# Iron Chelating Agents for Patients with Iron Overload

## QUESTION

What is the effectiveness of the different iron chelating agents in patients with iron overload due to frequent blood transfusions?

## CONTEXT

**Iron overload due to frequent blood transfusions**

Patients receiving regular blood transfusions can suffer damage to major organs such as heart and liver due to the accumulation of iron over the toxic levels.

Iron overload is treated with chelation therapy, which reduces iron stores while maintaining iron balance. Chelation therapy includes deferoxamine and deferiprone, but these medications are sometimes not well tolerated and are associated with adverse events. Deferasirox is an alternative for patients that cannot tolerate the aforementioned therapies.

## INTERVENTION

**Iron chelating agents**

<table>
<thead>
<tr>
<th>Changes in serum ferritin:</th>
</tr>
</thead>
<tbody>
<tr>
<td>There were no significant differences between deferiprone and deferoxamine in reducing serum ferritin in patients with thalassemia. <em>Very low quality evidence.</em></td>
</tr>
<tr>
<td>Combination therapy (deferoxamine and deferiprone) was superior to deferoxamine in reducing serum ferritin at one year in patients with thalassemia. <em>Very low quality evidence.</em></td>
</tr>
</tbody>
</table>
### Summary of the Evidence

#### Benefits

A systematic review [1](#) (date of search: March 2007) identified 14 randomized controlled trials (RCT) with 1,480 participants that compared deferasirox, deferoxamine, deferiprone and a combination therapy (deferoxamine and deferiprone).

A total of 5 RCT compared the effectiveness of deferiprone and deferoxamine as a chelation therapy in adults and children suffering from thalassemia and requiring multiple transfusions. Due to differences in reporting, a pooled estimate could only be obtained from two trials at 6 months and three trials at 12 months. Differences in the reduction of serum ferritin were not significant between treatments groups at 6 months (Mean Differences MD 1.18, 95%CI –0.42 to 2.78) nor at 12 months (MD –0.10, 95%CI –0.57 to 0.38).

A total of 6 RCT compared the effectiveness of a combination therapy (deferoxamine and deferiprone) to deferoxamine. Studies mixed adults and children suffering from thalassemia and due to differences in reporting, a pooled estimate could only be obtained from three trials. At 12 months there was a significant benefit from combination therapy in the reduction of serum ferritin (MD –0.71, 95%CI –1.10 to -0.41).

#### Risks

Trials that examined deferiprone or combination therapy reported adverse events inconsistently. Only three trials reported on all adverse events which in all instances were more common in patients receiving deferiprone or combination therapy, the most common being gastrointestinal events. No numerical data were provided.

#### Applicability

Chelation therapy seems effective for removing iron from the blood and a combination therapy seem more effective than a single treatment. Elucidating the long-term benefits of chelation therapy, including issues of adverse events and adherence, should be the primary focus for future research. Iron blood levels is an indirect measure of longer term clinical benefits.

#### Commentaries

There was a high degree of heterogeneity between trials in terms of trial design and outcome reporting. A common estimate of effect was only obtained from few studies that analized serum ferritin and compared deferiprone and deferoxamine and a combination therapy (deferoxamine and deferiprone). Moreover, due to differences in outcome reporting, pooled results were expressed as standardised mean differences that are of difficult interpretation.

#### Costs

The review developed a short-term (1 year) model to assess the cost effectiveness different chelation therapies. There were some differences between deferasirox and deferoxamine mainly due to route of administration of deferoxamine (traditional pump is less costly). Similarly differences between deferasirox and deferiprone were not clear and depending on age (favoring deferasirox in the youngest patients and deferiprone for older children and adults).

Unit costs for each of the chelators (2007, UK pounds) reveals that deferoxamine (500 mg and 2 g) costs £4.26 and £17.05 respectively. Deferasirox (28-tablet packs of 125 mg, 250 mg and 500 mg) costs £117.60, £235.20 and £470.40 respectively and deferiprone (500 mg/100-tablet) costs £152.39.

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<table>
<thead>
<tr>
<th>Number of Studies (N)</th>
<th>Variable</th>
<th>Comparison</th>
<th>Type of Evidence</th>
<th>Quality</th>
<th>Consistency</th>
<th>Direct Evidence</th>
<th>Size of Effect</th>
<th>GRADE</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 (79)</td>
<td>Serum ferritin (6 months)</td>
<td>Deferiprone vs deferoxamine.</td>
<td>4</td>
<td>-1</td>
<td>-1</td>
<td>-1</td>
<td>-1</td>
<td>Very Low</td>
<td>Limitations in methodology, significant heterogeneity, large confident intervals and/or low number of participants.</td>
</tr>
<tr>
<td>3 (260)</td>
<td>Serum ferritin (12 months)</td>
<td>Deferiprone vs deferoxamine.</td>
<td>4</td>
<td>-1</td>
<td>-1</td>
<td>-1</td>
<td>-1</td>
<td>Very Low</td>
<td>Limitations in methodology, significant heterogeneity, large confident intervals and/or low number of participants.</td>
</tr>
<tr>
<td>9 (42)</td>
<td>Serum ferritin (12 months)</td>
<td>Combination therapy vs deferoxamine.</td>
<td>4</td>
<td>-1</td>
<td>-1</td>
<td>-1</td>
<td>-1</td>
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Type of evidence: 4 = ECA; 2 = Observational studies; 1 = Non-analytic studies / Expert opinion