A Review of the Clinical Efficacy of Evening Primrose

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The oil obtained from the evening primrose (*Oenothera biennis*) plant is usually taken orally in a gel cap form. This herbal supplement is most commonly used for the treatment of mastalgia and atopic dermatitis. While recommending this supplement to patients for many years for the treatment of mastalgia, this author was interested in researching the plant and the evidence supporting its use for this complaint and its other potential uses. The oil is rich in omega-6 fatty acids, which are essential for many bodily functions; however, a lack of strong scientific evidence exists to support its use for the relief of mastalgia or atopic dermatitis. **KEY WORDS:** *dermatitis*, *evening primrose*, *mastalgia* *Holist Nurs Pract* 2008;22(3):171–174

In the United States, more and more individuals are using herbal therapies either instead of pharmaceuticals for specific symptoms, in conjunction with pharmaceuticals, or for general health maintenance. The National Center for Complementary and Alternative Medicine reported that Americans spent $5 billion in 1997 on herbal products.[1] Evening primrose (*Oenothera biennis*) is one of the more commonly used herbal medications. In 2005, evening primrose was ranked as the 12th top-selling herb in the United States with $5 303 904 in sales.[2] Allopathic providers are expected to practice evidence-based medicine; however, much of the data available to practitioners regarding herbal preparations are anecdotal. Scientific studies regarding the use of these preparations are now reported more regularly. Cohen et al[3] pointed out that many studies performed on herbals lack scientific rigor in that they may lack randomization, placebo control, sufficient numbers of participants, or significant length of time. Most allopathic providers were not provided with education regarding complementary and integrative therapies (CITs) in their medical curricula. Because of the fact that more patients are using herbal preparations (and many other forms of CITs), it is imperative that all healthcare providers learn as much as they possibly can about these popular medicinal plants. Evening primrose is popularly used for dermatologic and gynecologic complaints. It has a number of other potential benefits. This article explores the uses of this herb and reviews the current data supporting these uses.

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PLANT DESCRIPTION

Evening primrose (*O biennis*), a biennial plant, is a member of the Onagraceae family that is native to North America. Its lesser-known names are common evening primrose, fever plant, great evening primrose, King's cure-all, night willow-herb, scabish, scurvish, and tree primrose.[4] S. M. Ross, MH, HT, CNC (verbal communication, October 2007) noted evening star as an alternative name for evening primrose. In the United States, evening primrose plants are found from the Atlantic Ocean to the Rocky Mountains. These plants have also been naturalized around the world. The plant is in bloom from June to September, with the yellow flowers opening at sunset and closing up during the day (Fig 1). The flowers have a strong, sweet scent, which attracts moths for pollination. This biennial plant lives for 2 years and reproduces by natural propagation. It is the oil from the tiny seeds that is primarily used in herbal preparations, although the entire plant is edible.[4] According to Blumenthal,[5] the oil is obtained from the seeds by cold expression or solvent extraction. The golden, yellow oil is generally marketed as capsules for use. Jackson and

FIGURE 1. Evening primrose. Photograph by Karen Bergeron. Copyright 2001.

Bergeron noted that "the leaves are cooked and eaten as greens and the roots are said to be sweet, succulent and delicious when boiled like potatoes. Flowers are a sweet addition to salads or as a garnish and young seedpods are steamed."[4]

CHEMICAL CONSTITUENTS AND PHARMACOLOGIC ACTIONS

Evening primrose seed contains about 14% fixed oil (EPO), which is composed of about 65% to 75% linoleic acid, 7% to 10% γ-linoleic acid (GLA), plus oleic, palmitic, and stearic acids, and steroids campesterol and β-sitosterol.[5] Essential fatty acids (EFAs) are necessary for normal bodily functions. EFAs cannot be manufactured endogenously; therefore, they must be obtained exogenously from food sources. Evening primrose oil is a good source of omega-6 fatty acids, which is an EFA. EFAs "are generally necessary for stimulating skin and hair growth, maintaining bone health, regulating metabolism, and maintaining reproductive capability."[6]

