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Comparison the efficacy of *Hypericum perforatum* and *vitex agnus-castus* in hot flushes: A double-blinded randomized controlled trial

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Original Article

Abstract

BACKGROUND: Treating hot flushes in middle-aged women is an important health issue. Recently, *Hypericum perforatum* and *vitex agnus-castus* were investigated to decrease hot flushes. This study was conducted to compare the efficacy of *Hypericum perforatum* and *vitex agnus-castus* in hot flushes among menopausal women.

METHODS: This was a randomized, double-blinded, controlled trial. The Hypericum perforatum group received 330 µg Hypericum perforatum and second group received vitex agnus-castus in the same tablet forms. Data were analyzed using repeated measurement for comparing Greene Climacteric Scale.

RESULTS: Trend of Greene Climacteric Scale and hot flushness attack were decreased in both groups and it presented a decreasing trend within two months; however, no statistically significant difference was observed between the two groups.

CONCLUSION: It seems that Hypericum perforatum and vitex agnus-castus could be similarly effective in decreasing hot flushes. These two medicines did not have any special severe side effects.

KEYWORDS: Hypericum, Menopause, Plants, Randomized Controlled Trial, Vitex Agnus-Castus, Herbal Drug

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Introduction

Treating hot flushes in middle-aged women is an important health issue. Now, hormone therapy is used as the main method of treating menopause symptoms; however, these hormones may cause some side effects and complications such as temper changes, abnormal uterine bleeding, flatulence, breast tenderness, nausea, and headaches.[1,2]

Recently, a tendency toward alternative and complementary herbal treatment methods has emerged.[3,4] There are also some alternative treatment methods that use herbal medicines to decrease menopause complications including *Ginseng, Hypericum perforatum* (St John's wort), *vitex agnus-castus* (chaste tree/berry), black cohosh and *Dong quai (Angelica sinensis)*. Among these methods, Hypericum perforatum and vitex agnus-castus are the most favored.[5-7] These two herbs contain substances with selective serotonin reuptake inhibitors (SSRIs) or serotonin norepinephrine reuptake inhibitors (SNRIs). SNRIs are used as anti-depression drugs and they are used for treating menopause

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complications as well.[8,9] Therefore, Hypericum perforatum is used as an anti-depression drug in some countries and due to its two products i.e. Hypericin and Hyperforin which prevent and control mono-amino oxides enzyme, It exerts anti-depression effects.[10,11]

Vitex agnus-castus which is another herbal medicine could decrease hot flushes via its dopaminergic effects. Moreover, under-activity of dopaminergic system could cause psychological dysfunctions and it has been proved that dopaminergic effects of Vitex agnus-castus could be effective in decreasing emotional symptoms of menopause.[7] In previous studies, Vitex agnus-castus has decreased duration, severity and other complications of hot flushes.[12,13] In the United States and Europe, Vitex agnus-castus is used for treating premenstrual syndrome and hyperprolactinemia.[14] Hence, considering previous studies, this study was conducted to compare the efficacy of Hypericum perforatum and vitex agnus-castus in hot flushes among menopausal women.

Materials and Methods

This was a randomized, double-blinded, controlled trial. Protocol for the study was approved by the Ethical Review Board and the Dean of Faculty, the Deputy of Educational Affairs, and the Educational Affairs Administration of the University of Shiraz. Participants were selected in an outpatient academic medical center in Zeinabieh Hospital (Shiraz, Iran) from April 2009 to March 2010 by convenience sampling method. Sample size calculated 26 subjects in each group according to the assumption of type 1 error (alpha) 5%, power 90% and mean of difference between the two groups equal to 10 score [standard deviation (SD) ± 11]. In this study, 64 subjects were evaluated (Figure 1).

Informed consent was obtained and all the participants were ensured about the confidentiality of information during and after the study. Inclusive criteria were 1) age between 45-65, 2) last menstrual period 1 year ago, 3) serum follicle stimulating hormone level of more than 40 mIU/ml, and 4) informed consent. Exclusive criteria were 1) existing use of Hypericum or Vitex Agnus-castus, 2) severe diseases (e.g. heart, liver, kidney or metabolic diseases ,psychiatric disorders), 3) abnormal thyroid-stimulating hormone 4) smoking, and 5) using hormones ,vitamins or supplements drugs.

The participants were allocated by simple randomization by a nurse. Each patient received a package contain one group drug. These packages were prepared by the nurse. The Hypericum perforatum group received 160 mg Hypericum perforatum 3tab/day (Goldaru Co, Iran) and the second group received vitex agnus-castus 3tab/daily in the same tablet forms for 8 weeks.

