

# Evaluation of the effect of oral vitamin E and omega 3 supplement on postmenopausal hot flashes

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## Abstract

**Background and objectives:** Hot flashes and its complications are among the most annoying postmenopausal symptoms affecting the quality of life and mental state and mood. Anti-oxidants play an important role in the prevention and control of menopausal complications. In this study, the effect of oral vitamin E and omega 3 supplements on the hot flashes of postmenopausal women is evaluated. **Method:** This quasi-experimental interventional study was conducted on 80 postmenopausal women referring to gynecology and obstetrics clinic of Tamin-e-Ejtemaei Hospital of Zahedan in 2019. Patients I intervention group received and 850 mg capsule containing antioxidant supplement including omega 3 and Vitamin E. Demographic information questionnaires, personal information forms, and hot flashes severity weekly recording forms were used in this study for data collections. SPSS ver. 26 and chi-square, independent and paired T-test were used for data analysis and 0.05 was considered as significance level. **Results:** One week before the intervention, no significant difference in hot flashes severity was observed between the two groups. However, one week after the intervention, the hot flashes severity was significantly different between the two groups which further improved in the treatment period afterwards ( $P \leq 0.043$ ). **Conclusion:** Findings of this study suggests that vitamin E and omega 3 supplement therapy is effective in the prevention of postmenopausal complications especially hot flashes severity and it can be used as a complementary and alternative medical methods in reducing menopause complications.

**Keywords:** Menopause, Hot flashes, Oral Supplement, Omega 3, Vitamin

## INTRODUCTION

Women account for half of the population and most of them reach 65 years, i.e., they spent a third of their lifespan as postmenopausal women [1]. Menopause is defined as a persistent cessation of menstruation during which the level of FSH elevates and estrogen and progesterone declines. The most common postmenopausal complication is hot flashes [2]. These symptoms last 1-2 years in most women and sometimes lasts 10 years or more and disturbs daily activities, emotional imbalance, and sleep disorder. This symptom is reported in different studies on women above 45 years [1]. Postmenopausal hot flashes prevalence ranges from 0 to 80 percent depending on different factors including cultural, ethnical, and climate-related factors [2, 3]. Menopause is a physiologic period of a women's life. In this stage, some symptoms such as cessation of a reproductive period, vasomotor instability, facial and upper trunk erythema due to vascular dilation, psychological symptoms, increased blood flow, anxiety, and depression [4]. Elevated heartbeat, decreased blood pressure and cerebral blood flow increases the peripheral blood flow [5]. Estrogen deficiency and its associated disorders regarding neurotransmitter pathways such as noradrenergic and serotonergic pathways directly

affect temperature regulatory center in the hypothalamus and consequently results in hot flashes and night sweats [6]. Alternative therapy using estrogen leads to hot flashes in postmenopausal hot flashes in short term. Though, some evidences show that HRT increases the risk of uterine and breast cancer [6]. Also, unsaturated fatty acids balance the neurotransmitter and any factor which affects noradrenergic and serotonergic pathways, may improve the hot flashes

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symptom <sup>[7]</sup>. Omega 3 supplement, as an unsaturated fatty acid, balances serotonergic pathway and improves hot flashes by inhibiting abrupt changes in the temperature regulatory center in the hypothalamus <sup>[8]</sup>.

Moghadam *et al.* (2012) showed that omega 3 reduces the frequency of hot flashes and frequency and severity of night sweats, though it does not affect the severity of hot flashes <sup>[9]</sup>. Also, Jahdi *et al.* (2018) found in their study there is a significant difference between the effect of omega 3, folic acid, and placebo on the severity and duration and frequency of hot flashes, i.e. omega 3 and folic acid significantly reduces the severity and frequency of hot flashes <sup>[10]</sup>. Similarly, Ziaei *et al.* (2007) showed that vitamin E affects the frequency and severity of hot flashes <sup>[11]</sup>. Honarjo *et al.* (2015), in their study on the effect of antioxidant oral supplement (Vitamin E and Omega 3) on the frequency and severity of hot flashes, concluded that there is a significant relationship between the frequency of hot flashes ( $P=0.002$ ) and mean improvement in the severity of hot flashes ( $P=0.003$ ) in intervention and control groups.

