UNIKLINIK KÖLN

Klinik und Poliklinik für Kinder- und Jugendmedizin

Early treatment with intravenous bisphosphonates prevents severe postnatal bone loss in children with Osteogenesis imperfecta

Mirko Rehberg, Johanna Heistermann, Eckhard Schoenau, Oliver Semler, Heike Hoyer-Kuhn

[1] University of Cologne, Faculty of Medicine and University Hospital Cologne, Department of Pediatrics, Cologne, Germany,

Conclusion

- During first months after birth children with OI loose bone.
- Patients starting very early (first 3 weeks) with antiresorptive treatment showed less vertebral compression fractures than "late starters" (4 months).
- "Early starters" tended to have a better motor function development than "late starters".
- Therefore it can be assume that an early antiresorptive treatment might be beneficial for severely affected children.

Background

Osteogenesis imperfecta (OI) is characterized by hereditary skeletal fragility. Bisphosphonates (BPs) are the first line medical treatment in moderate and severe OI types III/IV. There is no consensus regarding start of treatment and treatment regimen in the first years.

Objective

Objective of the presented project was the evaluation of the therapeutic effect of 1 year of bisphosphonate treatment with neridronate (schedule see tab. 1) on vertebral shape and mobility in children with severe OI.

Age	Dose	Interval
0-11 months	1.0 mg/kg/day on two consecutive days	every three months
≥ 1 year	2.0 mg/kg/day as a single dose	every three months

Table 1: Schedule for neridronate treatment for children with OI

Methods

Matched pair analysis (retrospective; period 2009-2014) of 12 children depending on time of initiation of bisphosphonate treatment (early starters 0 - 3 months; late starters 3 - 5 months). Areal bone mineral density (aBMD) of the lumbar spine (L2-L4) was assessed by DXA (GE Lunar iDXA). Vertebral shape was assessed by x-ray of the lateral spine (Morphometry score "Körber") [1]. Mobility was analysed by age when children reached motor milestones.

Patients

|	Early therapy start	Late therapy start
number	n = 6	n = 6
male	n = 4	n = 3
female	n = 2	n = 3
OI-type III	n = 4	n = 3
OI-type IV	n = 2	n = 3
age therapy start	0.65 (±0.35) months	3.8 (±1.7) months

Table 2: Patient characteristics

Results

Late starters (mean age at start of BPs 3.8 +/-1.7 months) had a reduced aBMD at initiation of antiresorptive treatment compared to early starters (mean age at start of BP treatment 0.65 +/-0.35 months) (0.131 g/cm^2 vs 0.230 g/cm^2). After one year of treatment both groups reached the same level of mean lumbar aBMD (early starters: 0.244 g/cm^2; late starters 0.236 g/cm^2; table 3).

Vertebral morphometry score decreased from 1 to 24.8 and from 57.25 to 53.8 demonstrating a much more severely affected spine in the late starters.

Motor function assessment revealed "pulling to stand" with a mean of 13.6 months vs 15.0 months and "first supported steps" with a mean of 17.0 vs 22.5 months (table 4).

Results I - Radiographs

A   **B**
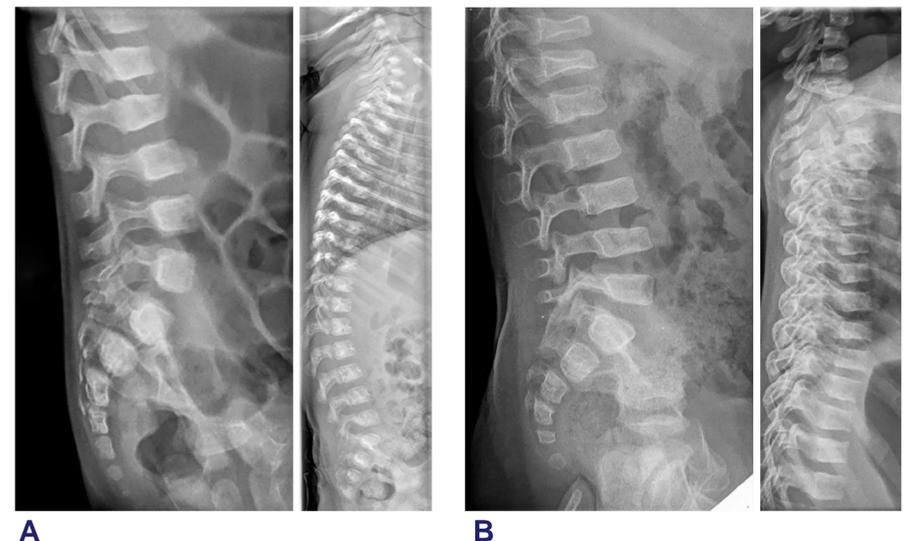
Fig. 1 A / B: Radiographs of the lateral spine in 2 children with OI treated with bisphosphonates
A Radiograph demonstrating vertebral shape after one year of treatment in a patient started at the age of 2 weeks. **B** Radiograph demonstrating vertebral shape after one year of treatment in a patient started at the age of 3.5 months.

Results II - Bone density and mobility

	Early starters		Late starters	
	Before start of therapy	After 1 year of therapy	Before start of therapy	After 1 year of therapy
Mean	0.2305 g/cm² n = 2	0.244 g/cm² n = 5	0.131 g/cm² n = 4	0.236 g/cm² n = 3
Mean	0.2305 g/cm² n = 1	0.298 g/cm² n = 5	0.1375 g/cm² n = 3	0.253 g/cm² n = 3

Table 3: Results of the lumbar aBMD early vs late starters.

Motor development	Early starters			Late starters		
	Mean [months]	Median [months]	Number of Patients	Mean [months]	Median [months]	Number of Patients
turn head	1.1	1	n = 4	2	2	n = 6
head control	10.8	3.2	n = 5	6.1	4	n = 5
grab an object	4.65	4.3	n = 4	5.6	4.25	n = 6
sit free	19.4	12	n = 5	15.6	8	n = 5
pull up to stand	13	13	n = 3	15.7	12	n = 3
first steps with support	17	17	n = 2	22.5	22.5	n = 2
first steps without support	23		n = 1	24.3	19	n = 3
Climb stairs with support	25		n = 1	28	28	n = 2

Table 4: Results of the motor function assessment

References: [1] Introduction of a new standardized assessment score of spine morphology in osteogenesis imperfecta. Koerber F, Schulze Uphoff U, Koerber S, Schönau E, Maintz D, Semler O., Rofo. 2012 Aug;184(8):719-25.

T-018
58ESPE
Bone, growth plate and mineral metabolism
Mirko Rehberg
Poster presented at:
PosterSessionOnline.com