



The effect of oral capsule of curcumin and vitamin E on the hot flashes and anxiety in postmenopausal women: A triple blind randomised controlled trial

Author links open overlay panelKhatereh Ataei-Almanghadim ^a, Azizeh Farshbaf-Khalili ^b, Ali Reza Ostadrahimi ^c, Elnaz Shaseb ^d, Mojgan Mirghafourvand ^e

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Abstract

Objective

The decline and eventual cessation of estrogen production cause a variety of symptoms during menopause, affecting each woman differently. Most women reported severe hot flashes and night sweats during menopause. The present study aimed to determine and compare the efficacy of curcumin and vitamin E on hot flashes and anxiety (primary objectives), sexual function, menopausal symptoms and adverse effects (secondary objectives).

Materials and methods

This was a triple-blind randomized controlled clinical trial. The participants consisted of 93 postmenopausal women in Ahar city-Iran. They were assigned into three groups (two intervention groups and one control group). The first intervention group received oral capsule

of curcumin (500 mg), the second intervention group was given oral tablets of vitamin E (200 IU/day), and the third group (control) received placebo twice a day for eight weeks. The participants completed the hot flash checklist one week before the intervention, and 4 weeks and 8 weeks after the intervention. They also filled out the Anxiety Scale, the Female Sexual Function Index (FSFI), the Greene Climacteric Scale before the intervention, and 4 weeks and 8 weeks after the intervention. One-way ANOVA, repeated measures ANOVA and ANCOVA tests were used for data analysis.

Results

There was no statistically significant difference between groups in terms of demographic characteristics, mean number of hot flashes, mean score of anxiety, sexual function index and menopausal symptoms before the intervention ($p > 0.05$). The mean age of participants was 51.7 years. Mean number of hot flashes in the curcumin group (adjusted mean difference = -10.7 , 95%confidence interval = -3.6 to -17.9 , $P = 0.001$) and in the vitamin E group (-8.7 , -0.6 to -15.0 , $P = 0.029$) was significantly lower than the placebo group after the intervention. The first significant effect of curcumin on hot flashes was observed after four weeks ($P = 0.027$). However, there was no significant difference between vitamin E group and placebo four weeks after intervention ($P = 0.052$) and the first significant effect of vitamin E on hot flashes was observed after eight weeks ($P = 0.025$). There was no statistically significant difference between the groups in terms of sexual function index, anxiety and menopausal symptoms ($P > 0.05$).

women but had no significant effect on anxiety, sexual function and menopausal symptoms.

Introduction

Menopause is a stage in life that all women experience as they age but in various ways.¹ Women face different challenges and undergo serious changes in their personal life, family and society during menopause.¹ Menopause refers to permanent cessation of menstruation that results from the loss of ovarian function. Clinically, menopause is diagnosed after 12 months of amenorrhea.² The average age of normal menopause is 50 and menopause typically occurs between 49 and 52 years of age.³ The decline and gradual cessation of estrogen production cause a variety of symptoms during menopause, affecting each women differently.^{4,5} Menopausal symptoms are hot flashes, sore breasts, vaginal dryness, irregular menstrual cycles, mood changes, vaginal atrophy, osteoporosis, and cardiac disease.^{4,5}

Vasomotor symptoms are hot flashes and night sweats that plague women during menopause.⁶ Hot flashes are sudden feeling of heat, burning and sweating with a slight increase in body temperature due to increased metabolic rate and peripheral vasoconstriction.⁷ Reduced levels of peripheral estrogen during menopause affect hypothalamus and central nervous system, which eventually alters neurotransmitter activity (serotonin, norepinephrine) and causes hot flashes.⁷ Hot flashes are present in as many as 55 % of women even before the onset of the menstrual irregularity that defines entry into the menopausal transition.⁸ The average duration of hot flashes is about 5.2 years.⁸ Hot flashes cause minor problems in some women while these symptoms disturb sleep, work, and daily activities in some other women.⁹ Vasomotor symptoms not only reduce quality of life due to cessation of estrogen production, but also are risk factors for cardiovascular disease.^{10,11} Anxiety is a common problem in menopause because women feel deprived and disabled to undertake their usual activities.¹² In other words, the risk of anxiety is higher in postmenopausal women due to lack of self-confidence, losing contact with their friends and relatives, lack of activity and mobility, lack of physical and financial independence and chronic illnesses.¹² Available studies had not addressed the prevalence of anxiety disorders (according to diagnostic criteria) in postmenopausal women. Available information on anxiety and menopause has not justified that menopause is a risk factor of anxiety.¹³ A study on postmenopausal women showed that anxiety was independently associated with severe impairment of quality of life and severe menopausal symptoms.¹⁴ Another study found a strong association between physical anxiety and menopause-related hot flashes.¹⁵

Available data showed that sexual disorders are very common in postmenopausal women.¹⁶ Postmenopausal hormonal changes can be effective in reduced sexual satisfaction and prevalence of sexual disorders in postmenopausal women.¹⁷ Common sexual complaints are decreased sexual desire, vaginal dryness, dyspareunia, orgasm, poor arousal, and low sexual satisfaction. Increased age and decreased estradiol levels have a significant detrimental effect on sexual function, desire and sexual responsiveness during normal menopause.¹⁸

