# Pilot Study to Evaluate the Effect of Vitamin E Supplementation on the Menopause Rating Scale Scores among Perimenopausal Women

**Marya Ahsan[1], Ayaz Khurram Mallick[2], Raj Ranjan Prasad[3]**


## ABSTRACT

**Introduction:** Post- Women's Health Initiative trial, Hormone Replacement Therapy (HRT) has fallen into disrepute. Other alternative therapies are being explored for the management of menopausal symptoms. We conducted a pilot study to evaluate the efficacy of vitamin E in the management of menopausal symptoms among perimenopausal women.

**Material and Methods:** A prospective randomized placebo-controlled single-blinded study was conducted. Thirty perimenopausal women aged between 35-50 years, who declined hormone replacement therapy for menopausal complaints were enrolled for the study. The selected patients were randomly distributed into two groups A and B. Group A (n=15) was given 800 IU of vitamin E per day in two divided doses for a period of three months while group B (n=15) was given placebo (soft gel capsules) orally once daily for three months. The Menopause Rating Scale (MRS) was used to evaluate the response to treatment. Paired t-test and independent t-test were applied for statistical analysis.

**Results:** Among the vitamin E administered group, the somatic and psychological scores improved by 22.44% ($p<0.05$) and 14.63% ($p<0.01$) respectively. Somatic and psychological scores also improved significantly among those on placebo treatment. The urogenital subscale scores did not improve among both the groups. Though the total scores improved by 18.34% ($p<0.05$) among vitamin E group, it was not significantly different from the 13.64% ($p<0.05$) total score improvement seen in the placebo group.

**Conclusion:** Vitamin E was not superior to placebo treatment for management of menopausal symptoms.


**Keywords:** Perimenopause, Vitamin E, MRS

## INTRODUCTION

Menopause, from the Greek word 'menos' meaning month and 'pausis' meaning cessation is defined as the last menstrual period. Though the diagnosis of menopause can be definitely made only retrospectively after one year of amenorrhea, the physiological changes culminating in the final menstrual period (FMP) begin at least a decade prior to it and continue even beyond the FMP.[1] This period of a woman's life is associated with distressing clinical problems such as hot flushes, night sweats, insomnia, mood swings, fatigue and urogenital complains.[1] Though a natural process, many women prefer not to bear them as part of their routine lives.[2]

The menopausal complains are most effectively treated by hormone replacement therapy (HRT). However, post Women's Health Initiative trial, HRT has fallen into disrepute for increasing the risk of breast cancer and not showing any beneficial effect on bone health or cardiovascular disease.[3,4] As a consequence of the confusions surrounding HRT, many women decline HRT and prefer alternative therapies. Prescribing practices of gynecologists have also largely been affected and they too are reluctant in prescribing HRT for menopause related symptoms.[5-7]

Numerous reports in medical literature and media have explored the effectiveness of various non-hormonal agents such as SSRIs, evening primrose oil, gabapentin, ginseng, vitamin E, acupuncture and reflexology in reducing menopausal symptoms, particularly hot flushes.[8,9]

In view of this, we conducted a pilot study to evaluate the efficacy of high dose of vitamin E against placebo in the management of menopausal complains among perimenopausal women in North India.

## MATERIAL AND METHODS

The pilot study was conducted as a prospective single-blinded randomized controlled trial over a period of one year in the Gynecology OPD of a tertiary care hospital in North India. Institutional Ethical Committee clearance was taken for the study. Patients participating in the study gave informed consent. A total of 30 perimenopausal women, between the age of 35-50 years, who declined HRT for menopausal complaints were enrolled for the study. Both early and late perimenopausal women according to the Stages of Reproductive Aging Workshop (STRAW) +10 criteria were included. Patients with irregular menses without skipping cycles and more than seven days difference in length of consecutive cycles were classified as early perimenopausal while those with ammenorhoea for more than two months were classified as late perimenopausal.[10] Patients with undiagnosed vaginal bleeding, history of breast carcinoma or other malignancies, cardiac diseases, liver disorder, diabetes mellitus, altered lipid profile were excluded from the study. Patients who had received any hormonal treatment or soy-bean derived products in the previous 12 months for menopausal symptoms were excluded. Those on antiplatelets or anticoagulants were also not included.

