Treatment of Sweating, Hot Flushing and Sleep Disturbance in Peri and Post Menopausal Women with Oral Pometone

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Abstract

Vasomotor symptoms, such as hot flushes and night sweats, are very common during the menopausal transition. One of the important alternative treatments is foods or supplements enriched with phytoestrogens.

Aim of the study

To assess the efficacy, safety and acceptability of pometone supplements for reducing sweating, hot flushes and sleep disturbance in peri and postmenopausal women.

Methods

This cross sectional randomized clinical therapeutic trail involved 44 peri and postmenopausal women. All patients took oral pometone capsule 500mg twice daily for one month period.

Result

The mean of hot flush, sweating score before treatment was 8.11±1.72. After four weeks of treatment, it became 1.36 ±2.10; P value was < 0.0001. The mean of sleep disturbance score before treatment was 4.40±3.03. After four weeks of treatment, it become 1.22 ±1.80 ; P value was < 0.0001 . No side effect was reported during the course of this study.

Conclusion

Pometone is effective, safe and cheep treatment to reduce hot flushes , night sweat and sleep disturbance in peri and postmenopausal women.

Keywords: sweating , hot flushing, sleep disturbance , menopausal women, pometone

الخلاصة

اعراض المحرك الوعائي، مثل الهبات الساخنة(الشعور بالحرارة) والتعرق الليلي، شائعة جدا خلال المرحلة الانتقالية ما بعد انقطاع الطمث .واحد من العلاجات البديلة المهمة هي الأطعمة أو المكملات الغذائية الغنية بالفايتواستروجين.

الهدف من الدراسة

لتقييم فعالية وسلامة ومقبولية البوميتون للحد من التعرق، والهبات الساخنة، واضطراب النوم في سن حول الياس ومابعد سن الياس

الطرق

تضمنت الدراسة 44 امرأة في سن حول الياس ومابعد سن الياس. تم اعطائهن 500 ملغم مرتين يوميا من دواء بوميتون لمدة شهر واحد.

النتائج

ان معدل الشعور بالحرارة والتعرق انخفض لدى المريضات من 8.11 قبل العلاج الى1.36 بعد شهر من العلاج. وان معدل الأضطرابات في النوم انخفض من 4.4 قبل العلاج الى1.22 بعد شهر من العلاج .

الاستنتاج

ان البوميتون مؤثر, أمين ورخيص لعلاج الشعور بالحرارة والتعرق واضطرابات النوم عند النساء حول سن الياس وبعده.

الكلمات المفتاحية:التعرق, الهبات الساخنة,اضطراب النوم,النساء في سن الياس, بوميتون.

Introduction

Natural menopause specifically, is confirmed after 12 consecutive months of amenorrhea in the absence of any obvious, pathological cause (NAMS).(2010). Surgical menopause results following surgical removal of the ovaries. In either instance, one result of the declining estrogen concentrations is the occurrence of vasomotor symptoms (VMS) that include hot flush and night sweats. Vasomotor

symptoms including hot flashes and night sweats occur in as many as 68.5% of women as a result of menopause (Blumel *et al*.,2011). While the median duration of these symptoms is 4 years, approximately 10% of women continue to experience VMS as many as 12 years after their final menstrual period (Politi *et al*.,2008). Severe VMS occur in 10.8% of women in perimenopausal time frame, in 12.3% of women during early menopause (1-4 years), and in 11.5% of women in late menopause defined as greater than 5 years from the final menstrual period (Blumel *et al*.,2011)