Lifestyle-related strategies such as keeping the core body temperature cool, regular physical activity and paced respiration without side effects are recommended for mild flushes.¹⁹ Available clinical trials did not either support or reject the efficacy of soy-containing food and isoflavone supplements (red clover), black cohosh or vitamin E on menopause-related flushes.¹⁹ However, no serious side effects were reported in short-term use of these treatments. Two antihypertensive drugs of clonidine and methyldopa had less effect but more side effects.¹⁹ Systemic estrogen either alone (ET: estrogen therapy), in combination with progesterone (EPT: estrogen and progesterone

therapy) or estrogen-progestin oral contraceptives significantly reduced moderate to severe hot flashes.¹⁹ Several non-hormonal drugs have been reported to relieve menopause-related hot flashes including selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), gabapentin, clonidine, and soy isoflavones.²⁰ Estrogen is a specific selective drug for treatment of menopausal symptoms in case that serious detrimental effects (risk factor for breast cancer and endometriosis) of the drug were eliminated in previous monitoring of the patients.⁵ Estrogen + progestin and estrogen alone reduce the risk of fractures but increase the risk of stroke, thromboembolic events, gallbladder disease, and urinary incontinence.²¹ Postmenopausal estrogen and progesterone therapy increases the risk of venous thromboembolism in women with cardiovascular disease.²²

It is recommended to use nonchemical treatments with fewer side effects instead of hormone therapy. A common treatment is curcumin derived from powdered roots of *Curcuma longa*.²³ It is a polyphenol found in turmeric.²⁴ Curcumin has anti-inflammatory and antioxidant properties.²⁴ It also provides targeted cardiovascular protection.²⁴ The effect of curcumin on endothelial function is not known yet.²⁴ Turmeric-derived curcumin was used for treatment of many diseases for centuries.²⁵ Curcumin is useful for a variety of purposes from molecular targets (e.g. transcription factors, growth factors and their receptors, cytokines and enzymes) to genes responsible for cellular proliferation and apoptosis.²⁵ Curcumin was also reported to treat various inflammatory diseases (e.g. cancer).²⁶ Findings have shown that curcumin is not toxic even at higher doses (8000 mg/day).²⁶

Vitamin E also belongs to chemical family of tocopherols (alpha-tocopherol) with antioxidant activity. It is one of the most important soluble lipids.^{27,28} This compound exhibits varying degree of antioxidant activity depending on the site and number of methyl groups and the type of isoprenoids.^{27,28} It has also shown various functions including neuroprotection, potent anti-inflammatory function, mediators in lipid metabolism and detoxification pathways, and antioxidant activity.²⁹ The lowest dose of vitamin E was reported as 400 IU/day³⁰ and the highest dose as 800 IU/day.³¹ Menopause is a risk factor for oxidative stress caused by the imbalance between free radicals and antioxidant activity.³² A strong cross-sectional analysis showed that vitamin E reduced the number of hot flashes.³³

Given the anti-inflammatory and antioxidant effects of curcumin and vitamin E,^{24,27,28} involvement of inflammatory and oxidative processes in the etiology of menopausal symptoms, anxiety, and sexual function,^{34,35} and side effects of chemical treatments,^{24,36} this clinical trial was designed to

assess the efficacy of curcumin extract and vitamin E on hot flashes, anxiety, sexual function, and menopausal symptoms.

Section snippets

Study design and participants

This was a triple-blind randomized controlled clinical trial (researcher, data collector, and analyst did not know the type of intervention in the three groups). The participants consisted of 93 postmenopausal women visiting Ahar-Iran health centers.

Inclusion criteria were women with normal menopause, enough literacy to fill out the questionnaires or accompanied by a literate person in the family, married, less than 6 years of menopause, at least 40 and at maximum 60 years of age, hot flashes

Results

Of 320 menopausal women, 160 women entered the study and 93 women were willing to participate in the study. They were randomly assigned to three groups. Each group consisted of 31 women. Four women were excluded from the study since they no longer were interested to cooperate in the study. Of these, two belonged to vitamin E group and curcumin group who did not attend the four-week follow-up. The other two belonged to vitamin E group and placebo group who did not participate in the 8-week

Discussion

This was the first study on the efficacy of oral curcumin capsule on hot flashes, anxiety, sexual function and menopausal symptoms in postmenopausal women. The results of the study showed that oral intake of curcumin and vitamin E significantly reduced hot flashes in postmenopausal women but had no significant effect on sexual function, anxiety, and menopausal symptoms. Considering the positive effect of vitamin E on menopausal symptoms has been reported in several studies,^{29,30,33} this study

Conclusion

The results of this study showed that oral intake of curcumin and vitamin E significantly reduced hot flashes in postmenopausal women but no significant difference was found between the two intervention groups and the control group in terms of anxiety, sexual function and menopausal symptoms. Therefore, curcumin and vitamin E capsules can be used as effective treatment to

reduce hot flashes in postmenopausal women. However, further studies are needed to reach a definitive conclusion.

Author contribution statement

KAA contributed to the study design, data collection, data interpretation and writing the manuscript. MM contributed to study design, data analysis, data interpretation and revising the manuscript. AF, ARO and ES contributed to study design, data interpretation and revising the manuscript.

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