

Hypericum extract was as effective as imipramine but had fewer adverse effects in mild to moderate depression

Woelk H for the Remotiv/Imipramine Study Group. Comparison of St John's wort and imipramine for treating depression: randomised controlled trial. *BMJ* 2000 Sep 2;321:536-9.

QUESTION: In patients with mild to moderate depression, how effective and safe is *Hypericum perforatum* (St John's wort) compared with imipramine?

Design

Randomised (allocation concealed*), blinded (patients)*, controlled trial with 6 weeks of follow up.

Setting

40 outpatient psychiatric, internal medicine, and general medicine clinics in Germany.

Patients

324 outpatients who were ≥ 18 years of age (mean age 45 y, 71% women) with mild to moderate depression (*ICD-10* criteria) without increased suicidal ideation, and who had a score of ≥ 18 on the 17 item Hamilton Depression Rating Scale (HDRS) on 2 consecutive visits. Exclusion criteria included pregnancy, allergy to the study drugs, abnormal thyroid function, bipolar disorder, serious psychiatric disease, and misuse of alcohol or drugs.

Intervention

157 patients were allocated to 75 mg of imipramine twice daily, and 167 were allocated to 250 mg of hypericum extract ZE 117 twice daily. Each group was also given placebos of the comparison treatment.

Main outcome measures

Change in scores on the HDRS, Clinical Global Impression Scale (CGIS), and Patient's Global Impression Scale (PGIS).

Main results

The 2 treatments were therapeutically equivalent with regard to overall effect on depression. The same improvement from baseline occurred with hypericum extract and imipramine at 6 weeks on the HDRS (least square mean change from baseline in HDRS score 12.0 v 12.8, 95% CI for the -0.8 difference -1.9 to 0.4), and similar mean scores were observed at 6 weeks on the CGIS (mean change 2.2 v 2.4, CI for the 0.2 difference -0.4 to 0.02) and on the PGIS (mean change 2.4 v 2.6, CI for the -0.2 difference -0.4 to 0.09). Response to treatment as measured by a $\geq 50\%$ decrease on the HDRS was similar in the 2 groups (table). The study had a power of 90% to detect a difference in improvement between the groups of > 3.5 points on the HDRS.

$\geq 50\%$ decrease on the Hamilton Depression Rating Scale at 6 weeks comparing hypericum extract with imipramine in mild to moderate depression†

Hypericum	Imipramine	RBI (95% CI)	NNT (CI)
43%	40%	8% (-4% to 17%)	Not significant

†Abbreviations defined in glossary; RBI, NNT, and CI calculated from data in article.

Patients tolerated hypericum extract better than imipramine ($p < 0.01$). More patients in the imipramine group reported adverse effects and more patients withdrew because of adverse effects (16% v 3%, $p < 0.01$).

Conclusion

In patients with mild to moderate depression, hypericum extract (St John's wort) was as effective as imipramine with fewer adverse effects.

*See glossary.

COMMENTARY

Previous studies of St John's wort indicate that it is an effective antidepressant when compared with placebo,¹ but studies comparing it with other active treatments have often been of poor quality and criticised for using inadequate doses of antidepressants and for concentrating on relatively mild illness.² To date this is the largest and best trial of St John's wort in depression and uses identical methodology to most antidepressant trials. Although the study does not mention the average dose of imipramine attained, they aimed to reach 150 mg/day. The study was limited to patients with *ICD-10* depressive episodes and scores of ≥ 18 on the HDRS, which is the standard cut off for severity in antidepressant trials. The main finding is a familiar one—St John's wort is as effective as imipramine, but better tolerated.

While many will be heartened that a herbal remedy is as effective as a well established antidepressant, some caution is needed. In many countries (including the UK), St John's wort is not licensed and therefore is not subject to the same pre and post marketing surveillance used with conventional antidepressants. Several preparations of St John's wort are available each containing different doses of hypericum. Some reports suggest that it may interact with other medications—sometimes with disastrous consequences.³ More information is also required on safety in overdose. There may well now be sound reasons to welcome St John's wort as a new antidepressant, but the double standard whereby effective herbal remedies escape the rigours of licensing must end.⁴

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- 2 Maidment I. The use of St John's wort in the treatment of depression. *Psychiatric Bulletin* 2000;**24**:232-4.
- 3 Ruschitzka F, Meier PJ, Turina M, et al. Acute heart transplant rejection due to Saint John's wort. *Lancet* 2000;**355**:548-9.
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