

The effect of different dosage of piascledine on hot flushes in postmenopausal woman of Jahrom, Iran.

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Abstract

Introduction: Menopause is one of the natural stages of women's life usually begins in 45-55 y old. The most common symptom is hot flushes. The aim of this study is to evaluate the effect of different doses of piascledine on hot flushes of post-menopausal women.

Method: 69 postmenopausal women referred to Dr. Rasekh clinic was entered to the study and were randomly divided into 3 groups, first group; 300 mg piascledine daily, second group; 300 mg piascledine twice a day and third group; hormone replacement therapy (1.25 mg conjugated estrogen for 25 d and 10 mg dydrogestrone for 15 d). Hot flushing symptoms were evaluated before and after intervention using Blatt-Kupperman Menopausal Index (BKMI). The data were analysed by SPSS 21 software.

Result: BKMI had a reduction of 17.91 in first group, 20.9 in second group and 20.96 in third group.

Conclusion: We found that a higher dosage of piascledine leads to a significant reduction in hot flushes rate and according to the effectiveness and also lack of side effects related to the higher dose of piascledine, it seems to be an appropriate alternative for hormone replacement therapy to treat the menopausal symptoms in high dosage.

Keywords: Hot flash, Menopause, Piascledine, Phytoestrogen. **Abbreviations:** HRT: Hormone Replacement Therapy; HR: Hormone Therapy; SSRI: Selective Serotonin Reuptake Inhibitors; CHD: Coronary Heart Disease.

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Introduction

Menopause is a natural stage in woman's life begins between the ages of 45-55 with a mean age of incidence around 51 years worldwide [1]. During this time the ovaries produce lower amount of female hormones specially estrogen which leads to menopause symptoms [2]. At the first menstrual cycle becomes irregular then it completely stops. When a woman doesn't experience menstrual period for 12 consecutive months, she is regarded as a menopause woman [3]. Most women spend more than one-third of their lives after menopause [4]. Estrogen reduction leads to some physical and emotional changes such as night sweats, mood changes, vaginal dryness, tachycardia, insomnia and hot flushes [5]. These symptoms can be severe enough to negatively impact quality of life, work performance, and personal relationships [6]. Hot flushes have been reported as the most bothersome symptom of menopause accounting for 75% of symptoms [7]. 40 percent of premenopausal women, 70 to 80 percent of women who naturally go through menopause and 90 to 100

percent of those who have had ovariectomy, will experience hot flushes. Frequency of the hot flushes varies from woman to woman. In about 30 percent of the women it occur more than ten times a day [8]. Hot flushes start by a sudden redness of skin on the face, neck and chest and is associated with a feeling of intense heat in the upper body; it sometimes ends with extreme sweating and usually last about 1 to 5 min [9]. Hot flushes usually occur during the night so they affect sleeping patterns and lead to perspiration and sleeplessness. Definitely, insomnia causes anger, restlessness and reduces mental functions, hence makes the body vulnerable to all sorts of stress disorders and can be indirectly related to coronary heart diseases [8].

Menopause does not require any medical treatment itself, the treatment is usually used to relieve the symptoms and to prevent or reduce complications caused by the menopause [10]. Both hormonal and no hormonal treatment modalities are available for management of the mentioned symptoms. Hormonal therapy includes estrogen and combined estrogen/progestin therapy. Non-hormonal therapy includes isoflavones,

gabapentin, clonidine, selective Serotonin Reuptake Inhibitors (SSRI's), black cohosh, and vitamin E [11]. Hormone Therapy (HT) is the most effective treatment for severe postmenopausal symptoms [12]. Hormone replacement therapy is contraindicated for the prevention of cardiovascular disease in postmenopausal women [13], moreover, with HRT the incidence of endometrial cancer, breast cancer, stroke and venous thromboembolism could be increased [14]. Despite the effectiveness of HRT on hot flashes, today there are disagreements about this type of treatment due to the mentioned complications caused by long-term use. It has been demonstrated that women's attitudes towards the menopause and their knowledge of the benefits and risks of HRT have a direct effect on their use of HRT [15]. Common side effects of estrogen include breast soreness, which can often be minimized by using lower doses. Vaginal bleeding occurs in almost all women receiving cyclic estrogen-progestin regimens and is common in the early months of a continuous estrogen-progestin regimen [10].

