

Review

Soy Consumption for Reduction of Menopausal Symptoms

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Abstract. *Aims:* To review current research on the effects of soy consumption on menopausal symptoms.

Methods: To review results of recent meta-analyses and individual clinical trials.

Main Results: One recent meta-analysis reported that isoflavone supplementation was associated with a 34% reduction in hot flashes, with increased efficacy as the baseline number of flashes and isoflavone dose increased. A second review concluded that consumption of at least 15 mg genistein, rather than total isoflavones, is responsible for the reduction in symptoms. Results of these two reviews are supported by most subsequent randomized controlled trials.

Conclusions: Consumption of 30 mg/day of soy isoflavones (or at least 15 mg genistein) reduces hot flashes by up to 50%. This total reduction includes that provided by “the placebo effect”. The greatest benefit may be realized when the isoflavone-rich food or supplement is taken in divided doses by subjects who experience at least four hot flashes/day.

Key words: Isoflavone – Phytoestrogen – Hot flash – Menopausal symptom – Soybean – Soy – Women – Menopause

Introduction

Menopause is often accompanied by vasomotor symptoms such as hot flashes and night sweats, psychological symptoms such as irritability, anxiety, difficulty sleeping and depression, and somatic symptoms such as decreased libido, fatigue and body aches. Although the symptoms of menopause can be merely nuisances, in some women they can be debilitating. As a result, in the most severe cases, exogenous estrogens are prescribed. Given recent reports suggesting that hormone replacement therapy may be associated with negative side ef-

fects, many women are hopeful that non-hormonal alternative solutions can be found.

It has been estimated that hot flash incidence is far lower in Asian countries than in the West. Although it is possible that these data are influenced by the reluctance of Asian women to discuss these issues, between 70–80% of women in the United States and Europe report having hot flashes, while only 10–20% of women in Japan, Singapore and China report such symptoms (Knight and Eden, 1995). Given the fact that the soybean, typically consumed in the Asian diet, contains the phytoestrogen isoflavones, it has been suggested that soy consumption may be responsible for this difference in symptoms. Recent data suggest that average consumption of isoflavones in Japan is between 15–30 mg/day, while in the United States and Europe, it is 1–2 mg/day. It has thus been suggested that soy consumption may be an effective substitute for postmenopausal hormone replacement therapy. In fact, recent studies performed in the United States and Australia suggest that between 16–34% of postmenopausal women consume soy foods and supplements, soy being the most common supplement taken by women who report vasomotor symptoms (Schonberg and Wee, 2005; Gold et al., 2007; van der Sluijs et al., 2007). Despite this widespread usage, controlled studies have shown inconsistent efficacy of soy supplements on menopausal symptoms.

Discussion and conclusions

Most studies on menopausal symptoms are limited to hot flash frequency and intensity, likely because out of all the symptoms, these can be measured most objectively. Early studies on soy effects on hot flashes showed enormous variability in results, thought to be due primarily to widely differing study designs and sample sizes. In order to overcome this, recent meta-analyses have been published that select out the very best trials, using specific pre-defined criteria, and pool the studies into one analysis in order to

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increase statistical power. One recent meta-analysis of 12 randomized, controlled trials (Murkies et al., 1995; Albertazzi et al., 1998; Scambia et al., 2000; Upmalis et al., 2000; Knight et al., 2001; St Germain et al., 2001; Faure et al., 2002; Han et al., 2002; Van Patten et al., 2002; Burke et al., 2003; Penotti et al., 2003; Colacurci et al., 2004) reported that isoflavone supplementation was associated with a reduction in hot flashes of 34% (95% confidence intervals -0.47 to -0.21, $P < 0.0001$), with an increase in efficacy as the baseline number of flashes and isoflavone dose increased (Howes et al., 2006) (Fig. 1).

A second critical review of 11 studies using well-characterized isoflavone supplements (Scambia et al., 2000; Upmalis et al., 2000; Faure et al., 2002; Han et al., 2002; Nikander et al., 2003; Penotti et al., 2003; Colacurci et al., 2004; Crisafulli et al., 2004; Petri Nahas et al., 2004; Secreto et al., 2004; Campagnoli et al., 2005) confirmed the importance of dose in determining whether or not isoflavones reduce hot flashes (Williamson-Hughes et al., 2006). In this review, all five studies providing more than 15 mg genistein showed significant decreases in hot flash frequency, while only one of the six studies providing less than 10 mg genistein showed a significant decrease. The conclusion of these researchers was that consumption of genistein, rather than total isoflavones, is responsible for the reduction in symptoms associated with soy intake, and that 15 mg genistein is the minimal quantity for benefit (Williamson-Hughes et al., 2006).

