

The Effect of Evening Primrose Plant on Physical Symptoms of Menopause

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ABSTRACT

BACKGROUND AND OBJECTIVE: Menopause is a global phenomenon for women and about 74 to 80% of women worldwide suffer from symptoms of menopause. The symptoms women experience during this period include night sweats, sleep disorders, heart problems and flushing. The treatment currently used for these complications is hormone replacement method, which has serious side effects. One alternative method for the hormone replacement method is the use of plants from the family of phytoestrogens such as evening primrose.

METHODS: This triple-blind clinical trial was conducted among 100 postmenopausal women with menopausal symptoms in both drug and placebo groups. First, the symptoms of menopause were measured based on scores of 0 – 16. The participants arbitrarily used placebo or evening primrose oil 1g perle twice a day for one month. After one month, the symptoms of menopause were measured and compared using Menopause Health Questionnaire. IRCT:1N2017012432161.

FINDINGS: The results of the study demonstrated that evening primrose has considerable effects on the reduction of flushing (3.33 ± 0.79 vs. 0.89 ± 0.64), sleep disorders (2.65 ± 0.6 vs. 1.3 ± 0.66) and musculo-skeletal disorders (3.41 ± 0.74 vs. 3.41 ± 0.73 vs. 0.82 ± 0.73) in evening primrose group compared with placebo group ($p < 0.001$). In this study, the mean physical symptom score before menopause was 11.15 ± 1.78 , while it was 4.78 ± 1.60 at the end of the study ($p < 0.001$).

CONCLUSION: Results of the study demonstrated that the use of evening primrose is effective in reducing the physical symptoms in postmenopausal women and can be used as a complementary therapy or an alternative method for hormone replacement method to improve the symptoms of menopause in women.

KEY WORDS: *Physical symptoms, Menopause, Evening primrose.*

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Introduction

Climacteric period is one of the most important periods in women's life and their health, since this period is accompanied by important physical, physiological and social changes (1, 2). In fact, menopause is a global phenomenon for women and about 74 to 80% of women are experiencing symptoms of menopause (3–5). This period starts from the appearance of the first symptoms of menopause and lasts until 5 – 10 years after menopause (6). The normal age of menopause was shown to be 54 in Europe (3).

According to world health organization, menopause occurs 12 months after amenorrhea. Although this period only refers to menopausal women, the age range usually includes 45 – 55 years (2). As life expectancy increased in recent years, women almost spent one third of their life in menopausal period (7).

In addition, since life expectancy is increasing, this part of world population is ever increasing (8). The symptoms women experience during this period include restlessness, forgetfulness, urinary symptoms, increased risk of osteoporosis, vaginal dryness, dyspareunia, moral fluctuations, joint pain, muscle and stiffness, palpitations, sleep disorders, flushing and night sweats (2, 9, 12, 14). Flushing symptoms include sudden redness on head, neck and chest skin along with a feeling of intense heat in the body, sometimes ends with a lot of sweating (15).

Vasomotor symptoms (VMS), commonly called hot flushes are the most common and the most problematic symptoms for menopausal women. About 80% of women experience flushing, 3 months after a normal menopause or created by surgery (16). On the other hand, sleep disorders caused by flushing at midnight or age increase may cause a lot of inconvenience in people, because people spend about one third of their life in sleep. According to studies, about 68–75% of menopausal women suffer from sleep disorders in this period (17).

Moreover, studies indicate increased spasmodic chest pain and irregular heartbeat after the beginning of flushing and over time, increased rate of cardiovascular diseases during this period (18). These complications, which are caused by reduction of androgens and estrogens, may influence social activities, joy of life and the overall quality of life in women and weaken the feeling of being useful and healthy (9–11). The treatment currently used for

improving the symptoms of estrogen reduction in menopausal women is hormone replacement method, which includes treatment with two hormones of androgen and estrogen.

Estrogens may increase the risk of breast cancer, gallbladder disease, thromboembolic events, stroke and coronary heart disease. If estrogen use is not allowed, the risks of administering progesterone include decreased intestinal activity, bloating, negative effects on lipids and lipase activity, breast pain, acne, etc. Moreover, before starting hormone therapy, some measures are necessary and examinations are required after therapy; every year, breasts and pelvis should be examined accurately, total cholesterol, cholesterol, triglycerides and blood pressure should be measured and mammography should be performed (11). In addition to the above-mentioned complications and consequences of these two hormones, this treatments requires continuous follow ups. Similar to all chemical medications, this method is also prohibited for some people (known or suspected breast or endometrial cancer, abnormal genital bleeding with unknown causes, thromboembolism disorders, active liver or gallbladder disease) and some people are not willing to use them (19).