CLINICAL APPLICATIONS

The primary uses of evening primrose are for atopic dermatitis, mastalgia, and lactation.[5] The other potential uses include diabetic neuropathy, premenstrual syndrome (PMS), rheumatoid arthritis (RA), EFA deficiencies, seborrhea, fortification of infant formula, dry eyes associated with Sjogren syndrome, Raynaud's disease, and uremic skin symptoms.[5] The University of Maryland Medical Center lists the following potential uses: anorexia nervosa, attention-deficit/hyperactivity disorder (ADHD), diabetic peripheral neuropathy, Sjogren syndrome, osteoporosis, menopausal symptoms, PMS, acne and psoriasis, eczema, alcoholism, allergies, RA, cancer prevention, weight loss, high blood pressure and heart disease, tuberculosis, and ulcers.[6] In addition, the Natural Medicines Comprehensive Database lists endometriosis, multiple sclerosis, Alzheimer disease, schizophrenia, chronic fatigue syndrome, asthma, ulcerative colitis, irritable bowel syndrome, prevention of pre-eclampsia, stimulation of and quickening of labor, and prevention of past due date births as still more reasons people use EPO.[7] A gel cap product is available for the treatment of dry eye syndrome. These gel caps contain omega-3 fatty acid from flaxseed oil and omega-6 fatty acid from EPO, with bilberry extract for combined anti-inflammatory effect.[8] EPO is also used as an ingredient in cosmetics and soaps.[7]

KNOWN CONTRAINDICATIONS AND PRECAUTIONS

According to the National Center for Complementary and Alternative Medicine, EPO is generally well tolerated by most individuals. Some individuals may experience mild stomach upset or headache. It is considered safe during pregnancy, but there is limited information.[9] Blumenthal[5] noted that, historically, EPO was not recommended in schizophrenic patients or those taking phenothiazines or other medications with potential to induce seizures. However, recent studies did not reveal any adverse effects in these populations. The author also noted that no limitations exist for its use during pregnancy. Omega-6 fatty acid is considered an important constituent of breast milk, therefore would likely be considered safe during lactation.[5] A team of researchers from the University of Maryland Medical Center warns against taking EPO or any omega-6 fatty acid in cases of seizure disorder. These researchers state that borage seed oil, and possibly other GLA sources, should be avoided during pregnancy because of possible harm to the fetus and risks for premature labor. Other potential interactions with omega-6 supplements include cephalosporins, chemotherapy, cyclosporine, and nonsteroidal anti-inflammatory drugs.[6] The Natural Medicines Comprehensive Database states that oral usage of EPO during pregnancy should be avoided because of

possible pregnancy-related complications. In addition, EPO should not be used in patients with a bleeding disorder or those who are taking anticoagulants. It is also possible that combining EPO with some herbs, including angelica, clove, danshen, garlic, ginger, ginkgo, red clover, and turmeric, may increase bleeding times and should be avoided.[7] Menopausal women should be aware of these potentially harmful interactions because they often take red clover for hot flashes, ginkgo for memory, and low-dose aspirin for anticoagulant therapy. The Natural Standard Research Collaboration states that allergy or hypersensitivity to EPO is not common but contact dermatitis is a possibility. Seizures have been reported with EPO use, mostly in patients with pre-existing seizure disorders or when taken with anesthetics. Based on these reports, individuals undergoing surgery with general anesthesia or those with seizure disorders should avoid EPO. Not enough information is available about EPO use during pregnancy.[10] Pearl et al confirmed that "proconvulsant effects have been associated with multiple commonly used herbal products including . . . evening primrose."[11]

