

Effect of Eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA) Supplementation on Hot Flashes in Menopausal Women: A Randomized, Double - Blind, Placebo- Controlled Clinical Trial

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Abstract: Background: Hot Flash is one of the compliance that impact on quality of life in menopausal women. This study investigated the effects of Eicosapentaenoic acid (EPA), and Docosahexaenoic acid (DHA) fatty acid supplementation on Hot Flashes in menopausal women. **Materials and Methods:** This is a Randomised, Double-Blind, Placebo- Controlled Clinical Trial study, on 83 menopause Women between 45-60 years old that had Inclusion criteria, and were randomly assigned to clinical group Ecosanoids or control group (placebo). Capsules of containing 300 mg (EPA) and (DHA) or placebo were prescribed to the participants for eight weeks one time per day. Of the 83 patients enrolled, 68 completed the study (Eicosanoid supplement, n=34; placebo; n = 34). Data collection method was demographic questionnaire, diary self report and food frequency questionnaire (FFQ). Data were analyzed by spss18: T tests, Chi-squared, Friedman and Mann-Whitney tests. **Results:** After 8 weeks intervention, There was significant difference HF frequency (P=0.003) between two groups. There was no significant difference in HF intensity between two groups (P=0.2) but it was significant reduction in intensity within two groups (P=0.003). **Conclusions** Eicosapentaenoic acid (EPA), and Docosahexaenoic acid (DHA) Supplementation affected on reduction of HF frequency and intensity, without significant difference on severity of HF.

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1. Introduction

Menopause is natural stage in every woman's life that the 55-48 age begins. This phase interrupt ovulation, menstruation, fertility decline, then cut, instability, mental health symptoms, anxiety, and depression that accompanies the meantime, hot flashes are the most common (1).

The main symptom is hot flashes during hot flushes women and more women are affected to varying degrees. The term "hot flushes" the sudden onset of a red cross on the scalp, neck and chest with

a feeling of intense heat with sweating bodies and sometimes extreme ends for a while (2).

The prevalence of symptoms at different studies, 75-18% of American women over age 50 reported that 75%, China 21%, Japan 18% (3).

Flushing mechanism, followed by disorders related to estrogen deficiency of neurotransmitters such as noradrenergic and path, which leads to a direct effect on the hypothalamus heat and hot flushes or night's, sweats (2). This can disrupt feel good and be healthy labor and sexual

activity and enjoyment of life and quality of life impact (4).

Although therapy, hormone therapy, estrogen alone or estrogen plus, due to side effects such as breast cancer risk in estrogen replacement Consumers (5), breast tenderness, bloating and depression in consumer PR (6), and hormones, many women either can not or do not want this treatment to use, so therapies such as alpha-2 adrenergic, dopamine antagonists such as Phenobarbital, Bromocriptine and naloxone orally, vitamin E, K supplements, minerals, alkaloids Belladonna with housing mild or antidepressants such as venlafaxine and Isoflavones or phytoestrogens such as soy, black etc. (6,5), various studies have been used to reduce or control vasomotor symptoms or complications, but have or seek answers Relative been treated. Therefore still need to investigate treatments that can reduce symptoms and fewer complications exist.

Eicosapentanoic Acid (EPA) and Docosahexaenoic Acid (DHA) is an essential fatty included as approved by the Food America Food and Drug Administration (FDA) is available to an approved Ministry of Health and Medical Education in Iran and the pharmacy capsule form a Grammy fish oil brand (Maxepa) and made from fish No mercury is (7) and adverse events specifically stated are not, and in many foodstuffs such as Fish, grains, vegetables, nuts, flax seed, and so on.

According to the mechanism of vasomotor symptoms seem to be any factor that noradrenergic and serotonergic influence on trails will be able to improve vasomotor symptoms (3).

Eicosapentanoic effect on the nervous system by touching the wall Eicosapentanoic neurons correct functioning and proper secretion of neurotransmitter production and balance amount will be reduced hot flashes (8, 9). Neurotransmitters central regulation of hypothalamic temperature seems to be the main cause of hot flashes is directly involved (3).

Studies have shown that the application successfully on hot flashes, such as the study of Lucas et al (10) studied in middle-aged women with mild and moderate depression and colleagues (11), but appears to be controlled clinical studies, not enough controlled clinical studies indicate that the increase in life expectancy in women after menopause and lifetime serving one-third of the complications and difficulties of this era, to improve the quality of life more attention.