On the other hand, hormone replacement therapy is forbidden for women with the following: a history of breast cancer, CHD (Coronary Heart Disease), a previous venous thromboembolic event or stroke, active liver disease, unexplained vaginal bleeding, high-risk endometrial cancer, or transient ischemic attack [10]. So in these cases HRT is not recommend and it's better to use other treatments instead. Phytoestrogens are polyphenols that are structurally similar to endogenous estrogen and have weak estrogenic properties [16]. It has a positive effect on the reduction of the symptoms related to the menopause like hot flashes and improves mood and quality of life in postmenopausal women [17]. A litany of health benefits including a lowered risk of osteoporosis, heart disease, breast cancer, and menopausal symptoms, are frequently attributed to phytoestrogens [18].

Nowadays, Soy foods and supplements have been the subject of much interest for the reduction of menopausal symptoms because of their high concentrations of phytoestrogens [19]. Piascledine is an herbal medicine derived from avocado and soy which is used to relieve the hot flash as menopausal symptoms in women [20]. This drug is made in France and has no side effects. The aim of our study was to evaluate the effect of different doses of piascledine on hot flashes in postmenopausal women To determine whether the higher dose of piascledine can be more effective in controlling hot flashes or not.

Materials and Methods

Sampling

This interventional study was approved by the Jahrom University of Medical Science Ethics Committee. The ethical code is Jums.REC.1393.121. This study was done from January 2011 to September 2012. After a complete explanation about the process of the study, a written informed consent was obtained from the patients so participation in this study was completely voluntary.

The patients were selected through convenience sampling and randomly divided into three groups. According to the previous researches, considering CI=95% and power=80% the sample size in each group was determined 23, so the total sample size was 69.

Study participants

All the menopause women with hot flashes who referred to the Dr. Rasekh clinic whose diagnosis was confirmed by the Kuperman index were entered to the study. We regarded them as the menopause ones if they didn't experience any menstrual flow for a minimum of 12 months.

Inclusion criteria

The patients who had not used hormone therapy (except first group), dietary supplements and herbal medicines to relieve menopausal symptoms were entered to the study.

Exclusion criteria

The women who were not able to use or continue their drugs due gastrointestinal symptoms were excluded.

Intervention

The patients were randomly divided into three groups. The first group received 300 mg piascledine once a day for 3 months. The second group received 300 mg piascledine twice a day for 3 months and the third group received HRT (1.25 mg conjugated estrogen daily for 25 d and 10 mg dydrogestrone daily for 15 d). All three groups were evaluated 4 times based on the Kupperman Index: before the intervention, 1, 2 and 3 month after that.

Questions

The Kupperman index is a numerical conversion index including 11 menopausal symptoms: hot flushes (vasomotor), paresthesia, insomnia, nervousness, melancholia, vertigo, weakness, arthralgia or myalgia, headache, palpitations, and stinging. Each symptom on the Kupperman index was rated on a scale from 0 to 3 for no, slight, moderate, and severe complaints. To calculate the Kupperman index, the symptoms were weighted as follows: hot flashes (4X), paresthesia (2X), insomnia (2X), nervousness (2X), and all other symptoms (1X). The highest potential score is thus 51. This index has been used widely in the studies of menopausal symptoms so its validity is confirmed [23-25].

Analysis

The statistical analysis was performed with SPSS software ver. 16. We used Mauchlys and ANOVA test to evaluate the consistency of the statistical data (p-value of $\leq /001$).

Results

This study was conducted on 69 eligible women, who were divided into three groups (23 patients in each group). From the participated patients, 67 of them were married and 2 were single. They were aged between 35-69 y old. The average age of the participants was 46.6 ± 87 SD (in terms of years). The average time from the last menstrual period was 19.5 ± 3.9 SD (in terms of month). The average Body Mass Index (BMI) of the patients was 27.05 ± 52 SD.

In general, from all three groups before the intervention, 21.7% were asymptomatic while 33.3% had severe symptom. But, at the end of the study all of the patients had no severe symptoms, 89.9% were asymptomatic, and mild symptoms of hot flushes remained in only 7% of patients.