The prevalence and severity of VMS is greater in women who are surgically menopausal compared to women experiencing natural menopause (Politi *et al*.,2008). As such, VMS have a significant impact on the quality of life and overall physical health of women experiencing VMS, leading to their pursuance of treatment to alleviate these symptoms. Management of VMS includes lifestyle modifications, some herbal and vitamin supplements, hormonal therapies including estrogen and nonhormonal therapies including clonidine, gabapentin, and some of the serotonin-norepinephrine reuptake inhibitors (Elena *et al*., 2012). VMS are theorized to result from dysfunction in the woman's tightly controlled temperature circuitry, leading to exaggerated activation of heat dissipation responses such as peripheral vasodilatation and sweating (Deecher *et al*.,2007). Hormone replacement therapy remains the most effective treatment for VMS. According to the most recent Cochrane review, hormone therapy reduces the frequency and severity of hot flashes by 75%-79 % (Maclennan *et al*.,2004). For decades, estrogen was used as a component of hormone replacement therapy to treat menopausal symptoms and for anticipated preventive health benefits in women with progesterone, or as a monotherapy hormone treatment in women after hysterectomy, but thereafter studies reported that long term estrogen increase the prevalence of cardiovascular events and breast cancer, many patients and researchers have looked into alternative treatments such as food or products containing phytoestrogens. Phytoestrogens are weak plant derived estrogens that are structurally similar to estrogen hormones produced by the body and bind to the estrogen receptors, acting like hormone regulators (Betty, 2009). The food most commonly known to contain phytoestrogens is soy, but beans, peas, lentils, and whole grains and seeds, especially flaxseed, rye, and millet, also contain these plant estrogens (Somjen *et al*., 2005). Pomegranate tree has been used extensively as indigenous medicine in many cultures, at least as far back as 1550 B.C (Wren, 1988) The oil from the seeds contains about 80% of a rare 18-carbon fatty acid, or punicic acid (Longtin., 2003). Also present in this oil are isoflavonic phytoestrogens (genistein & daidzein) and a phytoestrogenic coumestan called coumestrol (Moneam *et al*., 1988). Pomegranate is one of the only plants in nature known to contain the sex steroid estrone and has the highest botanical concentration of the steroid estrone at 14 mg/kg dried seed (Heftmann , 1966). The role of phytoestrogens has stimulated considerable interest since populations consuming a diet high in isoflavones such as the Japanese appear to have lower rates of menopausal vasomotor symptoms, cardiovascular disease, osteoporosis, and breast, colon, endometrial and ovarian cancers. The normal Japanese diet contains 200mg of phytoestrogens per day in comparison to the average Western diet, which contains less than 1mg. Efficacy for vasomotor symptom relief is lower than with traditional HRT (maximally 60-70% symptom reduction compared with 90-100% with traditional HRT). Beneficial effects have been shown on cardiovascular risk markers such as lipids and arterial compliance and on bone markers (density) , with possible SERM (selective estrogen receptor modulator) type effects (Somjen *et al*., 2005). Pomegranate juice and seed oil contain phytoestrogenic

compounds that have been shown to exhibit antioxidant activity (Schubert *et al*., 1999). Exert anti-proliferative effects on human breast cancer cells (Kim *et al*., 2002), significant anti-tumor activity against human prostate cancer (Albrecht *et al*., 2004), and heart disease prevention (Aviram *et al*., 2004). Also, pomegranate has been recommended as medicinal food for treatment of Acquired Immune Deficiency System (AIDS) patients (Lee *et al*., 1998).