The selected patients were randomly distributed in two groups A and B. Group A (n=15) was administered 800 IU vitamin E per day in two divided doses for a period of three months and group B (n=15) was given placebo (soft-gel capsules) orally

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twice daily for three months.

Patients were asked to fill a pre-tested questionnaire with sections A, B and C. Section A included socio-demographic data such as age, marital status, religion, education and occupational background. Detailed menstrual history was taken in section B. Section C included the English version of Menopausal Rating Scale (MRS) questionnaire for evaluating the menopausal symptoms.[11,12] In the MRS questionnaire 11 menopausal symptoms were graded from "0" (none) to "4" (very severe). Adding the scores of hot flushes, cardiac symptoms, sleep disturbances and rheumatic complains yielded the somatic subscale score. The psychological subscale score was obtained by adding scores of depression, irritability, anxiety and fatigue. Urogenital subscale score was obtained by adding scores given to symptoms of sexual dysfunction, bladder disturbance and vaginal dryness. Total score of the MRS questionnaire was obtained by adding scores of all the 11 symptoms.

The MRS questionnaire was administered to both the groups by face to face interview in the local language and responses were recorded at baseline i.e. before initiating the therapy and then after three months of therapy.

## STATISTICAL ANALYSIS

Validity of the MRS questionnaire was evaluated using chronbach's alpha. Paired t-test and independent t-test were applied to analyze the data using Statistical Package for Social Sciences (SPSS) software version 23.0 (SPSS Inc, Chicago, IL, USA). $P < 0.05$ was considered as cut-off value for significance.

## RESULTS

The average age of perimenopausal women in our study was 41.2 ± 1.51 years. The reliability analysis of the 11 item MRS questionnaire yielded a Cronbach's alpha 0.89 at baseline. As there was a drop rate of 23% and 23 patients out of 30 enrolled reported for follow up at three months. The total MRS score of group A (n=12) and B (n=11) were 20.50 (4.15) and 22.0 (5.60) respectively. The somatic, psychological and urogenital scores of both the groups were also comparable at baseline as illustrated in Figure 1.

As given in Table 1, after 3 months of treatment with vitamin E, group A (n=12) showed a 14.63% improvement in the total score of the MRS questionnaire ($P < 0.05$). The somatic subscale symptoms improved by 18.34% ($P < 0.05$) and psychological subscale symptom scores improved significantly by 22.44% ($P < 0.01$).

Patients of the placebo administered group (n=11) also showed a 13.64% improvement in the total MRS score ($P < 0.05$). The somatic scores and psychological scores improved by 20.54% ($p<0.05$) and 16.7% ($P < 0.01$) respectively. (Table 2)

There was no improvement in the urogenital subscale scores of both the groups. (Tables 1,2)

On comparing the MRS scores of group A and group B after three months of treatment, there was no significant difference between the groups with respect to total score, somatic subscale score, psychological subscale score or the urogenital subscale score as illustrated in Figure 2.

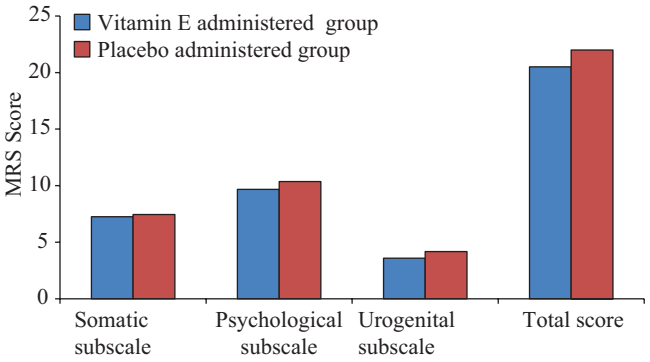


**Figure-1:** Baseline Menopause Rating Scale scores of group A (vitamin E administered, n=12) and group B (placebo administered, n=11).

