on bisphosphonate treatment, were not affected(8). During the treatment, the linear growth of our patient was in normal ranges and also the height SDS showed moderate improvement. The children with OI have bone deformities and short stature due to recurrent fractures. The minor improvement in our patient's height SDS is, probably, due to the decrease in fracture

frequency rather than the primary effect of alendronate.

Pamidronate is the most frequently used bisphosphonate in children with OI. Various studies revealed that, in children with OI, intravenous pamidronate treatment leads to an increase in BMD, a significant decrease in fracture frequency an improvement in life quality and a subjective decrease in bone pain. On the other hand this drug is expensive and 1 to 3 days of hospitalization is necessary for intravenous infusion(2-5).

The only report regarding the use of oral alendronate in children with OI included 15 children with OI, who received oral alendronate plus calcitriol treatment. It was reported that the BMD of all patients increased and a significant decrease in fracture frequency was observed(10).

The usage of oral bisphosphonates is inexpensive and easy to administer instead of intravenous (IV) form in selected cases of OI. We conclude that oral alendronate treatment decreases the bone turnover, improves the lumbar BMD and prevents new fragile fractures in type I OI.

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