There are controversial studies on the effect of vitamin E and omega 3 oral supplement on the severity of hot flashes which shows that the antioxidant effect of omega 3 and vitamin E on the reduction of the frequency and severity of postmenopausal hot flashes <sup>[12, 13]</sup>. Ciappolino *et al.* (2018) systematic review proved that omega 3 is effective on reducing the postmenopausal complications especially the frequency and severity of hot flashes <sup>[14]</sup>. Also, in P. Freeman *et al.* study in 2011 on the evaluation of the effect of omega 3 supplement therapy on the reduction of menopausal complications in 19 women for 8 weeks, it was reported that oral omega 3 supplement is effective in the reduction of postmenopausal complications, especially depression and hot flashes <sup>[15]</sup>. D Reed *et al.* performed a study on 355 postmenopausal women in 2014 and showed that oral omega 3 supplement derived from fish oil can significantly reduce the frequency and severity of hot flashes <sup>[16]</sup>. On the other hand, Parnan Emamverdikhani *et al.* study (2016) suggested that vitamin E supplement therapy relatively improves postmenopausal complications <sup>[17]</sup>. Also, B. Doshi *et al.* demonstrated in their study in 2013 that antioxidants, including Vitamin E plays role in reduction of postmenopausal complications such as hot flashes <sup>[18]</sup>.

As a result, considering the research priority of health improvement, postmenopausal care, and spending a third of life in the postmenopausal period with its known complications, it is tried in this study to assess the effect of Omega 3 and Vitamin E supplements on hot flashes.

## METHODS AND MATERIALS

This quasi-experimental interventional study was conducted on postmenopausal women referring to gynecology and obstetrics clinic of Tamin-e-Ejtemaei Hospital of Zahedan in 2019. The participants were selected by simple random sampling method. A written informed consent was taken from

all participants and they were informed how to take omega 3 and vitamin E supplements. They were informed that they can leave the study at any time. Based on a pilot study, sample size was calculated to be 80 (40 participants in the intervention group and 40 participants in the control group). Study inclusion criteria included: a minimum of 4 episodes of mild, moderate, or severe hot flashes experienced in 24 hours, 6 months to 3 years after menopause, aging 45-55, willingness to participate in the study, lack of HRT, lack of vaginal bleeding with unknown origin. On the other hand, vaginal bleeding, special diseases, unnatural menopause due to radiation or salpingo-oophorectomy, active liver or kidney disease, special diet, or opium use during study period.

Samples were divided into intervention and control groups. Participants in the intervention group received an 850 mg capsule counting antioxidant supplement (Omega 3 and Vitamin E). Hot flashes severity was measured in both groups before intervention, at the end of first week, second week, third week, first month, second month, and third month.

Data collection tools included a demographic information questionnaire (age, BMI, educational level, marital status, economic status, age at first and last menstruation, gravid, occupational status, longest duration of hot flashes, and mean number of daily hot flashes). Hot flashes measurement tool was a part of the scale developed by FDA which was used by Newton *et al.* <sup>[19]</sup>. Validity of this scale was approved by 8 faculty member of Zahedan University of Medical Sciences. Also, the reliability of this scale was acceptable with a Cronbach's alpha of 0.9. Data was analyzed using SPSS ver. 22. Descriptive statistics (frequency, frequency percentage, mean, standard deviation) were used for data analysis and inferential statistics (chi-square, independent and paired T-test) were used to determine statistical significance. Significance level was set at 0.05.

## RESULTS

Mean age of participants were  $49.587 \pm 4.272$  in the intervention group and  $50.175 \pm 4.924$  in the control group which were not significantly different. 59 (73.8%) participants were married, 29 (36.3%) were unlettered, 58 (72.5%) were housewife, and 43 (53.8%) of them had a low economic status. Mean BMI was  $27.660 \pm 1.392$  kg/m<sup>2</sup> in the intervention group and  $27.867 \pm 1.124$  kg/m<sup>2</sup> in control group, mean age of last menstruation was  $46.7 \pm 3.375$  years in the intervention group and  $47.175 \pm 3.918$  years in control group, mean age of onset of hot flashes was  $45.9 \pm 3.477$  years in the intervention group and  $46.65 \pm 3.752$  years in the control group, all of which did not show any significant difference between the two groups.

