Osteogenesis Imperfecta in the Bisphosphonate Era

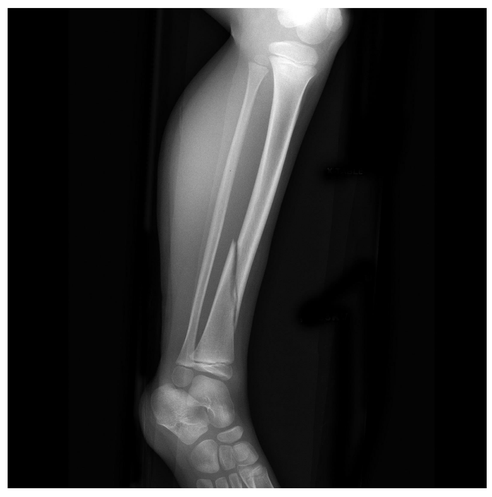
Andrew G. Feehan[1,2], Margaret R. Zacharin[1,2,3], Angelina S. Lim[1,4], Peter J. Simm[1,2,3]

[1]Hormone Research, Murdoch Children's Research Institute
[2]Department of Paediatrics, University of Melbourne
[3]Department of Endocrinology, Royal Children's Hospital
[4]Centre for Medicine Use and Safety, Monash University

BACKGROUND

Osteogenesis imperfecta (OI): a heritable connective tissue disorder characterised by increased bone fragility and low bone mass (1)

Skeletal features include frequent fractures, generalised osteopaenia, long-bone bowing, vertebral compressions and a varying degree of scoliosis (2).



Case courtesy of A.Prof Frank Gaillard, Radiopaedia.org, rID: 10344

- Bisphosphonate therapy: mainstay of treatment in OI, complemented by physiotherapy, rehabilitation & orthopaedic surgery (3)
- Bisphosphonates ↑ bone mineral density (BMD), ↓ fracture rates & improve mobility and ambulation in the short-term (4)
- It is unclear whether bisphosphonate treatment improves long-term outcomes in OI.

AIMS & OBJECTIVES

To demonstrate functional outcomes of adults with OI, stratified according to OI severity and treated with intravenous bisphosphonates as children.

To explore fracture incidence, bone mineral density outcomes and pain in this cohort compared to adults with OI who were never treated as children.

METHODS

- Adults with OI previously treated with bisphosphonates as children at RCH were invited to participate (*childhood treated cohort*).
- Adults with OI who were never treated with bisphosphonates as children were also invited to participate (*adult treated cohort*).

The study utilised four questionnaires:

- Validated quality of life survey: WHOQOL-BREF
- Validated functional surveys: Short Form (36) Health Survey, International Physical Activity Questionnaire (IPAQ) Short Form
- Study specific questionnaire assessing demographics and clinical history

Medical records were accessed to verify clinical data.

Results compared between groups & to controls in the literature (5-6).

RESULTS 1

Patient characteristics

- 52 adults (80% response) completed questionnaires. 33 adults treated in childhood, 19 adults treated in adulthood
- Median age (IQR): Childhood treated = 24 (21-28); Adult treated = 40 (34-46)
- Male:female = 18:15 (childhood treated) and 6:13 (adult treated)
- No significant differences in characteristics of childhood treated and adult treated cohorts.

Bony outcomes

- Childhood treated cohort started bisphosphonate treatment earlier than adult treated cohort (p<0.001).
- Pre-pubertal fracture incidence was reduced for all severities of OI but post-pubertal fracture incidence was higher for less severe OI.
- No significant differences in vertebral fracture incidence or diagnosis of scoliosis between childhood treated and adult treated cohorts.
- However, early bisphosphonate treatment improved BMD as assessed by dual-energy x-ray absorptiometry (DXA).

Table 1 Fracture incidence, scoliosis diagnosis and length of bisphosphonate treatment

	Childhood treated	Adult treated	P-value
Age at first fracture [months], median (IQR)	12 (0 – 36)	18 (6.8 – 22.5)	0.494
Fractures/ 10 person-yrs (95% CI)			
Before puberty,	5.2 (4.0 – 6.5)	8.3 (6.2 – 10.8)	**0.010**
Less severe OI	21.8 (20.1 – 23.5)	36.5 (33.3 – 39.9)	**<0.001**
More severe OI			
After puberty,			**<0.001**
Less severe OI	2.3 (1.4 – 3.5)	0.5 (0.2 – 1.0)	0.689
More severe OI	5.6 (4.7 – 6.6)	5.3 (4.5 – 6.3)	
Vertebral fracture, n (%)	15 (50)	5 (27.8)	0.308
Unknown, n (%)	6 (20)	6 (33.3)	
Scoliosis, n (%)	16 (48.5)	8 (44.4)	1.000
Bisphosphonates			
Age when started treatment in years, median (IQR)	9 (5 – 11.5)	28 (19 – 35)	**<0.001**
Length of treatment in years, median (IQR)	7 (4 – 11.5)	6 (3 – 12)	0.532