We used Blat Kuperman scale to measure the symptoms of the menopause. So including factor of four, the average rate of hot flushes in the three groups before the intervention was 22.63 ± 1.24 SD and at the end of the study it reached to 2.56 ± 39 SD with a significant reduction. all eleven variables related to each group (hot flushes, numbness, insomnia, nervousness, severe sadness, dizziness, weakness, muscle pain or arthritis, headaches, heart palpitations and tingling of the skin) had a significant decrease.

In the first group in which the patients had used one capsule of piascledine per day, the average number of Kuperman scale (including eleven variables) before and after intervention was 21.82 ± 2.20 and 7.69 ± 1.33 SD respectively which shows a significant reduction (Table 1).

Table 1. Comparison of BKM index before and after intervention in the first group.

		Mean	Std. deviation	Std. error mean	95% confidence interval of the t difference		df	Sig. (2-tailed)	
					Lower	Upper			
Pair 1	Prior	14.13043	6.06758	1.26518	11.50662	16.75425	11.169	22	0.000
	Post								

In the second group in which the patients had used two capsule of piascledine per day the average number of Kuperman scale before and after intervention was 24.69 ± 1.95 SD and 6.28 ± 56 SD respectively which shows a significant reduction (Table 2).

Pair 1	Prior	24.6957	23	9.39746	1.95951
	Post	6.2899	23	2.69924	0.56283

Table 2. Comparison of BKM index before and after intervention in the second group.

Mean	N	Std. deviation	Std. error mean
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In the third group in which the patients had received hormone replacement therapy, the average number of Kuperman scale before and after intervention was 62 ± 38 SD and 21.39 ± 2.29 SD respectively which shows a significant reduction (Table 3).

Table 3. Comparison of BKM index before and after intervention in the third group.

		Mean	Std. deviation	Std. mean error	95% Confidence interval of the t difference		df	Sig. (2-tailed)	
					Lower	Upper			
Pair 1	Prior	20.76812	11.43644	2.38466	15.82263	25.71361	8.709	22	0
	Post								

According to ANOVA test, the rate of hot flushes related to each group was not significantly different before the intervention. But after three months of intervention, the rate of hot flushes of third group (who received hormone replacement

therapy) was significantly different compared to first and second groups (P -value ≤ 0.05). Reduction in the rate hot flushes was not significantly different between the first and second groups (Table 4).

Table 4. Comparison of the hot flushes between 3 groups.

Dependent variable	(I) Drug	(J) Drug	Mean difference (I-J)	Std. error	Sig.	95% confidence interval	
						Lower bound	Upper bound
Sum q10	Pias 1 in every day	Pias 2 in every day	-2.86957	3.05368	0.351	-8.9664	3.2273

	Srerojen	0.43478	3.05368	0.887	-5.6621	6.5317	
Pias 2 in every day	Pias 1 in every day	2.86957	3.05368	0.351	-3.2273	8.9664	
	Srerojen	3.30435	3.05368	0.283	-2.7925	9.4012	
Srerojen	Pias 1 in every day	-0.43478	3.05368	0.887	-6.5317	5.6621	
	Pias 2 in every day	-3.30435	3.05368	0.283	-9.4012	2.7925	
Mean q1, q2, q3	Pias 1 in every day	Pias 2 in every day	1.4058	1.22478	0.255	-1.0395	3.8511
		Srerojen	7.07246*	1.22478	0	4.6271	9.5178
	Pias 2 in every day	Pias 1 in every day	-1.4058	1.22478	0.255	-3.8511	1.0395
		Srerojen	5.66667*	1.22478	0	3.2213	8.112
	Srerojen	Pias 1 in every day	-7.07246*	1.22478	0	-9.5178	-4.6271
		Pias 2 in every day	-5.66667*	1.22478	0	-8.112	-3.2213

*The mean difference is significant at the 0.05 level.

Then, the differences in the numbers of Kuperman scale were determined in all three groups before and after the intervention. Accordingly, the reduction of symptoms in both groups using piascledine was very sensible. However, the difference between these two groups is not significant. Meanwhile, the

difference between the groups taking piascledine and the group receiving hormone replacement therapy was significant. While the reduction rate of symptoms related to the second and third groups is not meaningful (Table 5).