Highest hot flashes frequency was 5-10 times in the intervention group and more than 10 times in the control group which shows a significant difference in terms of hot flashes frequency between intervention and control group ( $P \leq 0.002$ ) (Table 1).

**Table 1:** Mean demographic characteristics of the subjects in the intervention and control groups

| Group                           |              | Omega 3 and Vitamin E | Control group    | P-value |
|---------------------------------|--------------|-----------------------|------------------|---------|
|                                 |              | supplement (N=40)     | (N=40)           |         |
|                                 |              | Number (percent)      | Number (Percent) |         |
| <b>Age</b>                      |              | 49.587 ± 4.272        | 50.175 ± 4.924   | 0.258*  |
| <b>BMI</b>                      |              | 27.66 ± 1.392         | 27.867 ± 1.124   | 0.466*  |
| <b>Age at last menstruation</b> |              | 46.7 ± 3.375          | 47.175 ± 3.918   | 0.123*  |
| <b>Age at first hot flashes</b> |              | 45.9 ± 3.477          | 46.65 ± 3.752    | 0.357*  |
| <b>Marital status</b>           | Single       | 11 (27.5%)            | 10 (25%)         | 0.799   |
|                                 | Married      | 29 (72.5%)            | 30 (75%)         |         |
| <b>Educational level</b>        | Unlettered   | 10 (25%)              | 19 (47.5%)       | 0.188   |
|                                 | Diploma      | 15 (37.5%)            | 12 (30%)         |         |
|                                 | BS           | 8 (20%)               | 4 (10%)          |         |
|                                 | MA or higher | 7 (17.5%)             | 5 (12.5%)        |         |
| <b>Economic status</b>          | Low          | 18 (45%)              | 25 (62.5%)       | 0.178   |
|                                 | Middle       | 16 (40%)              | 13 (32.5%)       |         |
|                                 | High         | 6 (15%)               | 2 (5.0%)         |         |
| <b>Occupational status</b>      | Housewife    | 31 (77.5%)            | 27 (67.5%)       | 0.317   |
|                                 | Employed     | 9 (22.5%)             | 13 (32.5%)       |         |
| <b>Number of hot flashes</b>    | 10 or more   | 13 (36.11%)           | 23 (63.8%)       | 0.002   |
|                                 | 5-10         | 16 (42.8%)            | 17 (47.2%)       |         |
|                                 | 4 or less    | 9 (81.82%)            | 2 (18.18%)       |         |

ANOVA showed no significant difference in the mean hot flashes severity one week before the intervention between intervention and control groups ( $P \geq 0.649$ ), while a significant difference was reported one week after Vitamin E and omega 3 oral supplement therapy ( $P \leq 0.043$ ) which was more prominent later and hot flashes severity had a descending trend during the treatment course.

**Table 2:** Mean intensity of hot flashes per week before treatment and different weeks of treatment in the intervention group

| Group Time                            | Omega 3 and Vitamin E | Control group | P-value |
|---------------------------------------|-----------------------|---------------|---------|
|                                       | supplement (N=40)     | (N=40)        |         |
|                                       | Mean ± SD             | Mean ± SD     |         |
| <b>Before intervention</b>            | 2.075 ± 0.572         | 2.15 ± 0.863  | 0.649*  |
| <b>One week after intervention</b>    | 2.125 ± 0.563         | 2.45 ± 0.597  | 0.043*  |
| <b>Two weeks after intervention</b>   | 2.35 ± 0.733          | 1.925 ± 0.764 | 0.013*  |
| <b>Three weeks after intervention</b> | 1.875 ± 0.647         | 2.275 ± 0.598 | 0.005*  |
| <b>One month after intervention</b>   | 2.05 ± 0.677          | 2.35 ± 0.662  | 0.049*  |

|  |              |               |        |
|--|--------------|---------------|--------|
| <b>Two months after intervention</b>   | 2.04 ± 0.679 | 2.3 ± 0.723   | 0.052* |
| <b>Three months after intervention</b> | 2.05 ± 0.749 | 2.425 ± 0.635 | 0.018* |

## DISCUSSION

In this study, mean hot flashes severity decreased after receiving 850 mg Omega 3 and Vitamin E supplement for 2 months which may show the effect of antioxidant supplements in improvement of postmenopausal complications including hot flashes severity.