Patients and Methods

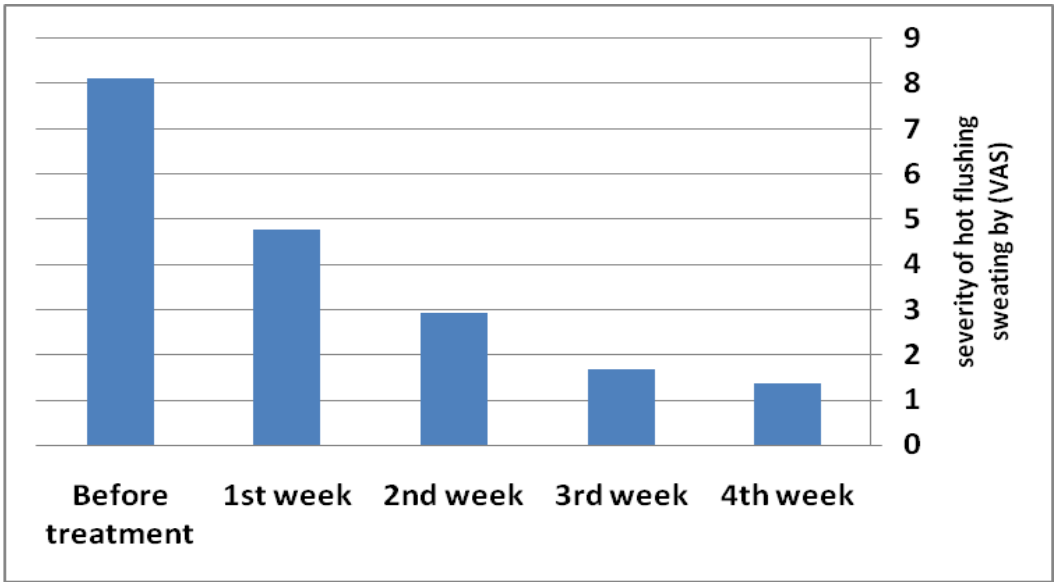
This is a cross-sectional randomized clinical therapeutic trial done at private clinic for a period extended from January 2013 to January 2014, involving 44 women; 7 of them were perimenopausal and the remaining 37 were postmenopausal, their age range from (40-65) years with means of 48.91 years ±6.38 SD. Four of the participitants had premature menopause. And 3 women had history of hysterectomy few months ago. They presented with hot flush, sweating and/or disturbances of their sleep. A verbal consent was obtained from all the participitants before the start of treatment. All the women took 500mg pometone capsules twice per day for a period of one month. All the patients were asked to record the severity of their hot flush , night sweat on a visual analogue scale twice per week ,the scale consisted of a 10 cm horizontal line marked from 0 (denoting absent symptoms) to 10 (denoting worst symptoms) and sleep disturbance by counting the numbers of awaking from sleep per night. Patients were assigned to receive 4 weeks of pometone capsule 500 mg twice per day. A reduction in scores of ≥ 50% was considered as the desired improvement in symptoms during treatment. Response to treatment was measured by using analysis of variance (ANOVA) test. P value <0.05 was considered as level of significance.

Result

The mean hot flush, sweating score before treatment was 8.11±1.72. After one week of treatment, it became 4.77±2.22. This score continued to decrease reaching to 2.93±2.13 by the end of second week; at the end of 3ed week the score became 1.68±2.12. The score continued to decrease reaching to 1.36 ±2.10 in the end of the fourth week. P value was < 0.0001,considered extremely significant as shown in table (1) and figure (1).

Table (1): Comparison response (hot flushing,sweating) to pometone treatment with one week interval. P value <0.05 was considered as level of significance.

	Time	No.	Mean of Hot Flushing, Sweating	SD	P	95% Confidence Interval
Pair I	Before	44	8.11	1.72	P<0.001	2.124-4.556
	1st week	44	4.77	2.22		
Pair 2	1st week	44	4.77	2.22	<0.001	0.6238-3.056
	2nd week	44	2.93	2.13		
Pair 3	2nd week	44	2.93	2.13	<0.001	0.03378-2.466
	3rd week	44	1.68	2.12		
Pair 4	3rd week	44	1.68	2.12	P>0.05	-0.8962-1.536
	4th week	44	1.36	2.10		
Pair 5	Before	44	8.11	1.70	P<0.001	5.534-7.966
	4th week	44	1.36	2.10		



Figure(1) patients response to treatment with one week interval.

The mean of sleep disturbance (numbers of awaking from sleep) score before treatment was 4.40±3.03. After one week of treatment, it became 4±2.94. This score continued to decrease reaching to 2.70±2.47 by the end of second week; at the end of 3ed week the score become 1.61±1.95. The score continued to decrease reaching to 1.22 ±1.80 in the end of the fourth week. P value was < 0.0001,considered extremely significant as shown in table (2) and figure (2). No side effect was reported during the course of this study.

Table (2): Comparison response (sleep disturbance) to pometone treatment with one week interval. P value <0.05 was considered as level of significance.

