

*Original Article***A comparative study on the effects of Hypericum Perforatum and passion flower on the menopausal symptoms of women referring to Isfahan city health care centers***Fariba Fahami**, *Zahra Asali**, *Abolfazl Aslani***, *Nahid Fathizadeh******Abstract**

BACKGROUND: With regard to an increase in the life expectancy for women and the consistency of the menopause age, a significant portion of women's age is passed after the menopause. Menopause is considered as a critical and sensitive period due to the changes and the disorders that are involved in it. Vasomotor symptoms, sleep disorders and psycho-mental changes are among the most prevalent symptoms of this period. Hormone therapy is a common treatment and it involves some problems for most individuals. The purpose of this study was to comparatively examine the effects of two herbal medications, Hypericum Perforatum and Passion Flower, on menopause symptoms.

METHODS: This study was of a clinical-experimental type which was done in 1388 in Isfahan. The sample included 59 menopausal women who had the conditions for entering into the study. The individuals were selected via simple sampling and were assigned randomly into two groups of Hypericum Perforatum treatment group (30 women) and Passion Flower group (29 women). The required data were filled out through interview, Personal Characteristics Questionnaire, and Cooperman's Index for menopause symptoms in three stages of pre-intervention, the third week of intervention, and the sixth week of intervention. The results were analyzed by descriptive and inferential statistical methods and the statistical software of SPSS.

RESULTS: The findings showed that the average score of menopause symptoms in two treatment groups of Hypericum Perforatum and Passion Flower had a significant decrease throughout the third and the sixth weeks of study ($p < 0.05$). In addition, there was no statistically significant difference between the two groups and both herbs equally resulted in a decrease in the menopause symptoms scores ($p > 0.05$).

CONCLUSIONS: With regard to the effects of Hypericum Perforatum and Passion Flower on treating menopause precocious symptoms (vasomotor signs, insomnia, depression, anger, headache, etc.), these two herbs can be used as an alternative treatment for individuals who cannot, whatsoever, use hormone therapy.

KEY WORDS: Menopause symptoms and treatment, hypericum perforatum and passion flower.

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Menopause is an undeniable period in women's lives. Nowadays, around 90 percent of women get to the age of 65 in the world. Thus, menopause is a stage in life that almost all women in the world experience it.¹ Menopause is a stage of a woman's life in which ovary functioning loss followed by a

permanent interruption of menstruation occur. The average age of menstruation in most industrial countries is 50 to 51.² A decrease in the level of ovarian hormones during menopause causes an increase in the physiologic and psychological changes that can significantly affect the quality and health of women.³ 85 percent of

* MSc, Department of Midwifery, School of Nursing and Midwifery, Isfahan University of Medical Sciences, Isfahan, Iran.

** PhD, Department of Pharmaceutics, School of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran.

*** MSc, Nursing and Midwifery Care Research Center, School of Nursing and Midwifery, Isfahan University of Medical Sciences, Isfahan, Iran.

Correspondence to: Fariba Fahami, MSc.

Email: fahami@nm.mui.ac.ir

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women complain from heatstroke, sleep disorders, and temperamental changes (anxiety, depression, irritability, etc.).⁴