Considering the increase in aging rate and the large population of menopausal women and considering the numerous harmful effects of these two hormones, it is necessary to prevent and treat menopause complications using natural plant. In addition, studies show that the number of women who are looking for alternative therapies to treat menopause complications is increasing (8, 20). On the other hand, since some plants contain substances with estrogen-like effects, plants such as vitagnus, red clover and valerian have been used by women in various societies to reduce flushing (10–17, 21,31).

Phytoestrogens are herbal estrogens with a structure and function similar to the estrogen created inside human body (26, 27). Therefore, many women use plants from phytoestrogen family as complementary treatment or an alternative for hormone replacement method to reduce menopause complications (28).

Evening primrose is one the plants with phytoestrogenic properties. Phytoestrogens are estrogen-like compounds in herbal products, often detected in bile, urine, semen, blood and stools of humans and animals. It seems that phytoestrogens

reduce the risk of cardiovascular diseases, breast or endometrial cancer and osteoporosis, relieve symptoms of menopause, particularly flushing, and improves memory, mood and sleep patterns. Evening primrose is one the important phytoestrogenic plants. Evening primrose is a member of Onagraceae family and different parts of this plant have positive effects on vasomotor symptoms in menopause, psoriasis symptoms, premenstrual syndrome, dysmenorrhea, inhibition of platelet aggregation and several other problems (15, 22–24).

Considering the general tendency for herbal compounds and all the above-mentioned issues, the present study was conducted to analyze the effect of evening primrose, which is a member of phytoestrogenic plants, on physical symptoms during menopause period.

Methods

After obtaining permission from the Ethics Committee of Shahrekord University of Medical Sciences (6-11.89) and obtaining written informed consent from patients, this triple-blind clinical trial was conducted among 100 menopausal women who referred to the medical center of Dastana (A city in Chaharmahal and Bakhtiari province). All healthy menopausal women, who have not used any hormonal drug and had no underlying disease and their Pap smear result was negative within the last one year and complained about their menopause symptoms, were willing to participate in the study and at least had the ability to read or write were included in the study. In cases of incorrect use of drug, severe gastrointestinal disorders, symptoms of sensitivity to drug and failure to complete the questionnaire, the patients were excluded from the study.

The drug and the placebo were used with similar labels for both cases. Since the manufacturer (Barij Essence pharmaceutical Co. Kashan–Iran) produced all the perls of evening primrose and placebo in similar shapes and similar numbers in boxes numbered 1 -100, neither the researchers nor women could identify them. The subject chose one of the boxes when they referred and started using it. Therefore, the subjects were provided with the necessary explanations about the goals and characteristics of the study, steps, demographic questionnaire, drug use checklist and the Menopause Rating Scale. In this study, the variable of mean age of menopausal women, mean period after the last menstruation, number of pregnancies, mean

number of pregnancies and education were used as demographic information. The participants were taught who to complete the questionnaire and they were asked return the questionnaire to the researcher in 24 hours. Then, the subjects were asked to choose one of the 100 boxes. There were 30 perls in each box for the 15 days use. When subjects received the box, they were provided with explanations regarding the side effects in addition to “how to use” instructions (one 1g capsule in the morning and one at night with a glass of water). The researcher’s phone number was also given to them for making contact in case of any problem. Within these 15 days, the researcher made sure about the correct use of drug and not using phytoestrogen-containing diet by telephone follow-up and weekly evaluation of the checklist.

After this 15-day period, the second questionnaire and the second box containing the drug or placebo with similar code was given to the subjects. Telephone follow-up and checklist completion was done similar to the first period and the third questioner was given to them on 30th day and after the second period of drug or placebo use.

In this study, Menopause Rating Scale (MSR) was used to determine the symptoms of Menopause. This scale consists of three subscales and was prepared in 1996 by the specialized committee of German-speaking countries. The validity and reliability of this scale was confirmed in various countries (Germany, Britain, France, Sweden, etc.) by calculating Cronbach's alpha in a large population. The English version of this scale, which was translated by Taavoni et al. in 2011 and its validity and reliability was measured (Cronbach's alpha 0.79), was used in the present study.