	Time	No.	Mean Number of Sleep Disturbance	SD	P	95% Confidence Interval
Pair I	Before	44	4.40	3.03	P>0.05	-1.064-1.864
	1st week	44	4	2.94		
Pair 2	1st week	44	4	2.94	P>0.05	-0.1641-2.764
	2nd week	44	2.70	2.47		
Pair 3	2nd week	44	2.70	2.47	P>0.05	-0.3741-2.554
	3rd week	44	1.61	1.95		
Pair 4	3rd week	44	1.61	1.95	P>0.05	-1.074-1.854
	4th week	44	1.22	1.80		
Pair 5	Before	44	4.40	3.03	P<0.001	1.716-4.644
	4th week	44	1.22	1.80		

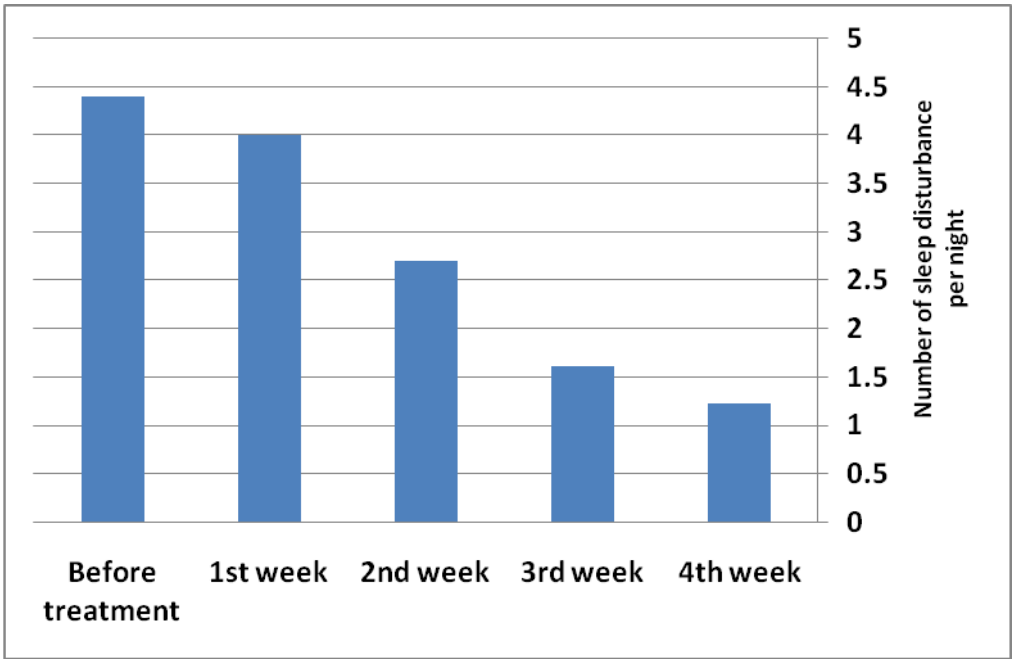


Figure (2): Comparison response (sleep disturbance) to treatment with one week interval .

Discussion

VMS are a disturbing part of menopause for many women and have a significant impact on the quality of life. Although hormone therapy is the most effective treatment for menopause related VMS, many women either cannot or do not wish to take this treatment. Therefore, the availability of effective alternative therapies for the treatment of VMS is of great importance such as phytoestrogens (Elena *et al*., 2012). Pomegranate is one of the only plants in nature known to contain the sex steroid estrone and has the highest botanical concentration of the steroid estrone at 14 mg/kg dried seed (Heftmann , 1966). Certain study showed the comparison with the placebo group, participants in the promensil group were 41%(isoflavones) but not in the rimostil group, thus 34% reduced hot flashes more rapidly (Tice *et al*., 2003). In our study the visual analogue score for hot flush before treatment was 8.11±1.72 decrease to 1.36 ±2.10 after 4 weeks treatment with pometone. While the score for sleep disturbances before treatment was 4.40±3.03 decrease to 1.22 ±1.80 after 4 weeks treatment with pometone capsules. The result of our study was in contrast to (Krebs *et al*., 2004) study, in which they found that phytoestrogens available as soy foods, soy extracts, and red clover extracts did not improve hot flushes or other menopausal symptoms. In an Italian study involve 51 women with severe hot flashes, the average number of hot flashes in the soy drinkers declined from 11 per day to six. In the placebo group it dropped from 11 to eight, which was statistically significant. But the soy had no effect on symptoms like anxiety, headaches or insomnia (David ,1999)

