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Research paper

Effect of *Viola odorata* vaginal suppository on menopausal vaginal atrophy: A Triple-blind randomized clinical trial

Fataneh Amindehghan [a], Samira Shahbazzadegan [a 1], Susan Houshmandi [a], Lili Amani [b]

[a] Department of Midwifery, School of Nursing and Midwifery, Ardabil University of Medical Sciences, Ardabil, Iran
[b] Department of Traditional Pharmacy, School of Persian Medicine, Tehran University of Medical Sciences, Tehran, Iran

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Abstract

Background

Vaginal atrophy is an often neglected symptom of menopause, which affected about 90% of women. Women tend to use alternative medicine such as herbs rather than estrogen replacement therapy to alleviate it. *Viola odorata* contains flavonoids in the form of phytoestrogens and probably can be effective in treatment of vaginal atrophy. This study was conducted to investigate the effect of *Viola odorata* vaginal suppository on menopausal vaginal atrophy.

Methods

This approved triple-blind randomized clinical trial, 8-weeks, study was conducted on 60 postmenopausal women from September 2022 until January 2023. Eligible participants were divided randomly into two groups of treatment (*Viola odorata* suppository) and placebo (glycerin suppository) after obtaining informed consent. Data of the socio-demographic questionnaire, vaginal pH, and vaginal maturation index (VMI) were collected before and at the end of the study. Subjective symptoms of vaginal atrophy (dryness, irritation, itching, and dyspareunia) were assessed before, 4^{th}, and 8^{th} weeks of intervention period by self-assessments. Data were analyzed using Independent t-test, Chi-square, Mann Whitney U, and Wilcoxon test by SPSS ver 23.

Results

There were no significant differences between the two groups at the beginning of the study in vaginal atrophy symptoms, vaginal pH, and VMI. Subjective symptoms of vaginal atrophy ($p<0.001$), vaginal pH ($p<0.001$), and VMI ($p<0.001$) were improved in the *Viola odorata* group 8 weeks of treatment.

Conclusion

Viola odorata vaginal suppository reduced the menopausal vaginal atrophy symptoms. Considering *Viola odorata* is a natural product with low cost, it can use in menopausal vaginal atrophy treatment.

Introduction

Menopause is one of the most important stages of a woman's life, which is characterized by changes in the level of sex hormones, cessation of menstruation, and infertility (Burger et al. 2007). Menopause occurs naturally in most women between the ages of 45 and 52 (Sussman et al. 2015). With the increase in life expectancy, the number of postmenopausal women is expected to reach 1.2 billion by 2030 worldwide and will increase by 47 million new cases each year (Johnson et al. 2019). Menopause is associated with many early and late symptoms (Speroff et al., 2020). Vaginal atrophy, as a late symptoms, refers to the structural changes in the vaginal epithelium caused by estrogen depletion. As a result of these changes, blood flow to the vagina and its moisture is decreased (Tan et al. 2012). 75% of postmenopausal women suffer from vaginal atrophy (Panjari and Davis, 2011). Vaginal atrophy leads to uncomfortable symptoms such as dyspareunia, vaginal dryness, burning and itching, and an increase in pH (Speroff et al., 2020). Vaginal atrophy can cause sexual dysfunction and have negative impact on women's quality of life. Considering to these symptoms appropriate intervention is necessary (Vizza et al. 2023).

There are different treatments for vaginal atrophy. Estrogen and hormonal drugs are the most common methods for the relief of vaginal atrophy (Karimi Afshar, 2015). There is an increasing concern regarding the side effects of hormones, so the desire for alternative treatments and complementary medicine including herbal treatments has been increased (Bae and Yoon, 2018, Lima et al., 2013, Poluzzi et al., 2014, Naumova and Castelo-Branco, 2018, Takacs et al., 2019, Sánchez-Borrego et al., 2014, Caruso et al., 2018).