Supplementation with omega-3 fatty acids medicine in the health field, is a special place, therefore, to determine the effects on hot flashes in postmenopausal women, the research on the referral

health centers in Zanjan University of Medical Sciences from 2010-2011 was performed.

Material and Methods

The study was double-blind, randomized controlled clinical trial. Population 60-45 years old, 83 women referred to health centers in Zanjan, the plaintiff and willing to treat hot flashes were formed. After obtaining informed consent from subjects who met inclusion criteria for the study were divided into groups randomly using a randomized clinical trial sample size based on a statistical test where alpha 0.05 and can test 80 with including a 10 percent drop, the total number of 70 samples taken, were selected. Inclusion criteria included: Iran, literate, eldest aged 45 to 60 years, cessation of menses for 12 months or more, or less than 12 months, with serum FSH greater than 40 IU and LH levels greater than 30 international units, at least 2 hot flashes per day (13 and 12), no known physical and mental diseases, Such as depression, diabetes, cardiovascular disease, hypertension, high cholesterol, thyroid disease, liver disease, blood disorders, cancer, digestive diseases, particularly, reflux, not using hormone therapy, anticoagulant medications, sedatives, antidepressants, anticonvulsants, lowering hypertension, agonists like clonidine, not using supplements such as soy, black, linseed, evening primrose oil and vitamin E. and do not use more than 2 fish per week. Exclusion criteria included the need for medical treatments, lack of proper use of drugs or placebo and unwillingness to continue the study.

The tool gathers information, demographic information - social and Obstetrics and Gynecology, daily registration forms registration number and severity of drug and placebo, food frequency questionnaire (FFQ), the content validity and test-retest and Cronbach's alpha Validity and reliability. Measurements of symptom severity using the proposed measure heater and colleagues (14), who were mild, moderate, severe had been considered. For qualitative variables into quantitative variables, severity of hot flashes, a slight 1 rating, average rating, 2 and 3 were given a severe rating.

For those who were enrolled in the study, the initial questionnaire was completed cards then they were asked to record the number and severity of hot flashes per day for 2 weeks to complete and After completing cards, daily capsules of 300 mg contains 120 mg acid (EPA) and 180 mg acid (DHA), for groups capsule placebo containing paraffin oral non-absorbed, for controls, day number 8 weeks was administered. During the study, participants were asked to record the number and severity of symptoms on daily cards and medication or placebo in the form and to report any side effects.

Methods of data analysis using independent and paired t-test, Friedman, Mann-Whitney, chi-square through SPSS software, version 18 was the minimum acceptable level of significance, 0.05 was considered. Finally, a total of 83 patients, only 68 patients (34 patients in each group) completed the study. 2 patients in group 1 were placebo therapies failed due to severe hot flashes and respectively third and fourth weeks of the study and were referred to a specialist. 12 subjects due to lack of proper use of capsules, by the researcher were excluded from statistical analysis. Individual characteristics and social and obstetric conditions in Table 1 are presented. Both groups of variables confounders such as age, body mass index (BMI), marital status, occupation, education, income, physical activity equal to or more than 3 times a week (3) the distance from the last menstrual interval starts flushing, age at menarche, number of pregnancies and abortions, number of live and dead possible time, congestion and possible actions to improve the stenosis (table 2) and from foods with no significant difference (Table 3). State the number and severity of

hot flushes per treatment group in Table 4 and Figure (1) is presented. Both groups had no significant differences in the number and severity before treatment.

Comparison between the groups in mean number of hot flashes in two weeks (first to eighth weeks) was compared between the two groups was significant from the fifth week ($p=0.04$). In relation to the severity of hot flashes (Figure 1) in the comparison between groups, the difference between the two groups was not significantly different in any of the weeks. However, this difference was significant within group comparison.

Additionally, the following measurements were taken, side effects of medication group, 2 had an upset stomach and obesity was reported by the placebo group, no complication was encountered. Well in studies performed to determine the number of capsules consumed and how to use it regular or irregular groups were not statistically different ($p=0.9$) comparison between the two groups was significantly higher treatment satisfaction ($p<0.001$).