P. Freeman et al. conducted a study to evaluate the effect of omega 3 supplement therapy in relieving postmenopausal depression and hot flashes. They concluded that omega 3 supplement therapy is helpful in reducing depression and hot flashes in the postmenopausal women [15]. D. Reed et al. conducted a study in 2014 to evaluate the effect of yoga, exercises, and omega 3 supplement therapy in postmenopausal women with a mean age of 57.4 years. Results of their study suggested that doing exercises is helpful in reducing menopausal complications, yet omega 3 supplement therapy in further effective in this regard, especially in the case of hot flashes [16]. Cohen et al. (2014) evaluated the effect of 12-week omega 3 oral supplement therapy in reducing postmenopausal vasomotor symptoms. They concluded that supplement therapy with fish oil derived

omega 3 effectively reduces the severity and frequency of hot flashes [20]. Results of Mohammady *et al.* study in 2018 indicated that oral omega 3 supplement in postmenopausal women aging 51 to 54 years exerts significant effects in reducing postmenopausal vasomotor symptoms such as hot flashes [21]. Ciappolino *et al.* in their study aimed to assess the effect of omega 3 fatty acids in the reduction of depression and hot flashes symptoms of postmenopausal women concluded that the effectiveness of oral supplement requires further investigations [14].

Rezasoltani *et al.* (2018) conducted a study on the effectiveness of vitamin E supplement therapy with 400 U daily for 4 weeks of 41 elderly women with menopausal complications; they concluded that vitamin E oral supplement is highly effective in reducing postmenopausal complications especially severity and frequency of hot flashes [22]. Parnan Emanverdikhani *et al.* (2016) performed a study aimed to evaluate the effect of vitamin E supplement therapy in reducing vaginal atrophy in postmenopausal women; they stated that 100 U vitamin E daily for 12 weeks relatively reduces vaginal atrophy and improves postmenopausal complications such as severity and frequency of hot flashes [17]. B. Doshi *et al.* systematic review (2013) demonstrated that oxidative stress is involved in formation and exacerbation of postmenopausal complications. On the other hand, antioxidants, such as Vitamin E oral supplement significantly improves these symptoms. As a result, antioxidant supplement therapy is effective in relieving postmenopausal complications such as pain and hot flashes [18].

## CONCLUSION

Hot flashes is among the most common postmenopausal complications and not only hormone replacement therapy is not accepted by most women, but also it even may lead to some adverse effects; thus, HRT is controversy for postmenopausal hot flashes. Results of this study suggest that vitamin E and omega 3 supplement therapy reduces postmenopausal complications especially hot flashes. Consequently, it is suggested that further studies be conducted on the role of different oral antioxidant supplements in reducing the postmenopausal complications.