Outcome of the study was Greene Climacteric Scale and its factors[15,16] and hot flushness attacks. Assessment of Greene Climacteric Scale and hot flushness attacks was done by one blinded investigator at the baseline, first and second months from the interview. Greene Climacteric Scale that developed by Green, measures psychological, somatic and vasomotor symptoms.[16]

Data were entered into SPSS for Windows (version 11.5, SPSS Inc., Chicago, IL, USA); independent t test was also used for comparing quantitative variables in the two groups and repeated measurement was used for comparing the trend of Greene Climacteric Scale and its factors during different visits in the two groups according to per-protocol analysis.

Results

In this study, 76 subjects participated with a mean age of 52.9 ± 4.7 years. The mean postmenopausal period was 4.2 ± 3.2 years. Body mass index (BMI) was 26.7 ± 4.6. The mean number of children was 4.3 ± 2 and the mean menarche age was 13.5 ± 1.6 years. There was no

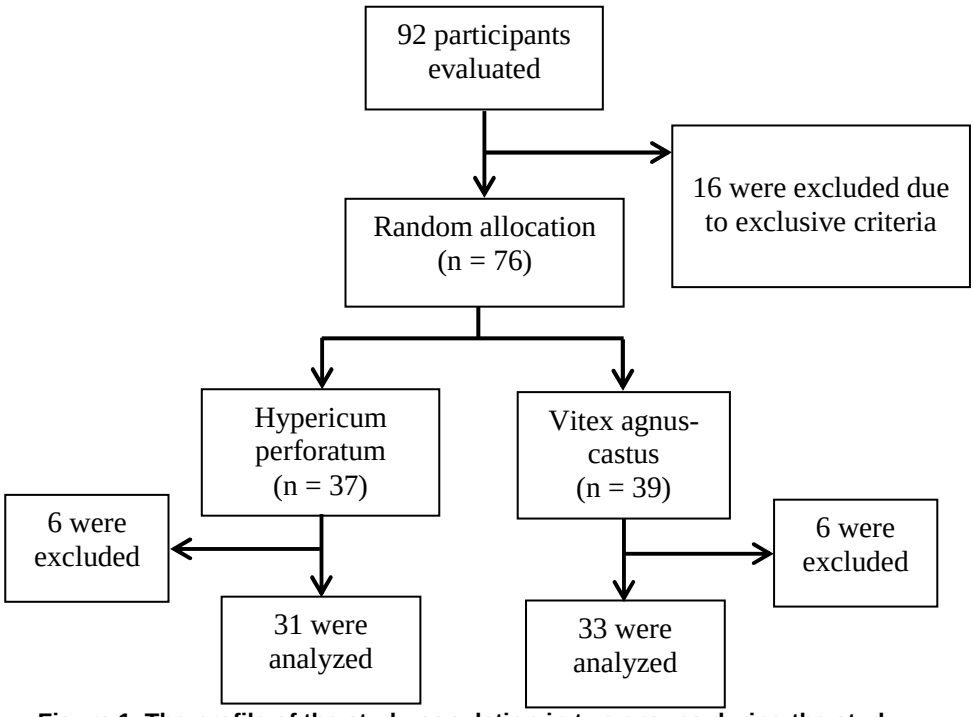

Figure 1. The profile of the study population in two groups during the study

statistically significant difference between the two groups regarding age, menopause age, menarche age and number of children.

The mean number of hot flushes was 3.6 ± 0.8 times. 62 subjects (81.6%) were married. No statistically significant difference was observed between the two groups of Hypericum perforatum and vitex agnus-castus regarding these variables (Table 1).

The general trend of Greene Climacteric Scale and its domains dropped in both groups and it presented a decreasing trend within two months; however, no statistically significant difference was observed between the two groups and the trend of reduction in both groups was similar. Both groups had a descending trend in hot flushes as well but there was no statistically significant difference between the two groups (Table 2) (Figure 2) and (Figure 3). Moreover, the percentage of successful treatment measured by Greene Climacteric Scale and its domains did not have any statistically significant difference between the two groups and at least 38% improvement was observed in each group. The maximum percentage of hot flush improvement was (58.7% and 55.5%) and the lowest percentage was in somatic domain (38.1% and 38.2%) (Table 3).

