RE: Rhubarb Extract Found Effective in Treating Anxiety in Perimenopausal Women


Women often experience anxiety, sleep disturbances, and other symptoms as they approach menopause. During perimenopause, the transition phase into postmenopause, the ovaries produce less estrogen and the levels of other hormones may fluctuate erratically. The special Siberian rhubarb (*Rheum rhaponticum* – a rare eastern European species) root extract (ERr 731) is used in Germany to relieve symptoms associated with peri- and postmenopause. One of the purposes of this clinical trial was to evaluate the effects of this special rhubarb root extract ERr 731 on anxiety and well-being in perimenopausal women. This publication uses the same dataset as the results on vaso-motor symptoms and menopause that were also published in *Menopause*. In addition, comparable positive results from a second randomized controlled trial were presented in October 2007 at the North American Menopause Society (NAMS) annual conference.

This randomized, double-blind, placebo-controlled trial was conducted at 9 gynecological clinics in the Ukraine. Women were eligible to participate if they were 45 to 55 years of age, had menopausal symptoms, and had irregular or no menstrual cycles during the previous 12 months. The subjects were randomly assigned to receive 1 enteric-coated tablet of either the rhubarb root extract ERr 731 or matching placebo daily for 12 weeks. Each tablet contained 4 mg of ERr 731 as the only active ingredient (tradename Phytoestrol N, since 1st September 2007 Phyto-Strol, Chemisch-Pharmazeutische Fabrik Göppingen Carl Müller, Apotheker, GmbH & Co, KG, Göppingen, Germany).

The subjects were asked to keep a diary throughout the study and record their hot flashes, bleeding, spotting, body weight, and tablet intake. They also completed the following assessments of anxiety and menopause symptoms: Menopause Rating Scale II, Hamilton Anxiety Scale, Psychological General Well-Being Index, and Women's Health Questionnaire. The subjects were examined at baseline and after 4, 8, and 12 weeks of taking the study medication. Women who had no response to treatment (defined as no change in the Menopause Rating Scale II total score) at 4 weeks could discontinue the study medication and continue on in a long-term observational study of 96 weeks. The authors state that results of the observational study will be reported later.
Fifty-five women were assigned to the ERr 731 group, and 39 completed the study as planned. Fifty-five women were assigned to the placebo group, and 7 completed the study as planned. Most of the women in the placebo group discontinued the study medication because of lack of efficacy after 4 weeks.

Total scores on the Hamilton Anxiety Scale and individual scores for psychic anxiety and somatic anxiety improved significantly from baseline to 12 weeks in the ERr 731 group compared to the placebo group (all P < 0.001). From baseline to 4 weeks, the severity of anxiety symptoms in the ERr 731 group improved but remained unchanged in the placebo group. Anxiety scores on the Menopausal Rating Scale II improved significantly from baseline to 12 weeks in the ERr 731 group compared to the placebo group (P < 0.001). Thirty-three of the 39 women in the ERr 731 group reported a reduction in the severity of anxiety symptoms from "moderate" or "severe" at baseline to "slight" at 12 weeks. This improvement in anxiety correlated well with reduced severity and number of hot flashes.

At baseline, the majority of women in both groups reported that they were "in low spirits mostly" or "up and down in spirits a lot" on the Psychological General Well-Being Index. At 4 weeks and 12 weeks, women in the ERr 731 group reported an improvement in general well-being but women in the placebo group did not. Scores on the Women's Health Questionnaire improved in the ERr 731 group at 4 weeks and 12 weeks, but no marked changes occurred in the placebo group. Scores on the Psychological General Well-Being Index and Women's Health Questionnaire were considered secondary outcomes and no statistical analyses were performed.

The authors conclude that ERr 731 is safe; the information on safety and adverse events were given in a previous article covering other outcome assessments (vaso-motor symptoms) of the same clinical trial.1 In addition a study evaluating long-term toxicity in dogs currently in press at Food and Chemical Toxicology found no toxicity.2

The authors conclude that ERr 731 is highly effective in reducing anxiety symptoms and improving state of health and general well-being in perimenopausal women. The authors hypothesize that ERr 731 exerts its effect by modulating neurotransmitter activity in the central nervous system. Recently, it has been demonstrated that ERr 731 is a highly selective activator of the estrogen receptor-β,3 which has been shown to reduce anxiety in animal models. The authors suggest that through this central nervous system pathway, ERr 731 may reduce the need for antidepressant and anti-anxiety medications currently prescribed for the treatment of anxiety related to menopause.

—Heather S. Oliff, PhD

Reference

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