Although the two reviews discussed above differ in their conclusions from a third systematic review reporting mixed results of 11 trials (Nelson et al., 2006), the results of the first two reviews are supported by most subsequent randomized controlled trials. For example, a randomized controlled double-blind study was performed in 51 Swedish postmenopausal women who consumed either 60 mg isoflavones or a placebo for three months. This study reported that hot flash symptoms were significantly reduced by half in the isoflavone group, while no change occurred in the placebo group (Cheng et al., 2007). A second randomized, placebo-controlled trial was recently performed over a 12-month period in 247 Italian women who reported at least four hot flashes/day at baseline (D'Anna et al., 2007). Although there was no change in hot flash number or severity in the placebo group, hot flashes were reduced by 57% and severity was reduced by 38% in the women who consumed 54 mg genistein daily (D'Anna et al., 2007). A third randomized controlled crossover trial was performed over an eight week period in the United States in 60 postmenopausal women. During the treatment period, the women consumed one-half cup of soy nuts (containing 25 g soy protein and 101 mg isoflavones) spread throughout the day (Welty et al., 2007). Although there was no change in hot flash frequency during the control period, the women experienced a 40% greater decline in frequency of hot flashes and significant improvements in a number of other menopausal symptoms while consuming the soy nuts (Welty et al., 2007). A fourth randomized, placebo-controlled crossover trial was performed in 100 postmenopausal Italian women who consumed 90 mg genistein or placebo for six weeks each (Albertazzi et al., 2005). In the 41 women with the greatest symptoms, hot flash score (frequency \times intensity) was reduced significant more in the

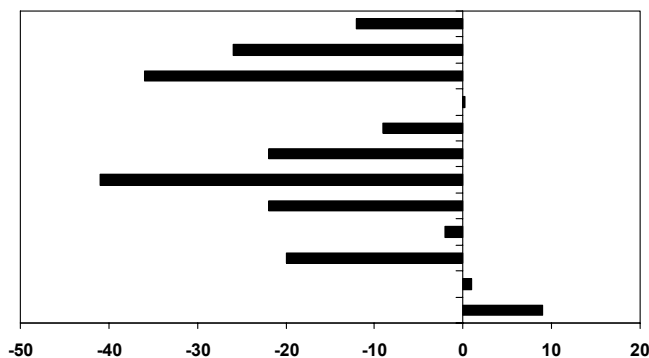


Fig. 1. Percent change in hot flashes, compared to control (bars from top to bottom show data from references Albertazzi et al., 1998; Han et al., 2002; Faure et al., 2002; Penotti et al., 2003; Upmalis et al., 2000; Knight et al., 1995; Colacurci et al., 2004; Murkies et al., 1995; St. Germain et al., 2001; Scambia et al., 2000; Burke et al., 2003; VanPatten et al., 2002, respectively) (Howes et al., 2006).

genistein group than in the placebo group (31% vs 20%) (Albertazzi et al., 2005).

These four controlled trials differ from a study that evaluated symptoms in 87 early postmenopausal women who consumed muffins containing either flaxseed, soy flour (containing 42 mg isoflavones), or wheat flour daily for 16 weeks (Lewis et al., 2006). In this study, there were no significant effects on hot flash frequency or severity in either the soy or flax group (Lewis et al., 2006). Another randomized double-blind controlled trial performed in 72 breast cancer patients who consumed 70 mg isoflavones/day or placebo for 12 weeks showed no significant effects of the isoflavones (MacGregor et al., 2005), consistent with other trials performed in breast cancer patients (Quella et al., 2000; Van Patten et al., 2002). These last studies suggest that breast cancer patients may respond differently to soy than healthy controls, particularly if they are on treatments such as tamoxifen or hormone inhibitors.

Although soy isoflavones have been shown to be effective in reducing menopausal symptoms, it is generally accepted that this effect is far smaller than that of exogenous estrogens. Countering this assumption are results of a randomized, controlled, double-blind pilot study published in 2006 in which the effects of soy consumption were compared directly with the effects of exogenous estrogen administration. Seventy-nine Brazilian women consumed either 100 mg isoflavones split into two doses, or 0.625 mg conjugated equine estrogens daily for six months (Kaari et al., 2006). In this direct comparison study, the Kupperman Menopausal Index of menopausal symptoms declined similarly in both the isoflavone and estrogen groups, by about 80% by the end of the trial.

These data suggest that consumption of as little as 30 mg/day of soy isoflavones (or at least 15 mg genistein), in soy protein or tablet form, may reduce hot flashes by as much as 50% or more. This total reduction includes that provided by "the placebo effect". The benefit increases with doses from 10 to 100 mg isoflavones/day and is greatest in women with a higher number of baseline hot flashes/day. The greatest benefit of soy isoflavones may be realized when the isoflavone rich food or supplement is taken in divided doses throughout the day by subjects who experience at least four hot flashes/day.

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