Traditionally various herbal treatments have been provided to eliminate vaginal atrophy, *Viola odorata* is one of them. *Viola odorata* was also known as Banfsaj in Old Persian. This plant grows natively or naturalized in large areas from Europe and the Middle East to Central Asia and in North America. All the aerial parts of the *Viola odorata*, including the stem, flower, and leaf, have valuable active ingredients including flavonoids, mucilage, violin alkaloids, saponin, and cyclotides (Ahmed et al. 2017). Flavonoids belong to the category of phytoestrogens, which have estrogenic activity but do not have the side effects of estrogens (Lobo, 2007). Mucilage is a compound that dissolves in contact with the desired tissue and produces a viscous and gelatinous substance that has anti-inflammatory, moisturizing, and softening properties (Paul, 2014). Saponin stimulates and increases the production of hyaluronic acid in the deep layers of the skin for a long time (hyaluronic acid restores the moisture of the skin) and has antibacterial properties (Boyer et al. 2017). This plant is used orally to treat cough, hoarseness, chest pain, sore throat, bronchitis, nervous tension, insomnia, hysteria, Alzheimer's, and also increased sweating (Ahmed et al. 2017). In a study, the Nasal spray of *Viola odorata* was effective in healing dry eyes (Saffar Shahroodi et al. 2019). Another study found that *Viola odorata* increased memory and can be used to treat Alzheimer's (Saleem et al. 2021). This plant is also used topically to heal various skin diseases. Its syrup, used as an expectorant, reduced bronchial inflammation in pediatric medicine. So far, there was no reported harmful or side effects caused by the use of this plant (Ahmed et al. 2017).

Regarding of *Viola odorata* as a rich source of phytoestrogens in the forms of flavonoid, mucilage with moisturizing properties, and saponin in the form of hyaluronic acid, it is possible that this plant is effective in treatment of vaginal atrophy and considering lack of similar study in the literature, this study was conducted to evaluate the effect of *Viola odorata* vaginal suppository on the treatment of vaginal atrophy in postmenopausal women.

Section snippets

Ethical aspects

The experimental protocol was approved by the Health Science Center (HSC) ethical committee and is registered for Clinical Trials. The research was conducted according to the principles outlined in the Declaration of Helsinki on human medical experimentation. Written informed consent was obtained from all participants and is presented in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines.…

Study design and sample size

This Triple-blind randomized, 8-weeks, controlled clinical trial was…

Results

54 postmenopausal women have completed the study. Demographic information of the participants in the two groups are shown in Table 1. There was no significant difference between the control and treatment groups in demographic variables.

The vaginal atrophy symptoms in treatment and placebo groups at different times (before, 4^{th} weeks, and 8^{th} weeks of using suppositories), are shown in Table 2. Vaginal atrophy symptoms were significantly decreased in the placebo and treatment groups over time,…

Discussion

In this randomized, -controlled- clinical trial, the *Viola odorata* vaginal suppository reduced the menopausal vaginal atrophy symptoms. Although no study was found on the effect of *Viola odorata* on vaginal atrophy symptoms, its effect has been reported in several diseases. *Viola odorata* has an effect to treat cough, hoarseness, chest pain, sore throat, bronchitis, nervous tension, insomnia, hysteria, Alzheimer's, and increased sweating (Ahmed et al. 2017). Lotfi et al. (2021) also showed…

Conclusion

In this study, *Viola odorata* vaginal suppository reduced menopausal vaginal atrophy symptoms. *Viola odorata* is recommended as a cheap and natural product to treat menopausal vaginal atrophy. A study with more samples and a longer time is suggested.

The results of this research can be used in the field of education and clinical practice, including the training of midwifery students, employees and midwifery practitioners in health-therapeutic centers, women's clinic, menopause care and service…

Ethics approval and consent to participate

Ethics approval was obtained from the Ardabil University of medical sciences, Human Research Ethics Committee on 2022-07-27 (IR.ARUMS.REC.1401.111). Participants indicated their informed consent to participate in the study by filling out the informed consent form according to the Ardabil University Ethics Committee. Informed consent was

obtained from all subjects. The International Clinical Trials Registry platform's Main ID is (IRCT20220814055687N1) in the Central Register of Controlled Trials …

Consent for publication

Not applicable.…

Uncited references

(Bosak et al. (2019))…

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CRediT authorship contribution statement

Fataneh Amindehghan: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Samira Shahbazzadegan:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review &…

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.…

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Author's contributions

SS, FAD, and SH made substantial contributions to the conception and design of the study. LA, SS, FAD, and SH are responsible for the overall logistical aspect of the trial and general acquisition of data. SS drafted the manuscript. FAD and LA are local investigators for the participating sites and are responsible for the implementation of the study and the inclusion of participants. All authors critically revised the…

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1 0000-0002-0634-5355

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