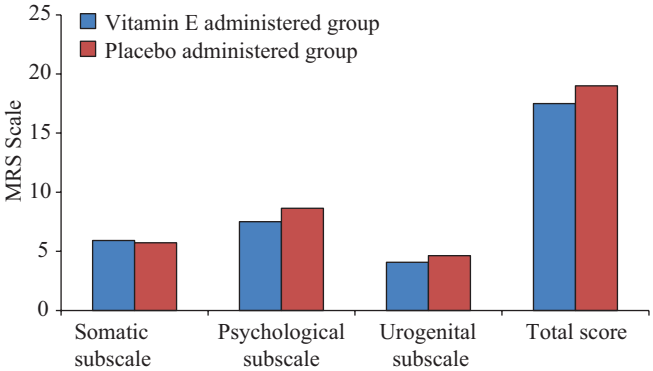


**Figure-2:** Menopause Rating Scale scores after 3 months of treatment of group A (vitamin E administered, n=12) and group B (placebo administered, n=11).

| | Scores before treatment | Scores three months after treatment | Absolute improvement | Percentage improvement |
|---|---|---|---|---|
| Total score | 20.50 (4.15) | 17.50 (4.72) | 3.00 (4.75)* | 14.63* |
| Somatic subscale | 7.25 (1.81) | 5.92 (1.68) | 1.33 (1.97)* | 18.34* |
| Psychological subscale | 9.67 (1.72) | 7.50 (2.07) | 2.17 (2.33)** | 22.44** |
| Urogenital subscale | 3.58 (1.38) | 4.08 (1.78) | -0.50 (1.45) | No improvement |

**Table-1:** MRS scores of perimenopausal women (n=15) on Vitamin E. (*=p<0.05, **=p<0.01)

| | Scores before treatment | Scores three months after treatment | Absolute improvement | Percentage improvement |
|---|---|---|---|---|
| Total Score | 22.00 (5.60) | 19.00 (4.60) | 3.00 (2.90)* | 13.64* |
| Somatic subscale | 7.45 (2.51) | 5.73 (1.95) | 1.53 (1.49)* | 20.54* |
| Psychological subscale | 10.36 (1.75) | 8.64 (1.50) | 1.73 (1.35)** | 16.70** |
| Urogenital subscale | 4.18 (1.72) | 4.64 (1.80) | -0.46 (0.52) | No improvement |

**Table-2:** MRS scores of perimenopausal women (n=15) on placebo. (*=p<0.05, **=p<0.01)

## DISCUSSION

Vitamin E (Tocopherol) is a fat soluble vitamin, present in many food products and is also available as dietary supplements. Sunflower oil, nuts, green leafy vegetables and fortified cereals are common sources of vitamin E. Being a naturally existing antioxidant, vitamin E plays a pivotal role in preventing lipid peroxidation.[13] Studies have shown encouraging reports of beneficial effects of vitamin E on the cognitive abilities, mental alertness and emotional stabilities in various forms of dementia specially in the elderly.[8,14,15]

This study was conducted to evaluate the efficacy of vitamin E for menopausal symptoms among perimenopausal women using the MRS scale. The MRS scale is composed of 11 items which covers three dimensions i.e. somatic, psychological and urogenital. In our study, the psychological subscale scores was the highest followed by the somatic subscale scores among both the groups as illustrated in Figure 1. The results were in line with studies done in other parts of India.[16-18]

Symptoms reported commonly by the perimenopausal women in our study were depression, irritability, anxiety and fatigue mostly ranging from moderate to severe grade thus yielding a high psychological subscale score. Large scale studies evaluating mood changes in perimenopausal women have found that the menopausal transition phase is associated with increased risk of depression.[19,20] After three months of treatment with vitamin E, there was an improvement by 22.44% in the psychological subscale scores ($p<0.01$). Though the improvement was statistically significant it was clinically not significant as the patients were not satisfied with the improvement. Patients in the placebo group also reported a 16.7% improvement in the psychological subscale score ($p<0.01$). The improvement seen in psychological symptoms among the vitamin E group was statistically not different from the placebo group in our study. This could be because the psychological symptoms are largely attributed to the fluctuations in the estrogen levels during the transition.[19,20] Moreover, oxidative damage is not important in the pathogenesis of psychological symptoms associated with menopause and hence similar effects were seen with both vitamin E and placebo. Besides fluctuating estrogen levels, apprehension towards menopause also contributes to depression and anxiety. Role of estrogens and its fluctuation has also been demonstrated to affect the cognitive abilities in these women.[21]