Some unexpected side effects were observed in the study illustrating in table 4. In the first month, some complications and side effects were observed in four subjects in the Hypericum perforatum group and four other subjects in the

Table 1. Comparison of demographic characteristics of the two groups

Variables	Hypericum perforatum	Vitex agnus-castus	P
Age	53.2 ± 4.7	52.7 ± 4.8	0.63
BMI	27.2 ± 4.8	26.2 ± 4.4	0.34
Age of menarche	13.4 ± 1.6	13.7 ± 1.6	0.39
Years after menopause (median)	4 (1-12)	3 (1-14)	0.65
Number of Children (median)	4 (0-8)	4 (1-10)	0.97
Married	29 (78.4%)	33 (84.6%)	0.48

Analysis was done by independent t test and mean ± SD; BMI: Body mass index; SD: Standard deviation

Table 2. Changes of value of Greene Climacteric Scale and its factors in the two groups during the study

Factors	Time	Hypericum perforatum	Vitex agnus-castus	P
Total	Baseline	29.54 ± 8.5	29.25 ± 8.7	0.88
	Month 1	22.13 ± 6.8	21.12 ± 7.0	0.53
	Month 2	15.86 ± 5.2	15.94 ± 5.6	0.95
Psychological	Baseline	15.08 ± 5.3	14.84 ± 5.9	0.85
	Month 1	11.1 ± 4.1	10.94 ± 4.8	0.87
	Month 2	7.83 ± 4.0	8.17 ± 3.8	0.7
Somatic	Baseline	6.81 ± 3.3	6.82 ± 3.3	0.99
	Month 1	5.27 ± 2.8	4.71 ± 2.5	0.37
	Month 2	4.05 ± 2.1	4.1 ± 2.4	0.92
Vasomotor	Baseline	6.64 ± 1.5	6.64 ± 1.7	0.98
	Month 1	4.86 ± 1.6	4.69 ± 2	0.48
	Month 2	3.56 ± 1.5	3.25 ± 2.2	0.34
Hot flushness	Baseline	3.67 ± 0.74	3.58 ± 0.84	0.64
	Month 1	1.59 ± 1.38	1.58 ± 1.63	0.98
	Month 2	1.4 ± 1.1	1.53 ± 1.71	0.68

Analysis was done by independent t test and mean ± SD; SD: standard deviation

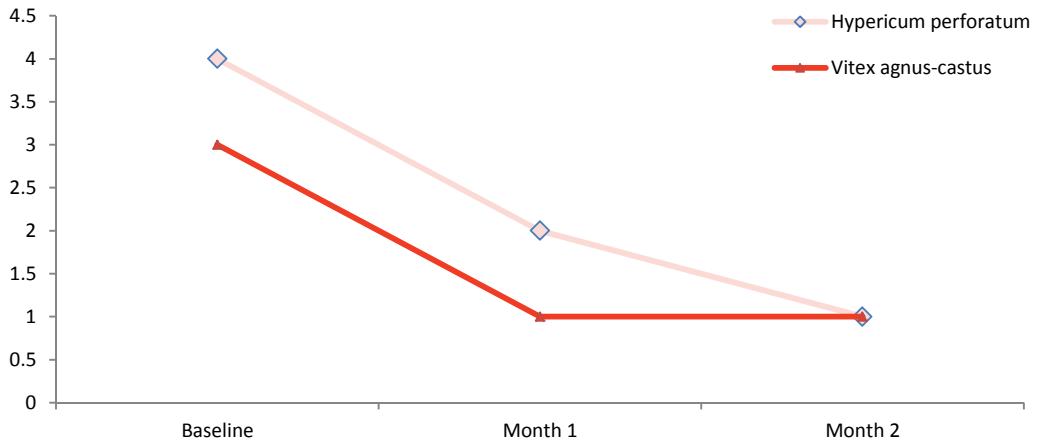

Figure 2. Comparing the frequency of hot flushness trend between the two groups

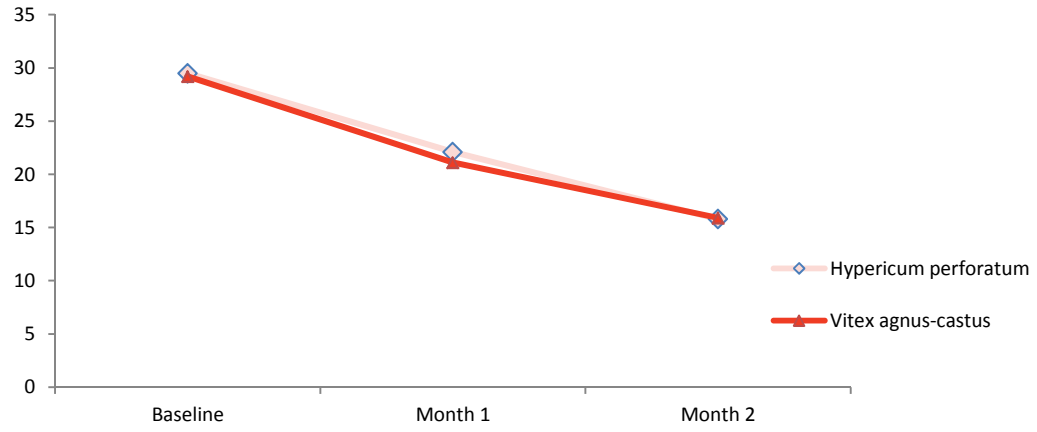

Figure 3. Comparison of Greene Climacteric Scale trend between the two groups

Table 3. Comparing the percentage of improvement in Greene Climacteric Scale and its factors and hot flushness between the two groups

