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

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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 assumed 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.

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 - 6 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

<table>
<thead>
<tr>
<th>Age</th>
<th>Number</th>
<th>Gender</th>
<th>OI-type</th>
<th>Age therapy start</th>
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</thead>
<tbody>
<tr>
<td>0-11 months</td>
<td>n = 6</td>
<td>n = 4</td>
<td>n = 4</td>
<td>n = 6</td>
</tr>
<tr>
<td>≥ 1 year</td>
<td>n = 2</td>
<td>n = 2</td>
<td>n = 2</td>
<td>n = 3</td>
</tr>
</tbody>
</table>

Table 1: Schedule for neridronate treatment for children with OI

Results I - Radiographs

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

<table>
<thead>
<tr>
<th></th>
<th>Early starters</th>
<th>Late starters</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before start of therapy</td>
<td>After 1 year of therapy</td>
</tr>
<tr>
<td>Mean</td>
<td>0.2305 g/cm²</td>
<td>0.244 g/cm²</td>
</tr>
<tr>
<td></td>
<td>n = 2</td>
<td>n = 5</td>
</tr>
<tr>
<td>Mean</td>
<td>0.2305 g/cm²</td>
<td>0.298 g/cm²</td>
</tr>
<tr>
<td></td>
<td>n = 1</td>
<td>n = 5</td>
</tr>
</tbody>
</table>

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

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/cm² vs 0.230 g/cm²). After one year of treatment both groups reached the same level of mean lumbar aBMD (early starters: 0.244 g/cm²; late starters 0.236 g/cm²; 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).

Table 4: Results of the motor function assessment