Other study included 30 women who took 40 grams of crusted flax seed daily for 6 weeks. The mean decrease in the hot flash frequency was 50% from 7.3 to 3.6 (Pruthi *et al*., 2007), in this study some side effects were recorded, 50% experienced mild or moderate abdominal distention, 30% of the them showed mild diarrhea and 20% did not complete the study because of side effects. While in our study there was no side effects of pometone, and no patient left the treatment because of side effects. Because phytoestrogens act similar to estrogen in certain tissues in the body, they

theoretically could increase the risk of breast cancer, and overall safety required further assessment. Reassuringly, however, the authors in the Cochrane Database Systematic Review did not find evidence that treatment with phytoestrogens caused estrogenic stimulation of the endometrium when used for up to two years (Lethaby *et al.*, 2007; Tice *et al*., 2006; Nelson *et al*., 2006)

A recent review indicated that black cohosh root extract demonstrated good efficacy in relieving menopausal symptoms, such as vasomotor instability, with little or no toxicity (Hardy ,2000). Another study showed that black cohosh had estrogen like activity and some efficacy in treating vasomotor menopausal symptoms, possibly by reducing the secretion of luteinizing hormone (Petho,1987). Phytoestrogens formulations and herbal products may be attractive alternatives for perimenopausal and postmenopausal women who want to delay use of HRT because of concerns about estrogen's effects on the progression of breast and uterine neoplasm and its tendency to increase coagulability (Lissin *et al*., 2000). However there is insufficient safety data exist to support long-term therapy with phytoestrogens and other herbal medications (Edyta *et al*., 2000) .

Conclusions

1. Pometone is effective, safe and cheap drug to reduce the hot flashes and sweating in perimenopausal and postmenopausal women.
2. Pometone also is effective in improvement of sleep disturbances in peri and postmenopausal women.
3. No side effects of pometone were noted during the study.

References

Albrecht, M., W. Jiang, J. Kumi-diaka, E.P. Lansky, L.L. Gommersall, A. Patel, R.E. Mansel, A.A. Geldof and M.J. Campbell, 2004. Pomegranate extracts potently suppress proliferation, xenograft growth and invasion of human prostate cancer cells. J. Med. Food, 7: 274–283

Aviram, M., M. Rosenblat, D. Gaitini, S. Nitecki, A. Hoffman, L. Dorufeld, N. Volkova, D. Presser, J. Attias and H. Liker, 2004. Pomegranate juice consumption for 3 years by patients with carotid artery stenosis reduces common carotid intima-media thickness, blood pressure and LDL oxidation. Clin. Nutr., 23: 423–433

Betty Wang, MD. Phytoestrogens and menopause. January 20, 2009.

Blumel JE, Chedraui P, Baron G, et al. A large multinational study of vasomotor symptom prevalence, duration, and impact on quality of life in middle-age women. Menopause. 2011; 18(7): 778-785.

David Schardt. Phytoestrogens for menopause.Menopause 6, 7, 1999.

Deecher DC, Dorries K. Understanding the pathophysiologyof vasomotor symptoms(hot flush and night sweats)that occur in perimenopause, menopause, and postmenopause life stages. Arch Womens Ment Health. 2007; 10: 247-257.

Edyta J. Frackiewicz, Neal R. Culter.Women's health care during the perimenopause.J. Am. Pharm. Assoc. 2000; 40(6).

Elena M Umiand and Laura F alconieri. Treatment options for vasomotor symptoms in menopause: focus on desvenflafaxine. Int J Womens Health. 2012; 4: 305-319.

Hardy ML. Herbs of special interest to women. J Amer Pharm Assoc. 2000; 40:234-42.