Index	Hypericum perforatum	Vitex agnus-castus	P
Greene Climacteric Scale	45.5 ± 12.0	44.8 ± 14.5	0.82
Psychological	48.3 ± 16.9	44.1 ± 16.8	0.28
Somatic	38.1 ± 23.7	38.2 ± 23.6	0.98
Vasomotor	45.8 ± 21.0	49.4 ± 34.9	0.58
Hot flushness	58.7 ± 34.0	55.5 ± 49.9	0.73

Analysis was done by independent t test and mean ± SD; SD: standard deviation

Table 4. Occurrence of side effects in the two groups during the study

Side effect	Side effects leading to withdrawal				Side effects not leading to withdrawal			
	Hypericum perforatum		Vitex agnus-castus		Hypericum perforatum		Vitex agnus-castus	
	First month	Second month	First month	Second month	First month	Second month	First month	Second month
Pain over eyes	0	1	0	0	0	0	0	0
Rashes	1	0	0	0	0	2	0	0
Nausea	0	1	0	0	3	3	1	0
Dry month	0	0	0	0	0	0	0	0
Dizziness	0	0	2	1	2	3	4	1
Loss of appetite	0	0	0	0	0	0	0	0
Headache	1	0	1	1	4	3	4	1
Lethargy	1	0	0	0	0	0	0	0
Constipation	1	0	1	0	4	0	2	1
Diarrhea	0	0	0	0	2	1	2	2
Total	4	2	4	2	15	12	13	5

vitex agnus-castus group and consequently they discontinued medicines. Common mild side effects were headache and constipation in the Hypericum perforatum group and headache and dizziness in the vitex agnus-castus group.

Discussion

Our results showed that Hypericum perforatum and vitex agnus-castus could reduce Greene Climacteric Scale in menopausal women. This improvement was observed in all items of Greens questionnaire but there was no statistically significant difference between the two groups. Previous studies have supported that Hypericum perforatum is useful in relieving the symptoms of menopausal syndrome.[7,9]

In our study, the percentage of improvement in Greene Climacteric Scale was 45.5% and 44.8% in Hypericum perforatum and vitex agnus-castus groups, respectively. There was no statistically significant difference between the two herbal drugs. The reasons for using vitex agnus-castus in our study were the efficiency, safety, and inexpensiveness of this combination since Hypericum perforatum is extensively found in the mountains of Iran. Furthermore, previous studies suggested further investigation about these herbal drugs.[7]

Previous studies compared Hypericum perforatum and placebo[7,9] but there are few studies comparing Hypericum perforatum and vitex agnus-castus.[7] Abdali et al.[9] showed that Hypericum perforatum was an effective treatment for vasomotor symptoms and hot flushes in premenopausal or postmenopausal women; this result was similar to our study results. In Abdali et al.[9] women who had used Hypericum perforatum showed more improvement in their frequency of hot flushes than the placebo-receiving group.

Al-Akoum et al.[10] indicated that Hypericum perforatum ethanolic extract can improve 30% of hot flushes. In addition, they found improvements in quality of life and its domains (vasomotor, physical, and psychosocial aspects) using the menopause-specific quality of life

(MENQOL) questionnaire. However, they suggested that further studies with larger clinical trials are needed.

Besides, our findings are in accordance with Grube et al.[17] They reported improvement in psychological and psychosomatic symptoms in menopausal women. Van Die et al.[7] measured Hypericum perforatum with vitex agnus-castus within menopausal symptoms. They showed that Hypericum perforatum and vitex agnus-castus were not superior to placebo in alleviating menopausal symptoms.

In a study[18] concerning the effects of vitex agnus-castus on hot flushes and nightly sweating among 50 pre and postmenopausal women, it was found that vitex agnus-castus was more efficient than the placebo. In Chopin [19], 33% showed major improvements and 36% mild to moderate improvements in symptoms. The most important improvement after hot flushes was regarding emotional symptoms. In our study, the most significant improvement was observed in hot flushes and then in psychological symptoms.

Based on the results of our study and other studies, it seems that Hypericum perforatum and vitex agnus-castus could be similarly effective in decreasing hot flushes. Therefore, taking these two substances could be helpful. These two medicines do not have any special severe side effects and their observed complications such as headache might be removed by simple medicinal treatments. Similar side effects have been observed in other studies as well.[10]

Conclusion

It seems that Hypericum perforatum and vitex agnus-castus could be similarly effective in decreasing hot flushes. These two medicines do not have any special severe side effects.

Conflict of Interests

Authors have no conflict of interests.

Acknowledgments

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