Table 1: Characteristics of subjects attending outpatient clinics in Zanjan University of Medical Sciences in 2010-2011

Group Variable	Eicosanoid n=34 Mean(SD)	Placebo n=34 Mean(SD)	P
Age (years)	52.15 (3.03)	51.09 (2.84)	0.14
BMI (Kg/m)	26.02 (3.77)	26.82 (2.67)	0.37
last menstrual length (Years)	2.65 (2.34)	2.73 (2.53)	0.95
Start flushing interval (years)	2.66 (2.58)	2.54 (2.3)	0.9
Parity	4.32 (2.41)	3.56 (1.71)	0.14

Table 2: Frequency of time and effort to improve hot flashes in menopausal women referred to outpatient clinics in Zanjan University of Medical Sciences, 2010-2011

Group Variable	Eicosanoid n=34 Mean(SD)	Placebo n=34 Mean(SD)	S.D.
Flushing time			
Day	16 (47.1%)	16 (47.1%)	0.91
Night	4 (11.8%)	3 (8.8%)	0.91
Day & Night	14 (41.1%)	15 (44.1%)	0.91
hot flashes treatment			
Yes	7 (20.6%)	9 (26.5%)	0.57
No	27 (79.4%)	25 (73.5%)	0.57

Table 3 Mean and standard deviation of the daily intake of food items in the third period Eicosanoid before, middle and end of the study in postmenopausal women with hot flashes who were referred to outpatient clinics in Zanjan University of Medical Sciences, 2010-2011

Group Variable	Eicosanoid n=34 Mean(SD)	Placebo n=34 Mean(SD)	S.D.
Eicosanoid amount of food intake (grams per day)			
EPA,DHA	0.68 ± 0.64 0.155 ± 0.146	0.68 ± 0.35 0.155 ± 0.079	0.96
Middle of the study (Week 4)			
EPA,DHA	0.72 ± 0.53 0.164 ± 0.12	0.76 ± 0.48 0.173 ± 0.11	0.79
End of the study (week 8)			
EPA, DHA	0.66 ± 0.54 0.151 ± 0.123	0.64 ± 0.51 0.146 ± 0.116	0.87

Table 4 compares the change in the number of hot flashes in 2 Eicosanoid and placebo groups, before and after intervention in postmenopausal women with hot flashes who were referred to outpatient clinics in Zanjan University of Medical Sciences in 2010-2011

Group Variable	Eicosanoid n=34 Mean(SD)	Placebo n=34 Mean(SD)	P
The number of hot flashes daily pre intervention	9.37 (7.05)	9.19 (5.45)	0.71
The number of hot flashes daily by the end of intervention	3.71 (5.9)	7.13 (5.96)	0.003
The comparison group	0.001	0.001	