Hormone therapy is often the most appropriate treatment for vasomotor symptoms which is forbidden to be used for most women or they don't have any interest towards it.⁵ Hormone therapy has potential side effects such as the risk of getting endometrial and breast cancers which limit its application.⁶ In recent years, serotonin reabsorbing selective preventive agents have become popular in treating heatstroke.⁷ Although these medications are totally effective, they are implicated in side effects like serotonin syndrome, etc.⁸ Nowadays, the use of supplementary treatments is increasing among women and it seems that they have become alternatives to hormonal treatments for controlling menopausal symptoms.⁹ *Hypericum Perforatum* has been used orally to treat light to moderate depression, anxiety, pre-menopause syndrome, seasonal psychic disturbances, restlessness, and viral infections.¹⁰ *Passion Flower* has anti-pain, anti-spasm, tranquilizing and sleep-inducing properties and is traditionally used for treating neural pain, general epilepsy, and spasm.¹¹ These two herbs lead to an increase in the level of available serotonin by controlling mono-amino oxides.¹⁰ The role of a reduction in serotonin in causing menopausal symptoms has been significantly proved.¹² Numerous studies have been conducted about the effects of antidepressants and tranquilizers on menopausal symptoms but research in this realm, especially about the effect of these medications on vasomotor symptoms, still continues. These two herbs have similar properties as the above-mentioned medications; they have fewer side effects, and individuals are more interested in herbal medications. Most of the conducted studies (both nationally and internationally) about the use of herbal medications in menopausal period pertain to photo-estrogenic herbs (soya, fenugreek, fennel, sweet root, etc). By virtue of this point that no other studies had been done on the effects of these kinds of herbs on menopausal symptoms throughout the country, except for Kazemian's study about the effect of

Passion Flower on heatstroke, the researchers decided to examine this issue, hoping that it would be a treatment method for reducing the menopausal symptoms and improving the women's health in this period. In our country, most women in this period refer less to health care centers due to the cessation of reproducing and pregnancy periods and our access to them was very difficult in spite of their large number and a high outbreak of these symptoms.

Methods

The aim of this research was to pinpoint and compare the effects of *Hypericum Perforatum* and *Passion Flower* on menopausal symptoms. The present study was a three-phase, two-group quasi-experimental clinical trial conducted in 1388 in Isfahan City Treating and Hygienic Centers. 59 menopausal women completed the study. The entrance conditions to the study were as follows: the women who had not experienced menopause in the last year, women who were at first 5-year period of menopause, those who had the score of 15 from Cooperman's index for menopausal symptoms, women who did not have any known psychological disturbances and did not have any record for these problems, women who didn't suffer from thyroid diseases, psychosomatic disorders, pheochromocytoma, carcinoid syndrome, leukemia, cancer and any known systemic diseases such as blood pressure, diabetes, cardiovascular problems, those who did not take hormonal treatments, nutritional supplements, herbal drugs, homeopathy for soothing their menopausal symptoms and did not take medications that could have intervention with *Hypericum Perforatum* and *Passion Flower* and finally, did not have a BMI more than 30 kg/m² and precocious menopause (before the age of 40 years). Those women who were suffering, whatsoever, from severe gastrointestinal problems or were not able to take the medications or had side effects following using the two medications of the study were omitted. After giving complete explanations to the qualified women about the stages and the kind of research and taking written consent, the Personal Fertility Features

Questionnaire and the Cooperman's index were filled out and individuals were randomly assigned into two groups. Randomization was done by using the random number table, so that the odd numbers were assigned to Hypericum Perforatum Group and the even numbers to Passion Flower Group. The procedure for taking the medications was like this: Hypericum Perforatum, 160 mg effervescent tablet made by Goldaroo Company, three times a day, Passion Flower, 30 mg, 20% Pass P drop, made by Iran Daroo Company, 10 drops, three times a day and 30 drops before sleeping.

Afterwards, throughout the third and sixth weeks of intervention, the Cooperman's index was filled out again. The Cooperman's index consists of eleven symptoms of menopause (heatstroke, insomnia, fatigue, depression, palpitation, headache, muscular and joint-related pains, anger, vertigo, numbness and goose bumps, creeping sensation) and each of these symptoms in this index gets a score of zero to three, for weak, moderate and severe conditions without any signs, respectively. Then, the score of heatstroke is multiplied by 4, the score of numbness and goose bumps by 2, insomnia by 2, anger by 2 and the rest of symptoms are multiplied by 1; the highest score is 51. The above-mentioned grading is based on Cooperman's index innovated by Blat et al, in 1952 to assess the symptoms of menopause and accordingly, used in numerous domestic and international papers, the reliability and validity of which has been verified.¹³ In order to make sure of the groups' homogeneity with regard to quantitative variables, the independent t-test was used and by virtue of the qualitative variables, the chi-square and Mann-Whitney U tests were employed. The variance analysis and paired t-test were used to define the effects of Hypericum Perforatum and Passion Flower on menopausal symptoms and in order to compare these two groups, the independent t-test was used.