Table 5. Comparison of the mean differences of Blatt_Kuperman index between 3 groups.

(I) drug	(J) drug	Mean difference (I-J)	Std. error	Sig.	95% Confidence interval	
					Lower bound	Upper bound
Pias 1 in every day	Pias 2 in every day	-4.27536	2.69626	0.118	-9.6586	1.1079
	Srerojen	-6.63768*	2.69626	0.016	-12.0209	-1.2544
Pias 2 in every day	Pias 1 in every day	4.27536	2.69626	0.118	-1.1079	9.6586
	Srerojen	-2.36232	2.69626	0.384	-7.7456	3.0209
Srerojen	Pias 1 in every day	6.63768*	2.69626	0.016	1.2544	12.0209
	Pias 2 in every day	2.36232	2.69626	0.384	-3.0209	7.7456

*The mean difference is significant at the 0.05 level.

Discussion

Understanding menopause-associated pathophysiology and developing new strategies to improve the treatment of menopausal-associated symptoms is an important topic in the clinic [21]. Both hormonal and non-hormonal treatments are available for management of the symptoms. There are few studies which have shown the disadvantages of HRT in menopause women. The study of Schumacher et al. conducted in 2003, shows that Estrogen plus progestin therapy increased the risk for probable dementia in postmenopausal women aged 65 y or older [22].

Kim et al. worked on the effect of complementary and alternative therapy on the climacteric period. They find out that hormone replacement therapy increases the potential risk of thrombosis, cerebral infarction and breast cancer [23]. They

also mentioned that finding a new alternative for HRT in management of menopause symptoms is an important concern of nowadays.

Epidemiological studies have shown that some of the diseases are more common in the West (including breast, endometrial, colon and prostatic cancers) which are less visible in East Asia that is due to consumption of phytoestrogens such as soy [24]. In a study conducted by Rua et al. it reveals that phytoestrogens appear to reduce the frequency of hot flushes in menopausal women, without serious side-effects [25].

Piascledine is an herbal medicine derived from avocado and soy and almost all the related researches to the piascledine has concentrated on its effects on arthritis, rheumatoid arthritis and osteoarthritis [26-29]. Laurent et al. worked on the relationship between osteoarthritis and nutrition, they have used two different doses of piascledine, 300 and 600 mg per day [30].

In the Appelboom et al. study also which conducted in 2011 on the people with Knee Osteoarthritis and they have used two different doses of piascledine, 300 and 600 mg per day [31]. So the use of piascledine twice a day is permitted and it has no side effects.

Only in one study conducted by Panahi et al. the effects of conventional HRT on the treatment of hot flush was compared with piascledine, they also evaluate the safety of piascledine in relieving postmenopausal symptoms. The patients in that open label clinical trial, randomized to receive piascledine capsule 1 mg or HRT (0.625 mg oral daily conjugated estrogen tablets, plus 2.5 mg continuous oral daily medroxy progesterone acetate tablets) for 2 month. They revealed that due to low HRT compliance and its possible risks in long period of time and considering the same activity of soybean supplement and HRT in relieving the hot flush as menopausal symptoms in women, it seems that soybean supplements can be an alternative therapy to hormone [20]. Their findings were compatible with our results.

In the recent study we compared the effect of two different doses of piascledine (300 and 600 mg) with hormone therapy in menopause women. And according to the results, all three groups had a significant reduction in the symptoms related to the menopause.

A significant difference was seen in all groups, so that the hormone therapy had the greatest effect, then in the second group that received piascledine twice a day the symptoms became disappear and finally in the first group received a capsule of piascledine daily the symptoms reduced. The important issue is that the use of piascledine was associated with no complication or side effect such as spotting or vaginal bleeding (the symptoms that we may see in HRT).

The patients using piascledine also doesn't have any concern about the different kinds of cancers related to the hormone therapy, Heart disease or thrombosis so they can confidently use this drug to reduce menopause symptoms.

Conclusion

We found that a higher dosage of piascledine leads to a significant reduction in hot flushes rate and according to the effectiveness and also lack of side effects related to the higher dose of piascledine, it seems to be an appropriate alternative for hormone replacement therapy to treat the menopausal symptoms in high dosage.

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The authors report no conflicts of interest.

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