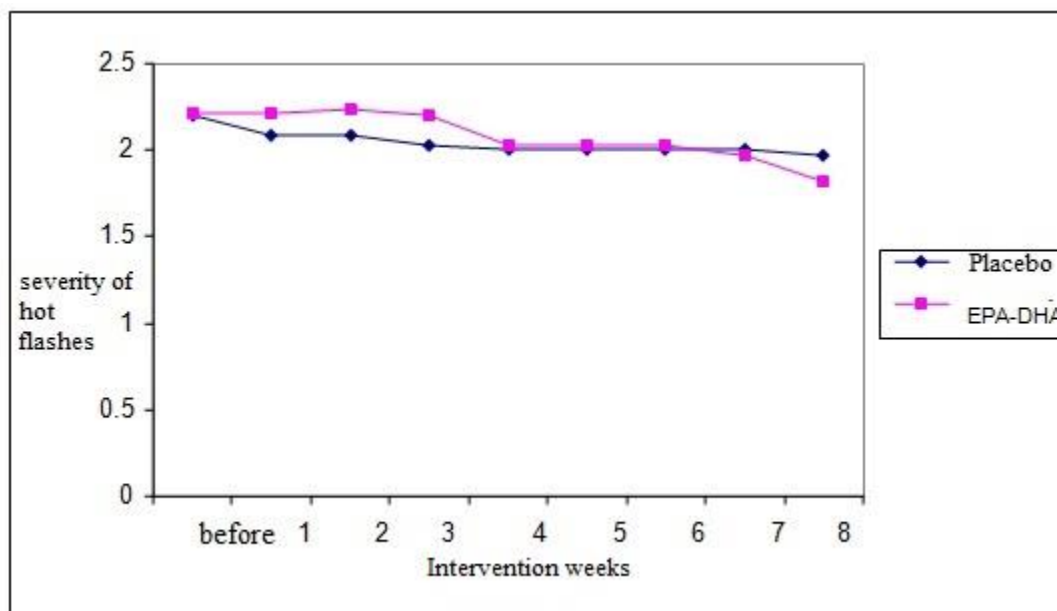


Chart 1: Comparison of changes in severity Eicosanoid and placebo groups, separated before treatment and one to eight weeks of treatment in postmenopausal women with hot flashes attending outpatient clinics in Zanjan University of Medical Sciences in 2010-2011

Discussion

The results showed that the mean number of hot flashes compared with pre-intervention and post-intervention between the two groups was significantly lower in the placebo Eicosanoid. So it seems Eicosanoid of EPA-DHA fatty acid is able to reduce the number of hot flashes in postmenopausal women. Based on test severity of hot flashes after the intervention compared with before the intervention and placebo was not significant between the two groups Eicosanoid, although the difference between the groups was significant. Our findings with the results of Lucas et al (10) investigated the effect of supplementation among women in Eicosanoid correspond. In this study, after 8 weeks, the mean number of daily hot flashes compared between the groups was significant. The study and colleagues (11) as compared to the combined effect of soy isoflavones on hot flashes in postmenopausal women without Eicosanoid, decrease in mean number of hot flashes after treatment with isoflavones combined with Eicosanoid 38.5% and Eicosanoid it without isoflavones reduction of 20% was reported. This decrease was significant for the comparison between groups, which is consistent with our study.

Linseed Flaxseed, isoflavones and a great source of essential fatty acids, linolenic acid, which handles fatty acids EPA-DHA is a type of Eicosanoid, (15, 16). The plant has 35% oil, 55 per cent of the fatty acids EPA-DHA Eicosanoid and 7.2 grams of flaxseed equal to 1 g of fish oil (17).

Dodean and colleagues (12) the effects of flaxseed supplementation on the severity of the significant within groups and between groups were insignificant, which was consistent with our study. The and colleagues (18) in a pilot study on the effect of flaxseed in 29 postmenopausal women with menopausal symptoms of hot flushes per week 14 60% decrease in hot flashes and loss of 57 percent of the total score (frequency and intensity) announced flushing his study of the control group.

Venlafaxine than those blockers selective reuptake serotonin reuptake inhibitors SSRIs, to treat depression is used, which is thought to be perhaps through interference with path neurotransmitter of the central heating hypothyroidism. Thalamic influence (3), ie, the direction of effect of fatty Eicosanoid the EPA-DHA is the same. Evans and colleagues (12) showed the effect of venlafaxine hydrochloride on hot flashes in postmenopausal women, Venlafaxine hydrochloride can reduce the severity of hot flashes compared to the group comparisons between groups were not significant, but this effect is consistent with our findings.

Neurotransmitters in the central regulation of the hypothalamic temperature seems to be the main cause of hot flashes is directly involved and

polyunsaturated fatty acids (Eicosanoid), balances the production of neurotransmitters that Eicosanoid perhaps the most important mechanism in menopausal symptoms (3). The strengths of our study are similar in the 2 groups in terms of daily food intake of fatty acids Eicosanoid, using food frequency questionnaires, followed up by regular sampling and examination by the physician and the limitations of this study, the problems created by the lack of placebo capsules daily use by some units due to the coarseness of the capsule (difficulty swallowing), who were forced to leave.

Conclusion:

Our research showed Eicosanoid (EPA, DHA) can reduce hot flashes in postmenopausal women. Due to the large population of adult, menopause problems from the standpoint of public health importance and the need for an appropriate solution and harmless felt important. Today, the approach is complementary and alternative medicine, Eicosanoid as supplements can be a good alternative in the treatment of hot flashes. Also according to the standard treatment of the sources of Obstetrics and Gynecology (5, 6, 19), hormone therapy is mentioned, the study compared the effect of hormone therapy in women who require hormone therapy Eicosanoid are recommended.

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