Results

30 individuals in Hypericum Perforatum group and 29 in Passion Flower group finally completed the study. 11 individuals in the Passion

Flower group and 12 in the Hypericum Perforatum group exited from the study.

In order to identify the homogeneity of qualitative features in both groups, such as occupational situation, marital status and exercising condition, the chi-square test and for educational level, the Mann-Whitney U test were used, the results of which were as follows: by virtue of occupation, most individuals in both groups were housewives (86.7 percent in the Hypericum Perforatum group and 93.1 percent in the Passion Flower group). With regards to marital status, most of the individuals in both groups were also married (96.7 percent and 100 percent, respectively). The highest frequency of educational level in the Hypericum Perforatum group was 33.3 percent junior high school and in the Passion Flower group, it was 37.9 percent elementary school education. 26.7 percent of individuals in the Hypericum Perforatum group and 27.6 percent in the Passion Flower group did regular exercise. There was no significant difference with regard to the aforementioned qualitative variables after conducting the statistical tests between the two groups. For examining the homogeneity of the two groups by virtue of quantitative variables like age, pregnancy records, the number of menopausal years, menopausal age, and the body mass index, the independent t-test was used which didn't show any significant difference (Table 1).

In Table 2, the average total score of menopausal symptoms before intervention, 3 and 6 weeks after intervention in both groups is presented. Considering the significant level of $p < 0.05$, the variance analysis showed significant difference of the average scores of the symptoms separately in each group and at the three specified times ($p < 0.00$). Moreover, the paired t-test showed that the average score of symptoms in the second referral compared with the first and in the third referral compared with the second had a significant decrease. This showed that Hypericum Perforatum and Passion Flower brought a significant decrease in the symptoms.

However, comparing the difference of symptoms' average score after intervention in both groups showed that both herbs equally decreased

Table 1. The average of quantitative variables in two groups

Variable	Group	Hypericum Tablet		Passion Flower Drop		P Value
		Mean	Standard deviation	Mean	Standard deviation	
Age		51.7	3.3	51.8	2.6	0.937
Pregnancy times		4.9	2.4	4.6	1.7	0.921
Number of menopausal years		3.1	1.5	2.8	1.6	0.58
Menopausal age		48.6	3.2	48.9	2.6	0.71
Body mass index		26.70	3.09	26.74	3.3	0.71

Table 2. Comparing the total score average of menopausal symptoms before and after the intervention in each group

Group	Before Treatment		3 Weeks after Treatment		6 Weeks after Treatment		P value
	Mean	Standard deviation	Mean	Standard deviation	Mean	Standard deviation	
Hypericum tablet	25.9	5.8	17.6	5.1	12.7	5.09	0.000
Passion flower drop	28.5	5.5	20.9	6.2	15.7	7.25	0.000

of the symptoms. The independent t-test alongside the significant level of $p < 0.05$ showed that symptoms average score in the second referral (three weeks after the treatment) compared with the pre-treatment and also the difference of the symptoms average score in the third referral (six weeks after the treatment) compared with the pre-treatment didn't have a significant difference in both groups ($p = 0.5$). Therefore, both herbs did not have any difference in decreasing the total score of the symptoms. Also, the intensity of each of the symptoms in both groups was examined before and after intervention by using the Freedman test. The intensity of heatstroke, insomnia, fatigue, depression, palpitation, headache, muscular and joint-related pains, anger, vertigo, numbness and goose bumps, and the creeping sensation was equally decreased at the significant level of $p < 0.05$ in both groups except for the vertigo in the Hypericum Perforatum group. By using the Wilcoxon test, interesting results were gained about the effects of both herbs on the symptoms. Although both herbs brought about a significant decrease in the symptoms at the time of intervention, the intensity of some symptoms had a more noticeable decrease in the first or the second three weeks. The intensity of some symptoms such as heatstroke, headache, weak-

ness and fatigue had a higher decrease in the second three weeks of intervention, meaning that these symptoms required more time than three weeks for recovery.

