Hearing Loss in Children with Osteogenesis Imperfecta (OI) Treated with Bisphosphonates

Christi A. Arnerich, Aaron C. Moberly, Linda A. DiMeglio, Richard T. Miyamoto
Indiana University, Indianapolis, IN, USA

• 21.4% of children developed hearing loss, a percentage similar to previous population studies.
• Since all received treatment, we cannot determine directly bisphosphonate effects on hearing loss over time.
• However, it appears that bisphosphonates neither increase hearing loss nor stop progression in these children.

CONCLUSIONS

Osteogenesis Imperfecta (OI) is a genetic disorder of collagen synthesis. It is commonly associated with increased fracture rate, decreased bone mineral density (BMD), and blue sclerae.

It is also associated with hearing loss, sensorineural and/or conductive, which progresses with age. Hearing loss is most prevalent in OI Type I.

There are several forms of OI ranging in severity:
- Type I, mild with blue sclerae
- Type II, perinatally lethal
- Type III, progressively deforming with white sclerae
- Type IV, severe with white sclerae
- Additional severe forms also described (Types V, VI, VII)

Treatment includes IV or oral bisphosphonates to increase bone density, decrease fracture rate, and decrease bony pain.

Bisphosphonates have been associated with osteonecrosis of the mandible and osteopetrosis of long bones in some cases.

Effects of bisphosphonates on hearing, specifically the middle ear ossicles and cochlea, have not yet been determined.

BACKGROUND

METHODS

• Children with OI types I (mild), or III/IV (moderate) underwent pure-tone audiometry with calculated pure-tone average (PTA), tympanometry, speech reception threshold (SRT), and acoustic reflex (AR) testing.
• Hearing loss was defined as PTA at 500, 1000, and 2000 Hz >15 dB.
• All patients received bisphosphonate therapy, either alendronate or pamidronate, for the duration of the study.

RESULTS

• 22 of 28 children had normal hearing.
• 6 of 28 children demonstrated hearing loss.
• 5 of these 6 had serial hearing assessments.
• All 6 have Type III/IV OI.
• 1 child displayed baseline hearing loss upon initial assessment.
• 1 child experienced hearing loss bilaterally.
• 1 child showed progression followed by a moderate degree of improvement.

SUBJECTS

• 28 children with OI
• Type I and Type III/IV represented
• Ages at first and last assessment were 2-17 years (mean 8.3) and 4-18 years (mean 11.1) respectively.
• 22 patients had multiple assessments.

INITIAL PTA ASSESSMENT

<table>
<thead>
<tr>
<th>Patient</th>
<th>Initial PTA assessment (right/left) (dB)</th>
<th>Last PTA assessment (right/left) (dB)</th>
<th>Time on bisphosphonate (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3/2</td>
<td>7/25</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>5/7</td>
<td>18/12</td>
<td>6</td>
</tr>
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<td>3</td>
<td>10/7</td>
<td>20/15</td>
<td>1</td>
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<tr>
<td>4</td>
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<td>1</td>
</tr>
<tr>
<td>5</td>
<td>5/5</td>
<td>13/22</td>
<td>6</td>
</tr>
</tbody>
</table>

Table 1: Initial and final PTA assessments of patients with hearing loss.

CONCLUSIONS

• 21.4% of children developed hearing loss, a percentage similar to previous population studies.
• Since all received treatment, we cannot determine directly bisphosphonate effects on hearing loss over time.

Figure 1: Blue sclerae typically found with OI Type I.

Figure 2: Femoral bowing in an OI type III patient. Lucencies between lines along the epiphyses signify bone growth following treatment with bisphosphonates.

Figure 3: Temporal bone CT demonstrating demineralization of otic capsule.

Figure 4: The hearing loss that appeared in the population did not show a pattern of steady progression in all cases. Hearing loss is defined as PTA >15 dB.

STUDY OBJECTIVES

• Determine the incidence of hearing loss in children with OI before and after treatment with bisphosphonates.
• Ascertain whether hearing loss progressed or improved during the course of therapy.