**Hypericum extract was better than placebo and equivalent to imipramine for moderate depression**


**Question**

In patients with moderate depression, how do the effectiveness and safety of *Hypericum* extract (St. John’s wort) compare with those of imipramine and placebo?

**Design**

8-week randomized [allocation concealed*†], blinded (clinicians and patients),* placebo-controlled trial.

**Setting**

18 general practitioners’ practices in Germany.

**Patients**

263 patients who were 18 to 65 years of age (mean age 47 y, 75% women) and had a diagnosis of moderate depression; score of ≥ 18 on the Hamilton Depression Rating Scale (HDRS); clinical global impression rating of moderate, marked, or severe; and depression lasting ≥ 4 weeks and ≤ 2 years. Exclusion criteria included bipolar disorders, alcohol or drug dependence, or suicidal risk. 230 patients (87%) completed the study; 251 (95%) were included in an intention-to-treat analysis.

**Intervention**

Patients were allocated to *Hypericum* extract (STEI 300, Steiner Arzneimittel, Berlin, Germany), 1050 mg/d (n = 106); imipramine, 50 mg/d titrated to 100 mg/d by day 5 (n = 110); or placebo (n = 47).

**Main outcome measures**

The primary end point was change from baseline in HDRS score. *Hypericum* was compared with placebo at 6 weeks and with imipramine at 8 weeks.

**Main results**

At 6 weeks, greater improvement from baseline occurred with *Hypericum* extract than with placebo (mean decrease in HDRS score of 13.4 vs 10.3, 95% CI for the 3.1 difference 1.5 to 5.4). At 8 weeks, *Hypericum* extract and imipramine had similar changes in score from baseline (mean decrease of 15.4 vs 14.2, CI for the 1.2 difference –0.6 to 2.6). More patients who received *Hypericum* extract had ≥ 50% improvement in HDRS scores than did patients who received placebo \(P = 0.027\)‡; the proportions did not differ between *Hypericum* and imipramine \(P = 0.14\)‡ (Table). Fewer patients in the *Hypericum* group than the imipramine group reported adverse effects \(P < 0.001\)‡ (Table).

**Conclusion**

In patients with moderate depression, *Hypericum* extract (St. John’s wort) was more effective than placebo and as effective and safe as imipramine.

*Source of funding: Steiner Arzneimittel, Berlin, Germany.*

For correspondence: Dr. K.O. Hiller, Steiner Arzneimittel, D-12207 Berlin, Germany. FAX 49-30-712-5012.

*See Glossary.

†Information provided by author.

‡P values calculated from data in article.

### Hypericum extract (HE) vs placebo at 6 weeks and HE vs imipramine (Imi) at 8 weeks for moderate depression§

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Comparison</th>
<th>Event rates</th>
<th>RBI (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 50% improvement in HDRS score</td>
<td>HE vs placebo</td>
<td>67% vs 48%</td>
<td>40% (3.5 to 101)</td>
<td>6 (3 to 50)</td>
</tr>
<tr>
<td></td>
<td>HE vs Imi</td>
<td>76% vs 67%</td>
<td>14% (~4.3 to 37)</td>
<td>Not significant</td>
</tr>
</tbody>
</table>

| Adverse effects                 | HE vs Imi                | 22% vs 46%  | 53% (30 to 69)  | 4 (3 to 9) |

§HDRS = Hamilton Depression Rating Scale. Other abbreviations defined in Glossary; RBI, RRR, NNT, and CI calculated from data provided by the author.

**Commentary**

The trial by Philipp and colleagues suggests that *Hypericum* extract may be considered as a treatment for moderate depression in primary care. To determine whether to prescribe *Hypericum*, some issues should be addressed.

The conclusion that *Hypericum* extract is safe in the long term is premature because of the limited duration of the study. Most patients are treated for many months. The fact that no data are available on concomitant pathology and drug treatments preclude statements about drug interactions. It has been shown that *Hypericum* induces the cytochrome P450, which might have serious clinical implications, for instance, in HIV-infected patients on protease inhibitors (1). Interactions with such other drugs as cyclosporin (2), warfarin, theophylline, and some contraceptives have been reported (3). Furthermore, such common foods as grapefruit influence the same enzyme system (3). Future studies might consider using a crossover design, comparison with a selective serotonin-reuptake inhibitor, or a higher dose of imipramine.

*Hypericum perforatum* is an herbal remedy that, although it is widely used and has promising results in this trial, is not yet completely understood. Because *Hypericum* products may vary considerably in composition, prescribers should be aware that study results may not be generalized to other extracts.

*Etienne Vermeire, MD*

University of Antwerp

Antwerp, Belgium

**References**

