Review: Pentoxifylline alone or as an adjunct to compression therapy improves healing in venous leg ulcers


**Question**

Is pentoxifylline (with or without compression therapy) effective for treating venous leg ulcers?

**Data sources**

Studies were identified by searching the central registers of the Cochrane Peripheral Vascular Diseases and Wounds Groups, which included trials found in MEDLINE, CINAHL, EMBASE/Excerpta Medica, conference proceedings, and hand searches of relevant journals. Bibliographies were also checked, and the manufacturer of pentoxifylline (Hoechst) was contacted.

**Study selection**

Randomized trials were selected if they compared pentoxifylline (with or without compression therapy) with placebo or another therapy in patients with venous leg ulcers and used an objective outcome measure for healing.

**Data extraction**

Data were extracted on study design and quality, interventions, patients, and outcomes.

**Main results**

9 studies (572 patients) were included. Studies varied in the method for diagnosis of venous ulceration; 3 studies reported their setting (community-based); and all studies used oral pentoxifylline, 1200 mg (1 study also used a 2400-mg daily dosage, and 1 study also used an intravenous route for 7 d). Follow-up ranged from 8 weeks to 6 months. In studies with and without compression therapy, pentoxifylline increased rates of healing or improvement (8 studies) and complete healing (6 studies) more than did placebo (Table). Analysis of only studies with compression therapy (5 studies) or of those without compression therapy (3 studies) still showed pentoxifylline as being more effective than placebo for healing or improvement (Table). 1 study that compared pentoxifylline and defibrotide with compression therapy showed no differences in healing at 3 months.

**Conclusion**

Pentoxifylline alone or as an adjunct to compression therapy is effective for healing venous leg ulcers.

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**Commentary**

Approximately 2% of men and women in the United States will have leg ulcers at some time in their life. Venous stasis ulcers are the most common type of leg ulcer and result from chronic venous insufficiency disease. Treatment by leg elevation, multilayer compression bandages, and local care produces complete healing in 40% to 70% of patients at 6 months with a 25% annual recurrence rate.

Jull and colleagues provide a provocative review of 9 small randomized controlled trials that compare pentoxifylline with placebo as systemic pharmacologic therapy for venous leg ulcers. Pentoxifylline was associated with greater complete ulcer healing or improvement than was placebo.

On the basis of this meta-analysis, should we broadly adopt this therapy? Only 2 of the studies included had > 100 patients, and both studies reported nonsignificant trends toward improvement. A large, multicenter, randomized controlled trial to confirm the results of this meta-analysis would be prudent.

**Oral pentoxifylline vs placebo for treatment of venous leg ulcers**

<table>
<thead>
<tr>
<th>Outcomes at 8 wk to 6 mo</th>
<th>Adjunctive use of compression therapy</th>
<th>Weighted event rates RBI (95% CI) NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healing or improvement</td>
<td>Absent or present</td>
<td>Pentoxifylline 60% 42% 41% (19 to 66) 6 (4 to 11)</td>
</tr>
<tr>
<td>Complete healing</td>
<td>Absent or present</td>
<td>Pentoxifylline 60% 46% 30% (10 to 54) 8 (5 to 19)</td>
</tr>
<tr>
<td>Complete healing</td>
<td>Present</td>
<td>Pentoxifylline 62% 47% 30% (10 to 54) 7 (5 to 18)</td>
</tr>
<tr>
<td>Healing or improvement</td>
<td>Absent</td>
<td>Pentoxifylline 51% 21% 142% (34 to 335) 4 (3 to 8)</td>
</tr>
</tbody>
</table>

*Abbreviations defined in Glossary; RBI, NNT, and CI calculated from data in article.*

Recent investigational therapies, such as growth factors, flavonoids, sulodexide, and skin grafts, have created renewed interest in venous stasis ulcers. The review by Jull and colleagues helps to highlight the limited data that support traditional therapies, including pentoxifylline, elevation, occlusive dressings, compression pumps, debridement, and compression bandages. In this list, compression measures have the most support. However, vascular medicine requires more standardized definitions, measurements, evaluations, and follow-up as part of adequately powered multicenter trials. These trials should examine the efficacy of traditional and new therapies, particularly when used in combination. On the basis of the systematic review, pentoxifylline (with or without compression) deserves careful study in patients with pre-ulcers or ulcers and as secondary prevention after ulcer healing.

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