

Agnus castus fruit extract was safe and effective for relieving symptoms of premenstrual syndrome

Schellenberg R. *Treatment for the premenstrual syndrome with agnus castus fruit extract: prospective, randomised, placebo controlled study.* *BMJ* 2001 Jan 20;322:134-7.

QUESTION: Is agnus castus fruit (*Vitex agnus castus* L extract Ze 440) effective and safe for treatment of premenstrual syndrome?

Design

Randomised (allocation concealed), blinded (investigators and patients), placebo controlled trial with follow up until the end of the third consecutive menstrual cycle.

Setting

6 outpatient general medicine clinics.

Patients

178 women ≥ 18 years of age who met *DSM-III-R* criteria for premenstrual syndrome. Exclusion criteria were participation in other trials, concomitant psychotherapy, pregnancy or breast feeding, inadequate contraception, dementia, alcohol or drug dependence, serious medical condition, hypersensitivity to agnus castus, fever, pituitary disease, or sex hormone use. 170 women (96%) (mean age 37 y) were included in the intention to treat analysis.

Intervention

Women were allocated to receive agnus castus fruit, 20 mg dry tablet once daily (n=91) (60% ethanol m/m, extract ratio 6-12:1; standardised for casticin), or matching placebo (n=87). Study medication was initiated at the start of the first cycle and continued until the end of the third consecutive cycle.

Main outcome measures

The main outcome measure was the change in composite score of 6 self assessment items from baseline to the end of the third cycle: irritability, mood alteration, anger, headache, other menstrual symptoms (including bloating), and breast fullness. Items were rated individually using a visual analogue scale (VAS), measured in mm (range 0=no symptoms to 10=unbearable) and summed for a total score. Secondary outcome measures were responder rate (defined as $\geq 50\%$ improvement in the 6 symptom composite VAS score from baseline), Clinical Global Impression (CGI) items 1 (severity of condition), 2 (improvement or deterioration), and 3 (overall assessment of risk or benefit), and adverse events.

Main results

Women in the agnus castus group had a greater reduction from baseline in the 6 symptom composite VAS score than those in the placebo group (128.5 v 78.1, $p=0.001$); this group also had a greater responder rate (table). Based on individual item VAS scores, women in the agnus castus group had greater reductions in 5 of the 6 symptoms (irritability, mood alteration, anger,

headache, and breast fullness; $p \leq 0.002$) and showed superiority of the treatment in each of the 3 GCI scores ($p=0.001$) compared with women in the placebo group. In both groups, adverse events were few (4.7% v 4.8% in agnus castus and placebo groups, respectively) and mild.

Conclusion

Agnus castus fruit extract was safe and effective for relieving symptoms of premenstrual syndrome.

COMMENTARY

This study by Schellenberg makes an important contribution to our knowledge of how premenstrual syndrome can be treated. Estimates of the prevalence of premenstrual syndrome are as high as 40%; therefore, any study that shows a treatment to be effective is important.¹ This study is the first double blind, placebo controlled, clinical trial of agnus castus.

The findings show that once daily agnus castus extract results in statistically significant improvement in 5 symptom categories, although the clinical significance of these changes in score is unclear. The scores were measured on a VAS with 10 mm representing the range of no symptoms (0) to unbearable symptoms (10). It is not immediately obvious to the reader how to interpret changes in the VAS scores, although Schellenberg states that a change in mean score of 12 mm would be clinically meaningful. Baseline VAS scores for the component items (irritability, mood alteration, anger, headache, and breast fullness) are not provided. As a clinician, I would want to see the baseline and final scores, and not just the difference scores. A clear description of how the CGI item of improvement or deterioration was measured and a clear description of the range of scores would have made me more confident of the effectiveness of agnus castus.

Overall, this study provides a foundation for discussing agnus castus with patients. Agnus castus is an ancient remedy mentioned by Hippocrates for use in "passing of the afterbirth" and other conditions.¹ It is noted as safe but should be used only by women using effective contraception because its effects on pregnancy have not been studied. Certainly, agnus castus is less expensive than selective serotonin reuptake inhibitors; for example, 90 capsules of fluoxetine, 10 mg, cost approximately US\$214 whereas 90 capsules of agnus castus cost US\$8.95.² A trial of agnus castus may be worthwhile for patients with mild to moderate premenstrual syndrome.

Gene Elizabeth Harkless, RN, ARNP, DNSc
Associate Professor/Family Nurse Practitioner
Department of Nursing, University of New Hampshire
Durham, New Hampshire, USA

- 1 On <http://www.thorne.com/townsend/oct/herbal.html>
- 2 Dimmock PW, Wyatt KM, Jones PW, et al. Efficacy of selective serotonin-reuptake inhibitors in premenstrual syndrome: a systematic review. *Lancet* 2000;356:1131-6.

Source of funding: Zeller AG, CH-8590 Switzerland through the Clinical Research Organisation Praxis Klinische Arzneimittelforschung, Polheim, Germany.

For correspondence: Dr R Schellenberg, Institute for Health Care and Science, 35625 Huttenberg, Germany. Fax +49 6403 72156.

A modified version of this abstract appears in *Evidence-Based Mental Health*.

Agnus castus fruit v placebo for premenstrual syndrome at the end of 3 consecutive cycles*

Outcome	Agnus castus fruit	Placebo	RBI (95% CI)	NNT (CI)
Responder rate	52%	24%	120% (45 to 242)	4 (2 to 7)

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