This scale measures the severity of menopause symptoms including 4 symptoms: night sweats and flushing (frequency of occurrence), heart disease (heart palpitations, increased heart rate and chest compression), sleep disorders (difficulty in falling asleep, difficulty during sleep and getting up early) and musculoskeletal disorders (joint pain and rheumatism problems). To use this scale, first the severity of each symptom was scored based on the level of dissatisfaction reported by the subjects as follows: 0=no symptom, 1=mild, 2=average, 3=severe, 4=very severe. Then, the sum of four symptoms of flushing and night sweats, heart disease, sleep disorders and musculoskeletal disorders constituted the total menopause physical symptom score, ranging from 0 to 16. Data collection for both questionnaires was done

using self – report techniques (18, 26). The collected data were recorded using SPSS program and were analyzed using T-test and ANOVA tests, while $p < 0.05$ was considered significant.

Results

Of 405 women with the necessary conditions for participation in the study, 209 women quit because of several reasons and finally, 100 women were willing to participate in the study. The participants were divided into two groups of drug ($n=50$) and placebo ($n=50$). After the beginning of intervention, 10 women were excluded from the study due to being scared of side effects and incorrect use of drugs and finally, 46 women received the drug and 44 women received the placebo (overall, 90 women).

The mean age of all women was 54.6 ± 12 and the mean period after the last menstruation was 3.50 ± 18.24 months. The study groups were homogenous in terms of demographic characteristics such as age, mean period after the last menstruation, mean age of menarche, number of pregnancies, number of deliveries and education level (table 1).

Table 1. Demographic characteristics of participants in the two groups of drug and placebo

| Variable | Group | Placebo Mean \pm SD | Drug Mean \pm SD | P-value |
|--|-------|--------------------------|-----------------------|---------|
| Age of menopausal women (year) | | 54.7 \pm 4.56 | 54.6 \pm 3.75 | 0.9 |
| Period after the last menstruation (month) | | 18.82 \pm 3.85 | 18.24 \pm 3.27 | 0.42 |
| Menarche age (year) | | 12.06 \pm 1.47 | 12.4 \pm 1.52 | 0.94 |
| Number of pregnancies | | 5.5 \pm 1.5 | 5.84 \pm 1.37 | 0.26 |
| Number of deliveries | | 5.88 \pm 1.64 | 6.02 \pm 1.5 | 0.98 |

The study groups were homogenous in terms of demographic characteristics

Considering that the number of participants in each group was not more than 30, Kolmogorov-Smirnov analysis was not necessary and the subjects were assumed to follow a normal condition. Independent T-test was used to evaluate the homogeneity of the demographic data and indicated that there was no significant difference between them in terms of demographic data and they were homogenous. There was no significant difference between drug and placebo group in terms of the four subscales before the

intervention. However, regarding flushing and night sweat, a significant decline was observed in drug group compared with placebo group, two and four weeks after the intervention ($p < 0.001$). Moreover, time had significant effect on decline in symptoms and the symptoms decreased as the time passed ($p < 0.001$) (table 2). In terms of heart disease, evening primrose had no significant effect on subjects. Based on these results, sleep disorder was faced with statistically significant decline during four weeks of using evening primrose ($p < 0.001$).

Table 2. Comparing the subscales of physical symptoms of menopause, before and after intervention in the groups of drug and placebo

| Group | Placebo Mean \pm SD | Drug Mean \pm SD | P-value |
|----------------------------------|--------------------------|-----------------------|---------|
| Flushing and night sweats | | | |
| Before intervention | 3.18 \pm 0.81 | 3.34 \pm 0.79 | 0.33 |
| Two weeks later | 2.77 \pm 1.05 | 1.60 \pm 0.53 | <0.001* |
| Four weeks later | 2.63 \pm 1.14 | 0.89 \pm 0.64 | <0.001* |
| P-value | 0.03 | <0.001 | |
| Heart disease | | | |
| Before intervention | 1.68 \pm 0.7 | 1.73 \pm 0.85 | 0.73 |
| Two weeks later | 1.81 \pm 0.58 | 1.56 \pm 0.68 | 0.06 |
| Four weeks later | 1.88 \pm 0.61 | 1.76 \pm 0.87 | 0.43 |
| P-value | 0.67 | 0.02 | |
| Sleep disorders | | | |
| Before intervention | 2.45 \pm 0.72 | 2.65 \pm 0.6 | 0.16 |
| Two weeks later | 3.04 \pm 4.85 | 1.78 \pm 0.62 | 0.8 |
| Four weeks later | 2.22 \pm 1.05 | 1.03 \pm 0.66 | <0.001* |
| P-value | 0.31 | <0.001 | |
| Musculoskeletal disorder | | | |
| Before intervention | 3.02 \pm 0.87 | 3.41 \pm 0.74 | 0.06 |
| Two weeks later | 2.7 \pm 1.04 | 1.82 \pm 0.52 | <0.001* |
| Four weeks later | 2.65 \pm 1.37 | 0.82 \pm 0.73 | <0.001* |
| P-value | 0.005 | <0.001 | |

