VERTEBRAL COMPRESSION AND RESHAPING IN CHILDREN WITH OSTEOGENESIS IMPERFECTA ON REGULAR ZOLEDRONIC ACID INFUSIONS

A. Baioumi[1], M. El Houssinie[2] and H. Elsedfy[1]

[1]Paediatrics Department, Ain Shams University, Cairo, Egypt

[2]Department of Community Medicine, Ain Shams Medical School, Cairo, Egypt

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INTRODUCTION

Osteogenesis Imperfecta (OI) is a group of rare hereditary collagen disorders which is mainly caused by mutations in genes involving synthesis of type I collagen or regulating osteoblast functions.

Vertebral compression fractures and vertebral deformities are well-known complications of OI. Vertebral compressions not only contribute to the development of scoliosis but also impact on the quality of life of patients by affecting their cardiorespiratory function which might shorten their life span.

Bisphosphonates increase bone mineral density (BMD) and reduce fracture risk of OI patients by inhibiting osteoclastic activities.

The effect of intravenous ZA on the shape of vertebral bodies in children with OI is still an area of evolving research.

AIM

This study aimed at assessment of the changes in vertebral compression and shape in children who received regular ZA infusions.

METHOD

This was a prospective study that ran over 5 years recruiting infants, children and adolescents with OI attending the Paediatrics Endocrinology Clinic of Ain Shams University (PECASU), Egypt.

The study included 23 patients with OI receiving regular ZA infusions. Patients < 3 years received ZA at a dose of 0.025mg/kg every 3 months and those ≥ 3 years received ZA at a dose of 0.05 mg/kg every 6 months. All patients were given the recommended daily doses of calcium and vitamin D.

Lateral X-rays of the thoracic and lumbar spine were done for each patient at initial enrolment then at the end of each year till they reached the minimum X-ray score then no further X-rays were done. The Score of Spine Morphology (SSM) developed by Koerber et al., 2012 (1) was used to assess the effect of ZA infusions on thoracolumbar spine morphology. The SSM relied on three criteria: vertebral compression, thoracolumbar kyphosis and deformity type to formulate a severity classification which is then used to develop a severity score.

RESULTS

The study included 23 patients, 13 males and 10 females. The mean age of the included patients was 5.3 ± 0.9 years. Their mean length/height SDS was -3.42±0.61 and their mean BMI SDS was -0.82±0.46 at inclusion in the study.

Children with OI showed significant increase in height / length on treatment.

There was no significant change in electrolytes, serum creatinine, ALT, calcium or phosphorus during the follow up period while patients were receiving ZA infusions. However, alkaline phosphatase (ALP) was significantly reduced compared to baseline on some visits starting from the third follow up visit.

ZA infusions were associated with a significant reduction in vertebral compression. The angle of kyphosis could be reduced through ZA treatment but the difference compared to baseline was not statistically significant.

The severity score which represented the mean values for thoracic and lumbar spines deformity and compression showed a significant reduction along the course of treatment (p = 0.001).

Table 1 The Score of Spine Morphology (SSM) in children with OI during follow up

	Baseline (N=23)	Follow up 1 (N=19)	Follow up 2 (N=14)	Follow up 3 (N=4)	*p*
Maximum point value for compression on X-ray spine	2.5 ± 0.3	1.8 ± 0.3 *	1.7 ± 0.3	1.1 ± 0.5	**0.026**
Average point value for compression on X-ray spine	2.2 ± 0.2	1.5 ± 0.2 *	1.5 ± 0.3 *	1 ± 0.5 *	**0.008**
The angle of kyphosis on lateral spine X-ray	2 ± 0.2	1.5 ± 0.2	1.3 ± 0.3	1.2 ± 0.5	0.067
Severity Classification	2.7 ± 0.4	2.2 ± 0.4	2 ± 0.5	0.9 ± 0.8	0.181
Severity Score	41.8 ± 6.6	20.7 ± 6.8 *	17.5 ± 7.6 *	4.8 ± 12.2 *	**0.001**

*p<0.05 compared to baseline value

CONCLUSIONS

Improving the deformed vertebral bodies in growing children with OI has important clinical implications.

This study showed that the different vertebral defects in patients with OI could be reshaped through regular ZA infusions without significant adverse effects or electrolyte disturbances.

Long-term therapy with ZA caused a significant reduction in ALP which could be explained by the reduced bone remodelling as an effect of ZA treatment.

CONCLUSIONS (CONT.)

Palomo et al., 2015 observed that vertebral reshaping did happen for growing children with OI on regular bisphosphonate therapy (2) with improvement in the number and severity of vertebral compression fractures over at least 6 years of IV pamidronate or ZA treatment.

Li et al., 2019 used quantitative vertebramorphometry which relied on different geometrical measurements of the vertebrae to assess the response to ZA infusions in children 3-15 years of age over a 2-year period. They used 5 mg annually of IV ZA to improve BMD. Additionally, patients also received calcium, vitamin D3 and calcitriol. Their study showed that vertebral dimensions were significantly improved after 1 year of treatment with ZA (3).

CONCLUSIONS (CONT.)

The SSM used in our study was easy to apply after a brief period of training. The severity score was a useful tool to assess the changes in vertebral bodies in children with OI.

It would be preferable to reach a consensus regarding the method of assessment of the changes in the shape of vertebral bodies in clinical and research settings in children with OI.

The authors recommend using the severity score for the clinical assessment of the changes in the shapes of vertebral bodies in children with OI.

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