Heftmann, E., S.T. Ko and R.D. Bennet, 1966. Identification of estrone in pomegranate seeds. Phytochem., 5: 1337–1340

Kim, N.D., R. Mehta, W.P. Yu, I. Neeman, T. Livney, A. Amichay, D. Poirier, P. Nicholls, A. Kirby, W. Jiang, R. Mansel, C. Ramachandran, T. Rabi, B. Kaplan and E.P. Lansky, 2002. Chemopreventive and adjuvant therapeutic potential of pomegranate (Punica granatum) for human breast cancer. Breast Cancer Res. Treat., 71: 203–217

Krebs EE, Ensrud KE, MacDonald R, Wit TJ. Phytoestrogens for treatment of menopausal symptoms: a systematic review. Obstet Gynecol. 2004 Oct; 104(4): 824-36.

Lee, J. and R.R. Watson, 1998. Pomegranate: A role in health promotion and AIDS? In: Watson, R.R. (ed.), Nutrition Food and AIDS, p: 179. CRC Press, Florida, USA

Lethaby AE, Brown J, Marjoribanks J, Kroneberg F, Roberts H, Eden J. Phytoestrogens for vasomotor symptoms. Cochrane Database of Systematic Reviews 2007, Issue 4. Art. No: CD001395. DOI: 10.1002/14651858. CD001495. Pub3.

Lissin LW, Cooke JP. Phytoestrogens and cardiovascular health. J Am Coll Cardiol. 2000; 35(6):1403-10.

Longtin, R., 2003. The pomegranate: Nature's power fruit? J. Natl. Cancer Inst., 95: 346–348.

Maclennan AH, Broadbent JL, Lester S, Moore v. Oral estrogen and combined estrogen/progestogen therapy versus placebo for hot flushes. Cochrane Database Syst Rev. 2004; 4: CDoo2978.

Moneam, N.M.A., A.S. El-Sharasky and N.M. Badereldin, 1988. Oestrogen content of pomegranate seeds. J. Chromatogr., 438: 438–442

(NAMS) The North American Menopause Society (NAMS).(2010). Estrogen and progestogen use in postmenopausal women: 2010 position statement of the North American Society. Menopause. 2010; 17(2): 242-255.

Nelson HD, Vesco KK, Haney E, Fu R, Nedrow A, Miller J, Nicolaidis C, Walker M, Humphrey L. Nonhormonal therapies for menopausal hot flashes: systematic review and meta-analysis. JAMA 295(17): 2057-2071, 2006.

Petho A. Climacteric complaints are often helped with black cohosh. Arztliche Praxis. 1987; 47:1551-3.

Politi MC, Schleinitz MD, Col NF. Revisting the duration of vasomotor symptoms of menopause: a meta-analysis.J Gen Intern Med. 2008; 23(9): 1507-1513.

Pruthi S, Thompson SL, Novotny PJ, Barton DL, Kottschade LA, Tan AD, Loprinzi CL. Pilot evaluation of flaxseed for the management of hot flashes. J Soc Inegr Oncol. 5(3): 106-112, 2007.

Schubert, S.Y., E.P. Lansky and I. Neeman, 1999. Antioxidant and eicosanoid enzyme inhibition properties of pomegranate seed oil and fermented juice flavonoids. J. Ethnopharmacol., 66: 11–17

Somjen D, Katzburg S, Livne E, Yoles I. DT56a (Femarelle/Tofupill) stimulates bone formation in female rats'.BJOG 2005; 112:981-985.

Tice JA, Ettinger B, Ensrud K, Wallace R, Blackwell T, Cummings SR. Phytoestrogens supplements for the treatment of hot flashes: the isoflavones clover extracts study: a randomized controlled trial. JAMA 2003 Jul 9; 290(2): 207-14.

Tice JA, Grady, D. Alternatives to estrogen for treatment of hot flashes. JAMA 295(17): 2076-2078, 2006.

Wren, R.C., 1988. Potter's New Cyclopedia of Botanical Drugs and Preparations. C.W. Daniel Company, Essex, UK.