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Efficacy of Omega-3 Fatty Acid Supplementation in Post-Menopausal Hot Flashes: A Randomized Clinical Trial

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Abstract: Hot flash is an unpleasant sense of hot feeling. The aim of this study was to assess the efficacy of omega-3 supplements in post-menopausal hot flashes. In this randomized trial, 60 post-menopausal patients with moderate to severe hot flashes randomly assigned to receive either 1000 mg omega-3 or placebo every day for 12 weeks. Main outcome measures were daily frequency and intensity of hot flashes at 12 weeks, 6 and 9 months after the intervention. At baseline, there was no statistically significant difference between the two groups in terms of age and duration, intensity and daily frequency of hot flashes. About 8 and 12 weeks after the intervention, omega-3 supplementation was associated with more reduction in the intensity of hot flashes compared to placebo ($p = 0.01$ and 0.004, respectively). However, it could not decrease significantly the number of daily hot flashes.

Key words: Omega-3, hot flash, post-menopause, intensity, Tehran

INTRODUCTION

Menopause is derived from the Greek words men (month) and pausis (cessation) which describes the end of monthly menstrual cycle following the loss of ovarian function. Menopause is an important phase of aging process in women and hot flash is a major symptom of it which can interfere with daily activities and adversely affects the quality of life. Approximately 2/3 of post-menopausal women experience hot flash which is intolerable in 20% of cases (Kronenberg, 1990).

Therefore, finding methods to prevent and/or alleviate troublesome hot flashes is of great importance. The current methods of management in hot flash include: Pharmacological intervention:

- Hormonal therapy including estrogen formulations, estrogen-progestin regimens, medroxyprogesterone acetate and megestrol acetate (Okeke *et al*., 2013; Prior and Hitchcock, 2012; Bertelli *et al*., 2002), tibolone (Swanson *et al*., 2006) and Selective Estrogen Receptor Modulators ($SERM_s$) (Kagan, 2012)
- Non-hormonal therapy including dopamine antagonist (veralipride) (Carretti *et al*., 2010), antidepressant medications (paroxetine, venlafaxine, fluoxetine and citalopram) (Cheema *et al*., 2007; Sterns *et al*., 2005), Bellergal (Loprinzi *et al*., 2005), antihypertensive (clonidine, methyldopa) (Loprinzi *et al*., 2005), naloxoe (De Fazio *et al*., 1984) and antiseizure medication (gabapentin) (Aguirre *et al*., 2010)

Complementary and Alternative Medicine (CAM) including phytoestrogens (D'Anna *et al*., 2009; Tice *et al*., 2003; Lethaby *et al*., 2007), isoflavones (Williamson *et al*., 2011) (soybeans, lentils), lignans (flaxseed, cereals, vegetables, fruits) and coumestans (sunflower seeds, bean sprouts); dong quai and evening primrose oil (Fugate and Church, 2004); ginseng; black cohosh (Leach and Moore, 2012); vitamin E (Kelley and Carroll, 2010; Aidelsburger *et al*., 2012); acupuncture (Venzke *et al*., 2010); yoga (Booth-LaForce *et al*., 2007); clinical hypnosis (Elkins *et al*., 2013) and meditation (Carmody *et al*., 2011).

At present, hormone therapy is the method of choice for hot flash. However, inability to take estrogen in certain conditions, such as history of breast cancer or concerns about the adverse effects of estrogen, such as increasing risk of breast cancer are responsible for increased tendency to use alternative therapies for prevention and treatment of hot flashes during recent years.

The aim of this study was to evaluate the effect of omega-3 supplementation on the frequency and severity of postmenopausal hot flashes.

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MATERIALS AND METHODS

This randomized, double-blind controlled trial was carried out in Shahid Akbar Abadi teaching hospital in Tehran, Iran from December, 2009 to November, 2010. This research study was approved by the Ethical Committee of Tehran University of Medical Sciences. A written informed consent was obtained from all participants.

All women aged 45-55 years old with symptom of hot flash for 6-18 months were eligible to participate in this study. Other inclusion criteria were as follows: FSH>20 IU mL^{-1} with amenorrhea for ≥12 months, BMI = 20-30 kg m^{-2}, intact uterus, at least one ovary and >4 hot flashes per day. Exclusion criteria were; use of any drug to alleviate vasomotor symptoms, such as clonidine or tamoxifen or hormone replacement therapy within the past 3 months; cigarette smoking; use of soya, vitamin E, black cohosh or flax; consumption of fish more than twice per week during the last 3 months, sensitivity to seafood or fish oil; use of anticoagulants; any vaginal bleeding during the last 6 months; history of breast cancer or receiving chemotherapy.