The etiology of hot flashes is not completely clear but is believed to result from the brain's response to decreasing estrogen levels. It has been hypothesized that a relative decrease in circulating estrogen levels alters the norepinephrine and serotonin levels, thus causing dysfunction of the thermoregulatory nucleus.[22] As the estrogen levels are fluctuating during the perimenopausal stage, the hot flashes are also more severe in this group.[16,23] Moderate to severe episodes of hot flashes and joint pains were the most common symptom of somatic domain. This was also accompanied by complains of sleep disturbances and mild cardiac symptoms like palpitation. The net somatic subscale scores of these symptoms improved significantly by 18.34% in the vitamin E administered group and by 20.54% in the placebo administered group after a period of three months (Tables 1, 2). As seen in figure 2, the improvement in the somatic subscale domain symptoms was comparable for both the groups. This indicates that the response of vitamin E and placebo were similar just as observed for the psychological subscale. Although very few research has been done to study the effect of vitamin E supplementation on menopausal symptoms, a placebo-controlled studies have demonstrated that vitamin E improved the hot flashes severity scores significantly when compared with a placebo.[8] Similarly in our study, improvement in hot flashes were seen but they were neither clinically nor statistically different from the placebo group.

The urogenital subscale scores were low as symptoms of vaginal dryness, irritation, soreness, dyspareunia, bladder disturbanceslike increased urinary frequency and urgency were not severe during the perimenopausal stage. These symptoms worsen during the postmenopausal stage with decreased estrogenization of the vaginal tissue.[16] There was no improvement in the urogenital subscale scores in our study. Some patients even reported a worsening of the symptoms of vaginal dryness as the menopausal stage progressed and the estrogen levels further declined. One study employing topical vitamin E gel applied locally improved the symptoms of vaginal dryness during menopause.[24,25]

The total score of the MRS scale improved by 14.63% for the vitamin E group (n=12) and a 13.64% improvement was seen in the total score for the placebo group after three months. Though these improvements were statistically significant within the group, there was no overall clinical or statistical difference in the improvement of menopausal symptoms between the vitamin E administered and placebo administered groups.

Our study is not without limitations. Firstly, the sample size is small because the study was undertaken as a pilot project due to scarcity of data in the Indian population. In addition, the MRS questionnaire was used for interview instead of a self-administered tool. Interviewer bias can be expected because of this.

## CONCLUSION

Though Vitamin E has recently gained points in the popular media as a non-hormonal and safe alternative for menopausal symptoms, there are very few studies to support this claim. We concluded from our study that vitamin E was similar to placebo in the management of menopausal complains during the perimenopause. However, large scale randomized controlled trials in the Indian population are needed to support or refute our findings.

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## REFERENCE

1. In: Edmond DK, editor. Menopause and the Postmenopausal woman. Dewhurst's Textbook of Obstetrics and Gynecology. 7th ed. Blackwell publishing; 2007. p. 492.
2. Singhal SR, Shullai WK. Comparative study of gabapentin and isoflavone in menopausal vasomotor symptoms. Journal of Mid-Life Health. 2016;7:132-139.
3. Saensak S, Vutyavanich T, Somboonporn W, Srisurapanont M. Relaxation for perimenopausal and postmenopausal symptoms. The Cochrane Library. 2014.
4. Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: Principal results from the

