Clinical Practice Assessment

Zoledronic Acid after a Hip Fracture

Clinical Question:
Does intravenous bisphosphonate therapy with zoledronic acid administered after osteoporotic hip fractures reduce the frequency of subsequent fractures or mortality?

Bottom Line:
Once-yearly IV zoledronic acid administered initially within 90 days of an osteoporotic hip fracture resulted in a significant reduction in subsequent fractures (ARR 5.3%; NNT 19) and mortality (ARR 3.7%; NNT 27) over 2 years. Strength of Recommendation- A (SORT).

Synopsis:
The HORIZON Recurrent Fracture Trial was a manufacturer sponsored multi-center, randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of zoledronic acid in preventing subsequent fractures following the surgical repair of a low-trauma hip fracture. The trial randomized 2127 patients to receive 5 mg zoledronic acid IV once yearly (n=1065) or placebo (n=1062). The infusions were first administered within 90 days after surgical repair of a hip fracture. All patients were followed up for a median of 1.9 years. Patients being treated with oral bisphosphonates or teriparatide were excluded, but other osteoporosis treatments were allowed at the discretion of the investigator. The two groups were well matched with regard to race, age, sex, bone mineral density and T-score but no information was given about co-morbidities such as cardiovascular risk factors.

There was a significant reduction in subsequent fractures, and a reduction in mortality (Table 1). An aspect of the study that could affect the generalizability of the findings is that the patients, on average, were slightly younger and healthier than hip fracture patients in the general population. There was also a slight imbalance in the randomization such that slightly more patients in the control group received other adjunctive therapies for osteoporosis than patients in the treatment group, but this imbalance would more likely to favor the placebo arm.

Table 1. Rates of Fracture and Death in the Study Groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo</th>
<th>Zoledronic Acid</th>
<th>HR (95%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fracture – no. (cumulative %)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>139 (13.9)</td>
<td>92 (8.6)</td>
<td>0.65 (0.50-0.84)</td>
<td>0.001</td>
</tr>
<tr>
<td>Nonvertebral</td>
<td>107 (10.7)</td>
<td>79 (7.6)</td>
<td>0.73 (0.55-0.98)</td>
<td>0.03</td>
</tr>
<tr>
<td>Hip</td>
<td>33 (3.5)</td>
<td>23 (2.0)</td>
<td>0.70 (0.41-1.19)</td>
<td>0.18</td>
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<tr>
<td>Vertebral</td>
<td>39 (3.8)</td>
<td>21 (1.7)</td>
<td>0.54 (0.32-0.92)</td>
<td>0.02</td>
</tr>
<tr>
<td>Death – no. (%)</td>
<td>141 (13.3)</td>
<td>101 (9.6)</td>
<td>0.72 (0.56-0.93)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

In this study, there was no significant difference in the rate of renal toxic or cardiovascular effects, including the incidence of serious atrial fibrillation. The most frequent adverse events in patients receiving zoledronic acid were pyrexia, myalgia, and bone and musculoskeletal pain. No cases of osteonecrosis of the jaw were reported.

The sustained value of zoledronic acid is supported by Grey’s report that 5 years after a single infusion of
Zoledronic acid 5mg benefit persists as measured by sustained depression of bone turnover markers and improved bone density.

**Source:**


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Reviewed: 11/23/11
Updated: 9/3/13