PUBLISHED RESEARCH DATA

A study regarding the effects of EPO and fish oil on severe mastalgia was completed in the Netherlands. One-hundred twenty women were enrolled in this double-blind, randomized, controlled trial of 6 months' duration. These women were divided into 4 groups. One group received EPO with a control oil, the second group received fish oil with a control oil, the third group received a combination of EPO and fish oil, and the fourth group received 2 control oils. At the conclusion of the study, EPO or fish oil or both were no better than placebo in relieving severe mastalgia because all women reported a decrease in both the severity of the breast pain and the percentage of pain days. The decrease in severity of pain was not statistically significant; however, an overall decrease of 13% was reported in the percentage of pain days for the entire study group.[12] In response to this published study, Graves[13] commented that although this study was in contrast to earlier claims, future studies should consider that all oils may have potential effect, and correct the ambiguity for that. This author also suggested that the attention and care these study participants received may have had an effect that might also be studied in the future.[13] Dickerson et al[14] declared that several dietary supplements including EPO have been reported to improve symptoms associated with PMS, but go on to state that "most studies have been small or poorly designed, efficacy needs to be confirmed in large, well-designed clinical trials before evidence-based recommendations can be made." These authors also pointed out that "a systematic review of placebo-controlled trials of EPO suggested lack of benefit in PMS, although mild relief was demonstrated in women with breast tenderness."[14]

The evidence for the use of EPO for atopic dermatitis is not much more promising. Williams[15] stated that it was "time to say goodnight" to the possibility that EPO was effective for treating atopic dermatitis. In evaluating 10 studies of EPO and atopic dermatitis, the researcher found no convincing evidence to support its use. This author further contended that most claims touting the benefits of EPO for the treatment of atopic dermatitis were made by Searle, the company responsible for marketing EPO, and that the studies funded by this company were never published. There was speculation that GLA needed to be taken in much higher doses to be effective; however, results from a randomized, double-blind, placebo-controlled trial by Takwale (as cited in Williams) still found no statistically significant effect. Williams[15] also noted that EPO product licensing has been withdrawn by the United Kingdom's Medicines Control Agency.

In a systematic review of the literature of herbal therapy use for RA, Soeken[16] noted that pooled results from 11 trials using GLAs found in borage seed oil, EPO, and blackcurrant seed oil "showed significant reduction in pain" when compared with placebo. Truscott-Brock[17] suggested that among other supplements, omega-6 fatty acids found in EPO are a good choice for individuals with Alzheimer disease because of neuroprotective and anti-inflammatory properties. In a study conducted in Australia, polyunsaturated fatty acids (PUFAs) were evaluated in children with ADHD. This study included data on 104 children aged 7 to 12 who were randomized into a placebo-controlled, double-blind, crossover study. Three groups were assigned: those taking PUFAs alone, those taking PUFAs plus micronutrients (a multivitamin), and finally the placebo group. The PUFA capsules contained 400 mg of fish oil, 100 mg of EPO, 29 mg of docosahexaenoic acid, 10 mg of GLA, and 1.8 mg of vitamin E. The groups were required to take 6 active or placebo capsules per day. The results indicated that treatment of ADHD with PUFAs showed significant improvement in

parental-evaluated ratings of attention, impulsivity, and hyperactivity.[18]

In a review of randomized controlled trials concerning the use of EPO for the treatment of diabetic neuropathy, Halat and Denneby[19] found that the evidence is "limited and inconclusive." They were able to find 2 of 3 studies that demonstrated beneficial results and conceded that EPO may be useful "in cases of mild diabetic neuropathy . . . or as an add-on therapy for patients with mild to moderate neuropathy who achieve only partial relief from prescription drugs."[19]

SUMMARY

Although evening primrose has been used for hundreds of years for a variety of complaints, the evidence base regarding its efficacy needs to be strengthened. This certainly does not mean that the efficacy is lacking; however, it does mean that more research needs to be completed. The evidence for use of EPO for diabetic neuropathy and ADHD sounds promising. The anecdotal evidence supports its use, and with a low adverse effects profile, EPO appears to be generally safe for use. Healthcare providers need to open a dialog with their patients to ascertain what methods of CIT they are using. Allopathic providers must realize that just because they were not taught about these modalities during their medical training does not necessarily mean that these options are not useful and efficacious for many patients. As such, allopaths must educate themselves regarding CIT modalities, conduct randomized, placebo-controlled trials, and support or even recommend their use by patients.