Moreover, passage of time had statistically significant effect in relieving the symptoms ($p < 0.001$). Furthermore, musculoskeletal disorder was faced with statistically significant decline during four weeks of using evening primrose ($p < 0.001$). Moreover, passage of time had statistically significant effect in relieving the symptoms ($p < 0.001$). According to the results of this study, the severity of physical symptoms of menopause showed a significant decline in drug group compared with placebo group, two and four weeks after the intervention ($p < 0.001$). Moreover, time had

significant effect on decline in physical symptoms and the symptoms decreased as the time passed ($p < 0.001$) (table 3).

Table 3. Comparing the severity of menopause symptoms, before and after intervention in the groups of drug and placebo

| Time Group | Before intervention | 2 weeks later | 4 weeks later | P-value |
|------------|---------------------|---------------|---------------|---------|
| Drug | 11.15±1.78 | 6.78±1.29 | 4.78±1.60 | <0.001 |
| Placebo | 10.34±1.69 | 10.34±5.83 | 9.40±3.49 | 0.28 |
| P-value | 0.65 | *<0.001 | *<0.001 | - |

Discussion

Results of the present study demonstrated that the use of 2 g per evening primrose oil twice a day for one month significantly decreased flushing, sleep disorders and musculoskeletal disorders. However, it had no significant effect on heart function, while the physical symptoms of menopause improved significantly. A study by Nahidi et al. demonstrated that the use of licorice during 4 months decreased the severity and frequency of flushing (29).

Furthermore, Kazemian et al. concluded that the use of valerian plant decreases the severity, period and frequency of flushing in menopausal women (22). In the study of Baghdari et al., the use of Flaxseed Powder also led to decline in severity and period of flushing in menopausal women (30). All these studies were consistent with our study and the use of phytoestrogenic plants led to decline in severity, period and frequency of flushing in menopausal women. However, the use of Flaxseed Powder in the study of Lewis, et al. did not lead to decline in severity and period of flushing, which might be due to low dosage of drug used in this study (30). The study of Taavoni et al. about the effect of red clover (a phytoestrogenic plant) concluded that this plant improved the quality of sleep in menopausal women (18). In addition, another study by Taavoni et al. measured the effect of valerian plant on sleep disorders during menopausal period and

proved the effectiveness of this plant (31). Both of these studies were consistent with our study. Another study by Taavoni et al. about the effect of red clover on heart diseases during menopausal period concluded that the use of this plant relieved heart diseases compared with control group. The questionnaire in this study was similar to our study (18).

In our study, evening primrose had significant effects on musculoskeletal disorders, which is probably due to anti-inflammatory effects of this plant (32). In the present study, to prevent the effects and interferences of phytoestrogenic foods, subjects' daily diet was recorded and assessed and in this way, this interfering variable was controlled and the subjects who used such food were excluded from the study. Therefore, we can say with more certainty that decline in severity and frequency of flushing is due to the effect of phytoestrogen in evening primrose. According to the above-mentioned subject matter and short period of using evening primrose and the positive effect on menopause complications, this plant can be prescribed as a non-invasive method for women with menopausal problems. It is worth noting that the dosage used in this study caused no side effects in women. Being a triple-blind study was one of the advantages of this study, which led to severe decline in the effects of any interventionist factor.

Relative control on environmental temperature was one of the limitations of the study, which could directly affect flushing. It seems that evening primrose can relieve flushing in menopausal women. However, further studies are required to prove the effect of this plant on flushing and specify the time of flushing relapse after the drug consumption is finished.

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