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Polyunsaturated fatty acids (PUFAs) might reduce hot flushes: an indication from two controlled trials on soy isoflavones alone and with a PUFA supplement

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Abstract

Objectives: To investigate the effect on hot flushes of a soy isoflavone extract alone (Study A) and with the addition of a supplement of polyunsaturated fatty acids, PUFAs (Study B).
Methods: Subjects were postmenopausal women (29 in Study A, 28 in Study B) with more than five troublesome hot flushes per day. Both studies were double-blind randomized placebo-controlled trials with cross-over design, of 24-week duration. After a 2-week observation period, they were randomized to receive two capsules per day providing 60 mg of isoflavones or placebo for 12 weeks; thereafter, women who had taken isoflavones were given placebo for a second 12-week period, and vice-versa. Women in the Study B were given also two capsules per day containing a PUFA supplement for the entire 24-week test period.
Results: Both studies showed the isoflavone extract to have no greater efficacy on hot flushes than the placebo. During the 24 weeks of the Study B there was a progressive and highly significant reduction in the number of hot flushes, independent of whether the women had begun with isoflavones or with placebo.
Conclusion: In these two trials the isoflavone extract did not show greater efficacy on the hot flushes than the placebo. The reduction of hot flushes observed in the Study B might be due to the PUFA supplement. PUFAs, particularly Omega (Ω) 3-fatty acids, could reduce hot flushes through their influence on neuronal membranes and/or the modulation of the neurotransmitter function and the serotoninergic system. Studies specifically designed to document the action of PUFAs on hot flushes would be welcome.

Keywords: Menopause; Hot flushes; Soy isoflavones; Polyunsaturated fatty acids (PUFAs)

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1. Introduction

Increasing numbers of women with contraindications to hormone therapy, or who prefer a more "natural" strategy to control hot flushes, are asking for alternative treatment. Among these, dietary supplements containing isoflavones are widely marketed. However, the efficacy of these preparations, apart from their placebo effect, is still debated.

The first studies demonstrating a slight efficacy of isoflavones to reduce hot flushes date to the second half of the 1990s [1–3]. These studies tested dietary soy supplementation in the form of flour or soy protein, administration methods which are not easily applicable in clinical practice. Dietary supplements in the form of tablets or capsules containing extracts from soy, as well as from other plants rich in isoflavones such as red clover, are more acceptable in our countries. At the end of 1999, we began a controlled 24-week cross-over study to verify the efficacy in reducing hot flushes of one of these preparations, capsules containing a standardized extract with known amounts of soy isoflavones (Study A). While recruitment was under way (which was completed at the end of 2000) the results of randomised trials on similar preparations appeared, and showed a substantial lack of efficacy versus placebo [4–6]. We therefore began a second study at the start of 2001, with the same design and using the same soy isoflavone preparation, but with the addition of a polyunsaturated fatty acid (PUFA) supplement for the entire 24 weeks of the trial (Study B). The reason for this addition was that studies in the rat had reported interesting data concerning increased pain threshold and improved thermoregulation functions, induced by diets rich in PUFAs, which can vary the composition of cell-membrane phospholipids, particularly in neurones [7]. Actually, phospholipid composition is of critical importance for the structural integrity of neuronal membranes, their fluidity, their enzymatic and receptor functions [8]. It was thus hypothesised that the effect of isoflavones on hot flushes could in some way be facilitated by the changes that PUFAs, and in particular Omega (Ω) 3-fatty acids, exercise on neuronal membrane functions.

Taken together, the two studies showed the isoflavone extract to have no greater efficacy than the placebo, whereas during the 24 weeks of Study B, a progressive reduction of hot flushes occurred that might be attributed to the PUFA supplement.

2. Subjects and methods

2.1. Subjects

The women participating in both studies were recruited among patients presenting to the Menopause Clinic of the Endocrinological Gynecology Unit, Sant'Anna Gynecological Hospital, Turin. Participants in Study A were enrolled between November 1999 and December 2000; those in Study B between January 2001 and December 2001. Eligibility criteria were: good general health, age between 45 and 58 years, BMI between 18 and 28, in surgical menopause for bilateral ovariectomy for at least 3 months or in spontaneous menopause with amenorrhoea for over 6 months and with menopausal hormone profile (estradiol <30 pg/ml and FSH >40 UI/l). All suffered a minimum of five moderate-to-severe hot flushes in 24 h. No use of drugs that influence vasomotor symptoms, such as veralipride, clonidine, antidepressants, tamoxifen and raloxifene; no hormone therapy or tibolone in the 6 months prior to enrolment. Those who consumed soy-based food more then once a week were excluded, as were those taking drugs that might reduce absorption of isoflavones (antibiotics, anti-acids).

All patients gave their signed informed consent to the study, which was approved by the Ethical Committee of the Piedmont Regional Government Health Department.

2.2. Study design and randomisation

Both studies were double-blind randomised placebo-controlled trials with cross-over design, of 24-week duration. Eligible patients who fitted the selection criteria were subjected to medical examination, during which the following were ascertained: reproductive history and history of past diseases, diet, use of alcohol and tobacco; pelvic gynaecological examination with clinical breast examination, measurement of blood pressure, weight and height with calculation of BMI [weight (kg)/height^2 (m^2)]. Patients were also given a daily diary in which to record the number of troublesome hot flushes experienced