Symptoms like anger, palpitation, creeping sensation, depressed mood, and muscular pain had a noticeable improvement in the first three weeks and these symptoms reacted more rapidly to treatment. In Kazemian's study, Hypericum Perforatum also caused a decrease in the intensity of heatstroke in the last month of intervention.¹⁴ In Chadahri's study, the mixture of Hypericum Perforatum and Passion Flower resulted in an improvement in depression and anxiety especially in the first two weeks.¹⁵

Discussion

The serotonin selective reabsorbing preventive agents are nowadays considered with regards to treating the menopausal symptoms as one of the non-hormonal medications.¹⁶ The Hypericum Perforatum and Passion Flower result in an increase in available serotonin by having preventive enzyme of monooxidize.¹⁰ It can be asserted that these two herbs brought a decrease in menopausal symptoms in this way. Most samples who had vasomotor symptoms alongside temperamental changes and sleep

disorders improved significantly after taking these two herbs but some samples who had only the severe vasomotor symptoms dispensed with the study in the initial stages of intervention due to lack of improvement. Lokonon also concluded in his study that only when the menopausal symptom of heatstroke is severe, antidepressants (flouxetine and citalopram) do not seem effective.¹⁷ Still, in Groub's study, Hypericum Perforatum had a significant effect on menopausal symptoms with a psycho-mental basis, especially heatstroke.¹⁸

Nonetheless, the absence of the placebo group in this study is attention worthy. We know that some symptoms, especially heatstroke, give a tangible response to placebo. But, this group was omitted from the study due to ethical reasons. However, by taking into account that the effect of Passion Flower on heatstroke had been compared with placebo in Kazemian's study and the Passion Flower was better than the placebo, we also compared hereby the Hypericum Perforatum with Passion Flower which yielded similar results on heatstroke. Moreover, it is mentioned in studies that the Cooperman's index is affected by placebo to a lesser degree. As it was mentioned in the results, some symptoms like anger, palpitation, creeping sensation, and a depressed mood respond faster to treatment than other symptoms. In Vazirian's study, in which Passion Flower was used to treat anxiety, the treatment period was 4 weeks while the effect of Passion Flower

was obvious from the seventh day of treatment.¹⁹ In Iran's Herbal Pharmacopoeia, the minimum time required for appearance of the effect of Hypericum Perforatum is mentioned from 4 to 5 weeks. But symptoms like heatstroke, headache, and muscular pain required a longer time of more than 3 weeks to respond to treatment. In most studies that have been done on heatstroke, the treatment period is long. For instance, in Brice's study, the mixture of black Kohoosh and Hypericum Perforatum with Kohoosh alone, the duration of the study was 6 months which had mentioned a 64 percent of improvement. In Kazemian's study, the intensity of heatstroke had also decreased in the end of the study (4 weeks). All in all, it can be claimed that the vasomotor symptoms require a longer time for treatment.

Conclusions

According to the results of the present study, it seems that the consumption of Hypericum Perforatum and Passion Flower can be effective in reducing the menopausal symptoms, especially when the symptoms of vasomotor, temperamental changes and sleep disorders are gathered together. In order to have a more accurate judgment about the effect of this set of tranquilizing herbs on vasomotor symptoms, more studies must be carried out comparatively with the placebo group

The authors declare no conflict of interest in this study.

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