REFERENCES

1. National Center for Complementary and Alternative Medicine. The use of complementary and alternative medicine in the United States. http://nccam.nih.gov/news/camsurvey_fs1.htm. Accessed November 12, 2007.
2. Blumenthal M, Grant KLF, Cavaliere C. Total sales of herbal supplements in United States show steady growth. *HerbalGram*. 2006;71:64–66.
3. Cohen SM, Rousseau ME, Robinson EH. Therapeutic use of selected herbs. *Holist Nurs Pract.* 2000;14(3):59–68.
4. Jackson D, Bergeron K. Evening primrose. http://altnature.com/gallery/Evening_Primrose.htm. Accessed November 12, 2007.
5. Blumenthal M. *The American Botanical Council Clinical Guide to Herbs.* New York: Thieme; 2003.
6. University of Maryland Medical Center. Omega-6 fatty acids. http://www.umm.edu/altmed/articles/omega-6-000317.htm. Accessed November 16, 2007.
7. Natural Medicines Comprehensive Database. Evening primrose oil. http://www.naturaldatabase.com. Accessed January 23, 2007.
8. Marketplace Department. Focus on dry eye medications. *Ophthalmol Manage*; 2007. http://www.ophmanagement.com/article.aspx?article=&loc=archive\2007\april\200704102.htm. Accessed November 16, 2007.
9. National Center for Complementary and Alternative Medicine. Evening primrose oil. http://nccam.nih.gov/health/eveningprimrose/. Accessed November 18, 2007.
10. The National Standard Research Collaboration. Evening primrose oil (*Oenothera biennis* L.). http://www.mayoclinic.com/print/evening-primrose-oil/NS_patient-Primrose/. Accessed November 18, 2007.
11. Pearl PL, Robbins EL, Bennett HD, Conry JA. Use of complementary and alternative therapies in epilepsy: cause for concern. *Arch Neurol.* 2005;62(9):1472–1475.
12. Blommers J, deLange-deKlerk ES, Kuik DJ, Bezemer PD, Meiger S. Evening primrose oil and fish oil for severe chronic mastalgia: a randomized, double-blind, controlled trial. *Am J Obstet Gynecol*. 2002;187(5):1389–1394.
13. Graves DS. *Evening Primrose Oil and Fish Oil Used for Mastalgia*. Austin, TX: American Botanical Council; 2003. HerbClip, HC 050333-245. www.herbalgram.com. Accessed October 15, 2007.
14. Dickerson LM, Mazyck PJ, Hunter MH. Premenstrual syndrome. *Am Fam Phys.* 2003;67(8):1663–1665, 1743–1752.
15. Williams HC. Evening primrose oil for atopic dermatitis. *BMJ.* 2003;27(7428):1358–1359.
16. Soeken KL. Selected CAM therapies for arthritis-related pain: the evidence from systematic reviews. *Clin J Pain.* 2004;20(1):13–18.
17. Truscott-Brock E. Naturopathic medicine and its complementary role in the care of persons with Alzheimer's disease. *Alzheimer's Care Q*. 2006;7(1):41–48.
18. Sinn N, Bryan J. Effect of supplementation with polyunsaturated fatty acids and micronutrients on learning and behavior problems associated with child ADHD. *J Dev Behav Pediatr*. 2007;28(2):82–91.
19. Halat KM, Denneby CE. Botanicals and dietary supplements in diabetic peripheral neuropathy. *J Am Board Fam Pract*. 2003;16:47–57.