A total of 65 women with moderate to severe hot flash (score ≥2) were enrolled in this study and observed for 1 week. They were asked not to use any kind of medications. However, five subjects could not tolerate hot flashes without hormone therapy and were excluded from the study. The remaining 60 participants were randomized in blocks of four using a random numbers table to create two groups of 30 subjects each. Allocation into each group was based on sealed and opaque envelopes indicating the type of intervention. Researcher and participants were blinded to the treatment allocation. Participants were instructed to take either 1000 mg omega-3 capsule (Zahravi Pharmaceutical Co., Tehran, Iran) or placebo (gelatin) with the same size, shape and color, every day for 12 weeks. Daily frequency and intensity of hot flashes were recorded by participants and analyzed every month during the study period, 3 and 6 months thereafter. For this study, researchers used Menopause Rating Scale (MRS), item No. 1 of the somatic subscale (range from 0 (none) to 4 (1 = mild, 2 = moderate, 3 = severe, 4 = extremely severe)) for evaluation of hot flash severity. The study outcomes were the daily frequency and intensity of hot flashes which measured by participant daily diaries.

Statistical analysis was performed using SPSS Version 16 software (SPSS Inc., Chicago, IL, USA). Student's t-test was used to analyze normally distributed continuous variables (presented as mean/SD) and Chi-square (χ^2) test was used for comparison of severity of hot flashes (presented as median (range)) between two groups. The p-value <0.05 was considered significant.

RESULTS AND DISCUSSION

At baseline, both groups were similar with regard to age and duration, intensity and daily frequency of hot flashes (Table 1).

During the study period, there was a progressive reduction in the frequency of hot flashes in both groups and at the end of study period, daily hot flashes in omega-3 group were somewhat less than control group, although the difference was not statistically significant. However, 6 and 9 months later, daily hot flashes were similar in both groups (Table 2). With regard to the intensity of hot flashes, 8 weeks after intervention there was a significant reduction in omega-3 group compared with the control group which last through the end of study period. However, 6 and 9 months post intervention there was no significant difference between the two groups (Table 2).

To the best of the knowledge, only a few studies have been done to evaluate the efficacy of omega-3 supplementation in postmenopausal hot flashes (Campagnoli *et al*., 2005; Lucas *et al*., 2009; Sternfeld *et al*., 2013). This study demonstrated that consuming omega-3 supplementation could not decrease significantly the number of daily hot flashes after 12 weeks, however it could significantly reduce the intensity of hot flashes with the maximum efficiency after 8-12 weeks. These results are in contrast to the findings in a previous study published by Lucas *et al*. (2009) in that omega-3 supplementation reduced the frequency of hot flash while had no effect on intensity of it. On the

Table 1: Baseline characteristics of two groups

Characteristics	Omega-3 N = 30	Placebo N = 30	p-value
Age (year; Mean±SD)	51.7±5.9	51.1±5.8	0.114
Duration of hot flashes (month; Mean±SD)	11.0±7.4	10.8±3.8	0.090
Intensity of hot flashes (MRS; median (range))	3(2-3)	3(2-3)	0.1
Frequency of hot flashes/day (Mean±SD)	5.3±2	6.9±4.7	0.1

Table 2: Comparison of frequency and intensity of hot flashes before and after intervention

Composition	Omega-3 (N = 30)	Placebo (N = 30)	p-values
Frequency of hot flashes (MRS, Mean±SD)			
Before intervention	5.3±2.0	6.9±4.7	0.10
After 4 weeks	4.5±1.7	4.6±2.6	0.80
After 8 weeks	2.3±1.5	2.5±1.8	0.70
After 12 weeks	0.8±1.1	1.3±1.0	0.07
After 6 months	1.9±2.2	2.6±3.7	0.30
After 9 months	2.4±1.6	2.2±3.4	0.70

other hand, this study is supported by the study published by Campagnoli *et al.* (2005) and Sternfeld *et al.* (2013) which showed the effectiveness of supplements and the balance of the evidence from these studies shows that the effectiveness of Polyunsaturated Fatty Acids (PUFAs), particularly omega 3-fatty acids is through their influence on neuronal membranes and/or the modulation of the neurotransmitter function and the serotoninergic system (Campagnoli *et al*., 2005). Furthermore, the study showed that during the first 6 months after the study period, omega-3 had no greater efficacy on hot flashes than the placebo. This means that omega-3 supplementation has not delayed effect and exerts beneficial effect during it is consumption.

Although, in comparison with hormone therapy, omega-3 has lower potency but regard to very few side effects and positive effect on cardiovascular health including lowering triglyceride levels, reduction of blood pressure levels and stabilizing the atherosclerotic plaques (Rizos and Elisaf, 2013), it might be useful in certain conditions such as contraindications to estrogen therapy.

CONCLUSION

Omega-3 supplements may be used effectively for reduction of severity of post-menopausal hot flashes.

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