

Review: St John's wort is more effective than placebo for mild to moderate depressive disorders

Linde K, Mulrow CD. *St. John's wort for depression*. (Cochrane Review, latest version 09 Jul 1998). In: *Cochrane Library*. Oxford: Update Software.

Question

Are extracts of *Hypericum perforatum* (St John's wort [SJW]) more effective than placebo and as effective as low dose antidepressants for mild to moderate depressive disorders?

Data sources

Studies were identified by searching Medline (from 1983), PsycLIT (1987–97), Embase/Excerpta Medica (from 1989), the clinical trial registry of the Cochrane Collaboration Depression, Anxiety, and Neurosis Group, the Cochrane Field for Complementary Medicine, and the private database Phytodok (Munich); by scanning bibliographies of relevant articles; and by contacting authors and pharmaceutical companies.

Study selection

Studies were selected if they were randomised controlled trials that compared SJW with placebo or other antidepressants in patients with depressive disorders. Studies with physiological outcome measures only were excluded.

Data extraction

2 reviewers extracted data on study characteristics and results and assessed the quality of each study. Missing or additional data were obtained from authors or sponsors.

Main results

27 of 45 studies involving 2291 patients with mild to moderate depression met the inclusion criteria. 17 trials compared SJW with placebo and 10 with antidepressants. Follow up ranged from 2 to 12 weeks in 26 studies (mean 5.5 wks)*, and 1 study had an unknown length of follow up. More patients responded to SJW than to placebo (14 studies, { $p < 0.001$ }*) (table). No differences in responder rate (treatment group response rate/

control group response rate) occurred for SJW compared with low dose antidepressants (5 studies, { $p = 0.79$ }*) (table). Side effects were fewer with SJW than with low dose antidepressants (7 studies, weighted event rate 28% v 45%, $p = 0.002$)*.

Conclusions

St John's wort (SJW) is more effective than placebo for patients with mild to moderate depressive disorders. SJW and low dose antidepressants had similar effectiveness, but SJW had fewer side effects.

Responder rates for St John's wort (SJW) v control in depressive disorders†

Comparison at a mean follow up of 5.1 weeks	Weighted event rates			
	SJW	Control	RBI (95% CI)	NNT (CI)
SJW v placebo‡	56%	25%	140% (70 to 239)	4 (3 to 6)

Comparison at a mean follow up of 5.6 weeks	Weighted event rates			
	SJW	Control	RBR (CI)	NNH
SJW v antidepressants	51%	52%	3% (-12 to 16)	NS

†NS = not significant. Other abbreviations defined in glossary; RBI, RBR, NNT, NNH, and CI calculated from data in article.

‡Heterogeneity existed among trials.

*Calculated from data in article.

Sources of funding: National Institute of Arthritis and Musculoskeletal and Skin Diseases and Karl und Veronica Carstens-Stiftung.

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A modified version of this abstract appears in *ACP Journal Club, Evidence-Based Medicine, and Evidence-Based Mental Health*.

Commentary

This review by Linde and Mulrow compares the effectiveness of SJW with placebo and low dose antidepressants across trials done primarily in Germany. Similar investigations are beginning in North America where public interest and use of herbal remedies are growing. SJW is classified as a food in North America, whereas it is regulated as a drug in Germany. This suggests possible differences in the strength of SJW preparations.

Limitations of the review include the heterogeneity among studies with respect to types and severity of depression, the variability of the diagnostic criteria used, and the accuracy of entry diagnosis based upon non-specialist and specialist clinical expertise. Of particular concern were the subclinical doses of antidepressant drugs in most of the studies, where 75 mg/day seemed to be "standard." Clinically, such

low doses of tricyclic antidepressants (TCAs) are considered starting doses and are increased to more therapeutic ranges of 150–300 mg (amitriptyline and imipramine).¹ The lack of difference between SJW and low dose antidepressants is therefore not surprising. TCAs have more troublesome side effects than the newer selective serotonin reuptake inhibitors, such as fluoxetine (Prozac) and sertraline (Zoloft), which are more commonly used today. Additionally, follow up for most studies was too short to determine clinical efficacy.

Longer and more tightly controlled trials are therefore needed to ensure valid comparisons of standardised doses of SJW with antidepressants for mild and moderate depression. The strong evidence for SJW over placebo holds promise and supports the need for further

studies of patients with similar illness severity and strict diagnostic criteria. SJW may be a viable option for those with mild depression who suffer minimal functional impairment and do not require or refuse antidepressants. The reduced side effects of SJW may enhance future treatment compliance if effectiveness is proved.

Increasingly, nurses are asked by patients about the use of herbal products, such as SJW, and should avail themselves of the most current, scientific evidence to support or discourage their use. Currently, SJW as a replacement for antidepressants is not recommended.

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1 Kuzel R. *Postgrad Med* 1996;99:179–92.