Review: diacerein is more effective than placebo and is as effective as NSAIDs for knee and hip osteoarthritis

David J Hunter and Barton Wise

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Review: diacerein is more effective than placebo and is as effective as NSAIDs for knee and hip osteoarthritis


Clinical impact ratings Rheumatology ★★★★★☆

In patients with knee or hip osteoarthritis, is diacerein more effective than placebo or other active treatments in reducing pain and improving function?

METHODS


Study selection and assessment: randomised controlled trials (RCTs), published or reported in English, French, or German between 1985 and 2004, that compared diacerein with placebo or another active treatment in patients with knee or hip osteoarthritis. 19 RCTs (n=3058, mean age range 48–67 y, 68% women) met the selection criteria, 16 of which were double blinded. Methodological quality of individual trials was assessed using the Jadad scale.

Outcomes: pain, function, and use of other medications for pain relief. Outcomes were assessed at 2 time points: at the end of active treatment (duration 1–36 mo, median 3 mo) and at the end of a treatment free follow up period (duration 1–3 mo, median 2 mo). Results were expressed as the Glass score, a standardised mean difference weighted by the Jadad quality score. A result >0 favours diacerein. Glass scores >0.8 are commonly regarded as clinically relevant.

MAIN RESULTS

During the active treatment period, diacerein reduced pain and improved function more than placebo and to a similar extent as non-steroidal anti-inflammatory drugs (NSAIDs) (table). During the post-treatment follow up period, diacerein reduced pain more than placebo or NSAIDs and improved function more than NSAIDs (no information for comparison with placebo) (table). Diacerein did not differ from placebo or NSAIDs for use of other medications during active treatment, but during the follow up period, patients in the diacerein group used other medications less often than those in either comparator group. Adverse events, mainly diarrhoea, were reported more frequently with diacerein than with placebo. Tolerability did not differ between diacerein and NSAIDs.

CONCLUSIONS

In patients with knee or hip osteoarthritis, diacerein reduces pain and improves function more than placebo and to a similar extent as non-steroidal anti-inflammatory drugs (NSAIDs) during the active treatment phase. Diacerein has a carryover effect, providing more pain relief than placebo or NSAIDs for several weeks after treatment is stopped.

Diacerein v placebo or non-steroidal anti-inflammatory drugs (NSAIDs) for knee or hip osteoarthritis

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Assessment phase*</th>
<th>Comparator</th>
<th>Number of trials (n)</th>
<th>Glass score (95% CI†)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>Active treatment</td>
<td>Placebo</td>
<td>8 (1847)</td>
<td>1.5 (0.8 to 2.2)</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>NSAIDs</td>
<td>10 (1037)</td>
<td>-0.4 (-1.1 to 0.4)</td>
</tr>
<tr>
<td></td>
<td>Follow up</td>
<td>Placebo</td>
<td>9 (1847)</td>
<td>2.7 (1.3 to 4.1)</td>
</tr>
<tr>
<td></td>
<td>NSAIDs</td>
<td>8 (1665)</td>
<td>2.1 (1.3 to 2.9)</td>
<td></td>
</tr>
<tr>
<td>Function</td>
<td>Active treatment</td>
<td>Placebo</td>
<td>8 (1847)</td>
<td>1.5 (0.8 to 2.2)</td>
</tr>
<tr>
<td></td>
<td>NSAIDs</td>
<td>8 (912)</td>
<td>0.1 (-0.7 to 0.9)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Follow up</td>
<td>NSAIDs</td>
<td>6† (-)</td>
<td>2.6 (1.7 to 3.5)</td>
</tr>
</tbody>
</table>

*Median duration was 3 months for active treatment and 2 months for post-treatment follow up.
†A standardised mean difference weighted by the Jadad quality score. A result >0 favours diacerein. Glass scores >0.8 are commonly regarded as clinically relevant. CI defined in glossary.
‡Information provided by author.

Commentary

The systematic review and meta-analysis by Rintelen et al of RCTs evaluating diacerein was performed to provide an evidence-based assessment of its symptomatic efficacy in the treatment of osteoarthritis. This oral formulation is widely prescribed in Europe; however, it is not available in North America.

Several methodological concerns raise questions in interpreting the results. It is unclear if data abstraction was performed by both reviewers on all available data, how any discrepancies were adjudicated, and what the congruence of the reviewers was. Although the authors mentioned investigating heterogeneity among the studies in the ‘Methods’ section, no results of these analyses were provided. Visual inspection of the data suggests that heterogeneity is present. The Cochrane review of this topic raised concerns about heterogeneity, and the conclusions reached were not as positive as those expressed in the review by Rintelen et al. Two of the best quality RCTs in the review (large sample size, long duration, and publication in peer reviewed journals) showed no difference in pain or function between diacerein and placebo.

Most importantly, however, given the real potential for publication bias and concerns regarding the involvement of industry in promoting this bias and supporting the publication of this meta-analysis, serious questions remain as to whether this review is truly impartial. The ‘Comment’ section had a consistently positive description of the efficacy of diacerein and relatively little discussion of the limitations of the analysis or the quality issues of the included studies. The authors raised legitimate concerns about the tolerability of NSAIDs and commented on the high frequency of adverse events associated with diacerein, particularly transient diarrhoea.

Diacerein may have possible benefit by improving pain and function in osteoarthritis, although this meta-analysis has not convincingly demonstrated its efficacy. Further research is warranted to investigate the short and long term effectiveness and toxicity of diacerein therapy in patients with osteoarthritis.

David J Hunter, MD
Barton Wise, MD
Boston University School of Medicine
Boston, Massachusetts, USA