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Treatment of Moderate to Severe of Premenstrual Syndrome with Echinophora platyloba

Masoumeh Delaram*[1]

1. Department of Midwifery, Faculty of Nursing and Midwifery, Shahr-e-Kord University of Medical Sciences, Shahr-e-Kord, Iran

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*Corresponding author at:
Department of Midwifery, Faculty of Nursing and Midwifery, Shahr-e-Kord University of Medical Sciences, Shahr-e-Kord, Iran.
E-mail:
masoumehdelaram@yahoo.com

Abstract

***Background*:** Premenstrual Syndrome (PMS) is the appearance of annoying symptoms, disrupting women's daily activities as well as inducing problems. Different treatment were suggested for its and the method with the least side effects will be preferred. The aim of this study was to determine the effect of *Echinophora platyloba* extract on PMS in the students of Shahr-e-Kord University Of Medical sciences in Iran.

***Materials and Methods*:** Sixty students having moderate to severe PMS, participated in a single-blind randomized clinical trial. The students were randomly assigned into two equal groups. The first group received the *Echinophora platyloba* (*E. platyloba*) extract and the second group received placebo. The Daily Record of Severity of Problem (DRSP) questionnaire was used to quantify PMS severity before and after the intervention. At the end of first and second cycles after the intervention, the severity of PMS was detected and compared with before intervention. Data analysis was performed by using Mann-Whitney *U*, Wilcoxon and Pearson correlation test.

***Results*:** There was not a significant difference in the severity of premenstrual syndrome between the *E. platyloba* and placebo group before the intervention (100.8±22.1 vs. 104.3±19.5). A significant difference was found between two groups after the intervention [(49.7±23.2 vs. 79.1±28.1), p=0.002].

***Conclusion*:** *E. platyloba* extract is probably effective in the treatment of premenstrual syndrome. Using of this herbal extract is suggested for the treatment of PMS.

Introduction

Premenstrual syndrome (PMS) is the appearance of physical and psychological symptoms recurring periodically before the menstruation and disappearing in the first days of menstruation [1, 2]. Headache, abdominal bloating, breast tenderness, sore muscles and joints, fatigue, lack of energy, change in appetite, and thirst are some of the physical symptoms. Psychological symptoms include anxiety, depression, irritability, nervousness, crying, poor concentration, aggression and suicidal tendencies [3, 4]. PMS is a psycho-endocrine disorder in which biological, psychological and social parameters play important roles. Symptoms usually appear in the last 7-10 days of cycle and during this time, most of women refuse to be present at work more than every other times, need to be rest and small number of them suffer from depression and have a great tendency to suicide [5]. PMS leads to deficiencies in job performance as well as disturbed relationships with spouse, children and others. A previous study reported 27.5% of women with premenstrual syndrome experienced lack of job efficacy, 22% suffered from relationship problems at work, 83% had conflict with spouse, 61% had conflict with children and 41% of them experienced disturbance in social communications [6].

Since the underlying pathophysiology of PMS is unknown, a variety of therapeutic protocols has been suggested. Non-pharmacological treatments including change in nutrition habits, reduction the in taking of salt and animal fat in diets, exercise, stress reduction and supporting system [1] Pharmacological treatments including GnRH analogues, spironolactone, danazol, alprazolam, mephenamic acid, gamalinoleaic acid, fluoxetine, vitamins, minerals, progesterone and serotonin reuptake inhibitors, are suggested [7]. Abstaining from sugar, alcohol, caffeine and augmenting dietary fruits, vegetables and grains have been prescribed. Triptophan, magnesium, potassium glauconite, calcium and certain pharmaceutical herbs have been reported to be effective in the treatment of PMS as well [8]. One study reported that *Hypericum perforatum* decreases the intensity of PMS [6]. Another study reported that Fennel and Chamaemelum are effective on treating of 3 symptoms of PMS [9]. Positive effects of *Agnus castus* for the treatment of PMS have also been reported [10]. *E. platyloba* belongs to the spiacese or Umbelliferae family and consists of four species including *E. cinerea*, *E. platyloba*, *E. orientalis* and *E. sibthorpiana*. Two former species are thought to grow exclusively in IRAN [11]. Platyloba spieces are used for flavoring the foods, cheese and yoghurt and known locally by different names such as Khosharize, Tigh Touragh, Tigh Masti, Koshander, Kouzang, Tanghez or Khousharouze [12]. In Chaharmahal-Bakhtiyari province, this herb grows actively from the beginning of September to the middle of October and then enters a phase of