## REFERENCES

- Ghasemi A, Haghighi L. Omega-3 Fatty Supplementation in Postmenopausal Hot Flashes: A Randomized Clinical Trial. *J Biological Sciences* 2013; 8(2): 46-49.
- Avis NE, Crawford SL, Greendale G, Bromberger JT, Everson-Rose SA, Gold EB, *et al.* Duration of menopausal vasomotor symptoms over the menopause transition. *JAMA internal medicine.* 2015;175(4):531-9.
- Freeman E, Sherif K. Prevalence of hot flushes and night sweats around the world: a systematic review. *review. Climacteric.* 2007;10(3):197-214.
- Wier E. Hot flash. *Canadian Medical Association Journal.* 2004;170(1):1-3.
- Lucas RA, Ganio MS, Pearson J, Crandall CG. Brain blood flow and cardiovascular responses to hot flashes in postmenopausal women. *Menopause (New York, NY).* 2013;20(3).
- Rossmannith WG, Ruebberdt W. What causes hot flushes? The neuroendocrine origin of vasomotor symptoms in the menopause. *Gynecological Endocrinology.* 2009;25(5):303-14.
- Utian WH. Psychosocial and socioeconomic burden of vasomotor symptoms in menopause: a comprehensive review. *Health and Quality of Life outcomes.* 2005;3(1):47.
- Lucas M, Asselin G, Mérette C, Poulin M-J, Dodin S. Effects of ethyl-eicosapentaenoic acid omega-3 fatty acid supplementation on hot flashes and quality of life among middleaged women: a double-blind, placebo-controlled, randomized clinical trial. *Menopause.* 2009;16(2):357-66.
- Moghadam R, Azgoli G, Molaie B, Hajifaraji M, Sori H, Ghanati K. Effect of Omega3 on vasomotor in postmenopausal women. *J of Arak UniMedSci* 2012; 15(1): 116-26. [In Persian].
- Jahdi F, Chamani M, Neisani Samani L, Haghani H, Mojab F. Comparing the Effect of Omega3 and that of Folic Acid on Menopause-Related Hot Flashes. *Complementary Medicine Journal;* 2018.28(3): 2331-2353.
- Ziaei S, Kazemnejad A, Zareai M. The effect of vitamin E on hot flashes in menopausal women. *Gynecologic and obstetric investigation* 2007; 64(4): 204-7.
- Lucas M, Genevieve A, cantal M, Marie JP, Sylvie D. Effect of ethyl-eicosapentaenoic acid omega3 fatty acid supplementation on hot flashes and quality of life among middle aged women. *The Journal of the North American menopause society* 2009; 16(2): 357-66.
- Moghadam R, Azgoli G, Molaie B, Hajifaraji M, Sori H, Ghanati K. Effect of Omega3 on vasomotor in postmenopausal women. *J of Arak UniMedSci.*
- Ciappolino V, Mazzocchi A, Enrico P, Syren ML, Delvecchio G, Agostoni C, *et al.* N-3 Polyunsaturated Fatty Acids in Menopausal Transition: A Systematic Review of Depressive and Cognitive Disorders with Accompanying Vasomotor Symptoms. *Int J Mol Sci.* 2018;19(7).
- Freeman MP, Hibbeln JR, Silver M, Hirschberg AM, Wang B, Yule AM, *et al.* Omega-3 fatty acids for major depressive disorder associated with the menopausal transition: a preliminary open trial. *Menopause.* 2011;18(3):279-84.
- Reed SD, Guthrie KA, Newton KM, Anderson GL, Booth-LaForce C, Caan B, *et al.* Menopausal quality of life: RCT of yoga, exercise, and omega-3 supplements. *Am J Obstet Gynecol.* 2014;210(3):244 e1-11.
- Parnan Emanverdikhani A, Golmakani N, Tabassi SA, Hassanzadeh M, Sharifi N, Shakeri MT. A survey of the therapeutic effects of Vitamin E suppositories on vaginal atrophy in postmenopausal women. *Iran J Nurs Midwifery Res.* 2016;21(5):475-81.
- Doshi SB, Agarwal A. The role of oxidative stress in menopause. *J Midlife Health.* 2013;4(3):140-6.
- Newton KM, Reed SD, LaCroix AZ, Grothaus LC, Ehrlich K, Guiltinan J. Treatment of vasomotor symptoms of menopause with black cohosh, multibotanicals, soy, hormone therapy, or placebo: a randomized trial. *Annals of internal medicine.* 2006;145(12):869-79.
- Cohen LS, Joffe H, Guthrie KA, Ensrud KE, Freeman M, Carpenter JS, *et al.* Efficacy of omega-3 for vasomotor symptoms treatment: a randomized controlled trial. *Menopause.* 2014;21(4):347-54.
- Mohammady M, Janani L, Jahanfar S, Mousavi MS. Effect of omega-3 supplements on vasomotor symptoms in menopausal women: A systematic review and meta-analysis. *Eur J Obstet Gynecol Reprod Biol.* 2018;228:295-302.
- Rezasoltani P, Elliyoun N, Ziaie T, Kazemnezhad Leyli E, Kazemi Aski S, Sobhani A. Effect of Vitamin E Supplementation on Plasma Nitric Oxide in Menopausal Women with Hot Flashes: A Cross-Over, Randomized Clinical Trial. *Iranian Red Crescent Medical Journal.* 2018;20(9).