

EDITORIAL

Herbs, Vitamins and Minerals in the Treatment of Premenstrual Syndrome: A Systematic Review

Up to 90% of women will, at some time in their lives, experience symptoms of premenstrual syndrome (PMS) with one-fifth having severe symptoms prompting medical treatment. Up to 200 premenstrual symptoms have been reported with most involving changes in mood, breast symptoms, bloating and pain. An unfortunate 5-8% of women will be diagnosed with premenstrual dysphoric disorder (PMDD), a DSM-IV-TR disorder with luteal phase symptoms severe enough to markedly interfere with work, school, usual activities or relationships.¹

Most women with mild or moderate PMS do not require treatment. For those women with severe PMS or PMDD, treatment is often required, the mainstay of which is psychopharmacologic therapy with antidepressant and anxiolytic medications or the use of hormonal therapies to suppress ovulation. Symptom control is sometimes obtained with non-steroidal anti-inflammatory drugs, diuretics or spironolactone. Occasionally, in the presence of severely debilitating disease, surgical management with total abdominal hysterectomy and bilateral oophorectomy accompanied by hormone replacement therapy may be required.

Women with mild to moderate symptoms are unlikely to seek medical intervention for PMS but do self-medicate with over-the-counter analgesics, mild diuretics, and natural health products. For those women who seek treatment, 10-15% do not start therapy due to fear of drug side effects or unwillingness to take antidepressant medications. For those that do start antidepressant medications, the majority quit within two years because of unacceptable side effects (43%), unwillingness to use antidepressant type medicines (20%), lack of improvement (18%), or fear of drug dependence (19%). Furthermore, almost one-quarter of women stop their medications to deal “naturally” with PMS.²

In this issue of the *Canadian Journal of Clinical Pharmacology*, (Can J Clin Pharmacol Vol 16 (3) Fall 2009:e407-e429; October 29, 2009) Whelan, Jurgens, and Naylor report their results of a systematic review of natural health products (NHPs) used to treat PMS/PMDD. This is a much needed update to previous attempts to summarize the literature on alternative and complementary therapies in the treatment of PMS/PMDD. Like previous reviews,³⁻⁵ they conclude there is little high-quality evidence from well-designed trials to support the use of natural health products by women suffering from PMS/PMDD. From 62 herbs, vitamins and minerals advocated for treatment of PMS/PMDD, only 10 products met the inclusion criteria set by the authors. Of those, calcium is the only product the authors conclude to be supported by randomized controlled trials (RCTs) to help with PMS symptoms including mood swings, water retention, bloating, mastalgia, food cravings and pain. Discrepant results between studies, lack of statistical power, poor methodology, unclear outcomes, or results from only a single small study precluded the authors from supporting the use of other agents including chasteberry, vitamin B6, ginkgo, saffron, St. John's wort, soy, and vitamin E, although preliminary data for those agents suggests the need for further investigation. Results from available evidence show no benefit from evening primrose oil or magnesium oxide, but the effect of magnesium pyrrolidone carboxylic acid is unclear.

Unlike the previous reviews that included all relevant RCTs and a description of their methodology, this study was novel in that it was limited to only RCTs of acceptable methodological rigor. Unfortunately, there are still some limitations to this study. It is unclear from the authors exactly how trial quality was determined, although they consistently, and in

duplicate, applied an instrument they developed for which they will soon publish validity data. The authors' focus was on natural health products and other potentially useful complementary therapies such as dietary change, acupuncture, massage therapy and homeopathy were not included. By restricting searches to only English and French the authors likely missed some relevant trials. Traditional Chinese Medicine, for example, has a long history of herbal product use and a recent systematic review identified two RCTs of Chinese herbal products with potential benefit in PMS.⁶ Also, in the absence of strict criteria for the diagnosis of PMS or a gold-standard outcome measure, the authors accepted previous researchers' definitions of PMS and outcome measures, rather than determining their own. In order to avoid problems with variation in ingredients, particularly with plant-based agents, the authors restricted inclusion to only single agent therapies. However, given the wide variety of symptoms of PMS/PMDD it is unlikely that a single agent can significantly reduce overall symptom scores – an outcome reported in some of the included studies. Further, most of the included studies did not use predetermined definitions of clinical response.

Despite the limitations, the article by Whelan et al is an important reminder to clinicians that it is imperative that we continually update our understanding of the evidence of complementary and alternative medicine. When these therapies have a pharmacologic basis for their effects it is imperative that we seek out information of the highest level – well-designed RCTs or systematic reviews/meta-analyses. There cannot be a double standard between natural health products and conventional pharmaceuticals. This study is an attempt by the authors to summarize the evidence base to date for NHPs used for PMS with similar rigor as would be used when examining, for example, the role of antidepressants for PMS. It is not surprising that there is little quality evidence to convince clinicians to recommend NHPs for their patients with PMS.

However, these results nicely summarize preliminary studies that do support ongoing research into complementary therapies for PMS. The authors remind us that the RCTs of the future

must overcome weaknesses of data quality that currently exist. They require adequate sample size, last for several menstrual cycles with reasonable wash-out periods, use well characterized products in carefully selected patients, and measure specific outcomes of clinical significance.

In North America, nearly one-half of women use complementary and alternative medicine.⁷ As clinicians, we must all be aware of the nature and quality of evidence for “natural” PMS/PMDD therapies so that we can help our patients make informed decisions about their care.

D. Perri, BScPhm, MD, FRCPC
Assistant Professor of Medicine
Clinical Pharmacology & Therapeutics
Department of Medicine
McMaster University, Hamilton, Canada

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