Women's Health Initiative randomized controlled trial. JAMA. 2002;288:321.
5. Meherishi S, Khandelwal S, Swarankar ML, Kaur P. Attitudes and practices of gynecologists in Jaipur toward management of menopause. Journal of Mid-Life Health. 2010;1:74-78.
6. Pimenta F, Maroco J, Ramos C, Leal I. Hot Flushes and Night Sweats in Midlife: Why do Some Women Have Them and Others do Not? Psicol. Reflex. Crit. 2014;28:753-63.
7. Singh B, Liu XD, Der-Martirosian C, Hardy M, Singh V, Shepard N, Gandhi S, Khorsan R. A national probability survey of American Medical Association gynecologists and primary care physicians concerning menopause. Am J Obstet Gynecol. 2005;193:693-700.
8. Ziaei S, Kazemnejad A, Zareai M. The effect of vitamin E on hot flashes in menopausal women. Gynecol Obstet Invest. 2007;64:204-7.
9. Nedrow A, Miller J, Walker M, Nygren P, Huffman LH, Nelson HD. Complementary and Alternative Therapies for the Management of Menopause-Related SymptomsA Systematic Evidence Review. Arch Intern Med. 2006;166:1453-1465.
10. Harlow SD, Gass M, Hall JE, et al. Executive Summary of the Stages of Reproductive Aging Workshop + 10: Addressing the Unfinished Agenda of Staging Reproductive Aging. The Journal of Clinical Endocrinology and Metabolism. 2012;97:1159-1168.
11. Heinemann LA, Potthoff P, Schneider HP. International versions of the Menopause Rating Scale (MRS). Health and Quality of Life Outcomes. 2003;1:28.
12. Heinemann LA, DoMinh T, Strelow F, Gerbsch S, Schnitker J, Schneider HP. The Menopause Rating Scale (MRS) as outcome measure for hormone treatment? A validation study. Health Qual Life Outcomes. 2004;2:67.
13. Szczubiał M. Effect of supplementation with vitamins E, C and β-carotene on antioxidative/oxidative status parameters in sows during the postpartum period. Polish journal of veterinary sciences. 2015;18:299-305.
14. Fata GL, Weber P, Mohajeri MH. Effects of vitamin E on cognitive performance during ageing and in Alzheimer's disease. Nutrients. 2014;28;6:5453-72.
15. Basambombo LL, Carmichael PH, Cote S, Laurin D. Use of Vitamin E and C Supplements for the Prevention of Cognitive Decline. Annals of Pharmacotherapy. 2017; 51:118-24.
16. Ahsan M, Mallick AK, Singh R, Prasad RR. Assessment of menopausal symptoms during perimenopause and postmenopause in tertiary care hospital. J Basic Clin Reprod Sci. 2015;4:14-9.
17. Sharma S, Tandon VR, Mahajan A. Menopausal symptoms in urban women. JK Sci. 2007;9:13-7.
18. Mahajan N, Aggarwal M, Bagga A. Health issues of menopausal women in North India. Journal of Mid-Life Health. 2012;3:84-87.
19. Gungor B, Gungor M, Taymur I, Askin R, Demirci H, Akpinar Y, Akgul A. The effect of perimenopausal estrogen levels on depression and anxiety: a pilot study. The European Research Journal. 2015 1(1).
20. Weber MT, Maki PM, McDermott MP. Cognition and mood in perimenopause: A systematic review and meta-analysis. The Journal of steroid biochemistry and molecular biology. 2014;0:90-98.
21. Epperson CN, Sammel MD, Freeman EW. Menopause Effects on Verbal Memory: Findings From a Longitudinal Community Cohort. The Journal of Clinical Endocrinology and Metabolism. 2013;98:3829-3838.
22. Morrow PKH, Mattair DN, Hortobagyi GN. Hot Flashes: A Review of Pathophysiology and Treatment Modalities. The Oncologist. 2011;16:1658-64.
23. Thurston RC, Joffe H. Vasomotor symptoms and menopause: Finding's from the study on Women's Health across the Nation. Obstet Gynecol Clin North Am. 2011;38:489-501.
24. Morali G, Polatti F, Metelitsa EN, Mascarucci P, Magnani P, Marrè GB. Open, non-controlled clinical studies to assess the efficacy and safety of a medical device in form of gel topically and intravaginally used in postmenopausal women with genital atrophy. Arzneimittelforschung. 2006;56:230-8.
25. Mac Bride MB, Rhodes DJ, Shuster LT. Vulvovaginal Atrophy. Mayo Clinic Proceedings. 2010;85:87-94.

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