Table 2 BMD outcomes, childhood treated versus adult treated

	Childhood treated	Adult treated	P-value
L_1L_4 BMD z-score	-0.4 at mean age 21.3 years	-1.9 at mean age 40.9 years	**0.003**
Less severe OI	0.4 at mean age 17.4 years	-2.0 at mean age 41.6 years	**0.002**
More severe OI	-0.8 at mean age 23.4 years	-1.9 at mean age 39.4 years	0.081

RESULTS 2

Quality of life outcomes

- No significant differences in quality of life scores between childhood and adult treated cohorts
- The childhood treated cohort scored lower than healthy controls in the physical domain.

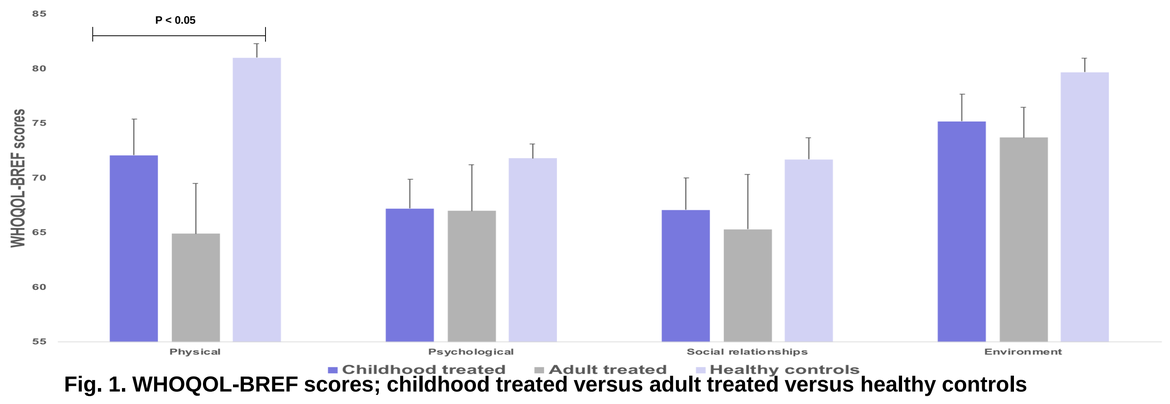


Fig. 1. WHOQOL-BREF scores; childhood treated versus adult treated versus healthy controls

Functional outcomes

- In less severe OI, childhood treated individuals had higher levels of physical functioning than adult treated individuals.
- In more severe OI, there were no differences in physical function between the two cohorts.

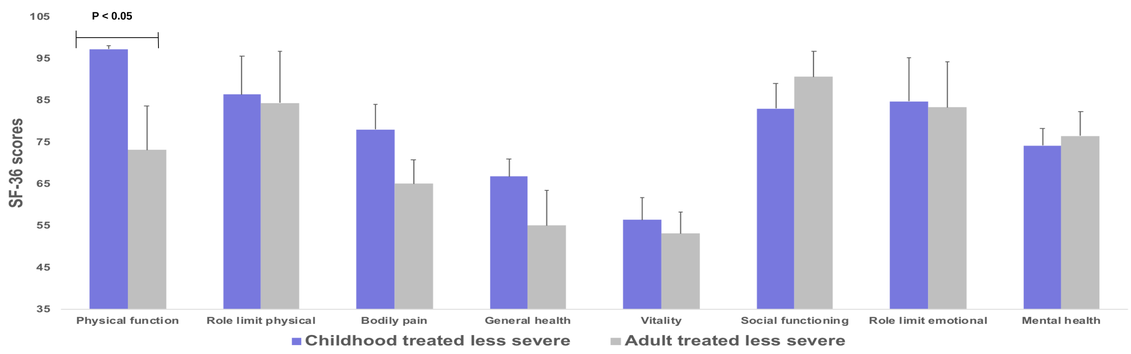


Fig. 2. SF-36 scores; less severe OI, childhood treated versus adult treated

CONCLUSIONS

- Adults with OI treated with bisphosphonates as children had improved BMD outcomes compared to adults with OI who were never treated in childhood.
- Improved BMD does not appear to influence prevalence of scoliosis.
- Results suggest that treatment with bisphosphonates at an earlier age improves physical activity, particularly in less severe forms of OI but may not alter quality of life

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