hibernation. It is believed that the herb's appearance is strongly influenced by temperature and the height of Chahrmahal-Bakhtiari from the sea level [13]. The previous studies on *E. platyloba* have demonstrated that saponins, flavonids and alkaloid components are present and hydro-alcoholic its extract controls the growth of three types of bacteria and fungi [14]. It is noted that the extract taken from the herbs leaves is much more potent than the extract taken from the herb stem [13]. The other existing antibacterial components in the herb includes trans-b-ocimene (67.9%), furanone (62%) and myrcene (6%) [14]. The extract of *E. platyloba* has been shown to be effective in reducing contractions of the rat ileum and other anti-spasmodic effects of *E. platyloba* have been demonstrated [15]. The anti-fungal effects of *E. platyloba* on common dermatophytes were examined and the findings showed the various density of *E. platyloba* extract are effective on *Trichophyton schoenleinii* and *Trichophyton verrucosum* dermatophytes [12]. The effectiveness of this herb in treating *Candida albicans* fungal infections was reported to be less than that of amphotericin [13]. *E. platyloba* has been utilized traditionally in Charmahal-Bakhtiari for the reduction of premenstrual symptoms, but there has been no scientific study to date on the effect of *E. platyloba* on PMS. Thus the aim of this study was to investigate the effects of *E. platyloba* on premenstrual syndrome in students of Shahr-e-Kord University of Medical Sciences.

Materials and Methods

This study was a single blind randomized clinical trial enrolling as subjects a total of 250 students ranging in age from 18-25 years, who are currently attending the Shahr-e-Kord University of Medical Sciences. The study design was approved by the Ethical Review Board in the Shahr-e-Kord University of Medical Sciences. All of participants gave signed consent. The participants were requested to fill the Daily Record of Severity of Problems form (DRSP) two cycles before the intervention and the severity of PMS symptoms was evaluated for all subjects. DRSP is a standard tool for detecting the intensity of PMS and its validity and reliability have been approved by Borenstien [16]. This form determines the severity of PMS symptoms using five items, including: [anxiety symptoms (tension, emotional changes, irritation, reduction in concentration, and fear), depressive symptoms (depression, hopelessness, amnesia, crying, dizziness, mood disorders, sleep disorders, insomnia, isolation and lose of interest to daily activities), emotional symptoms (headache, sweating, hot-flashes, increased appetite, heart palpitations, fatigue, reduction of energy and inability to do daily activities), fluid and electrolyte retention symptoms (increase in weight, edema, breast tenderness, backache, abdominal cramps, and pain in muscles and joints) and somatic symptoms (acne, urinary frequency, constipation and inflammation of nose)] [16]. Based on the DRSP form, scores ranging from 0 to 4 were allocated to evaluate the severity of symptoms as it follows; 0: absence of symptoms, 1: mild (the women seldom has problems in daily activities, 2: moderate (the women has problem in doing daily activities, but can go to work or school), 3: severe symptoms (the woman is not able to do daily activities), and 4: very intense (the woman is confined to bed). All of the participants were also asked about their menstrual patterns; such as duration of menstruation, amount of bleeding, menstrual intervals, dysmenorrhea, family history of PMS, and use of drugs for the reduction of PMS. Finally sixty students with highest PMS scores, were selected and their PMS scores was evaluated at the first and second cycles before the intervention by DRSP form and then, they were randomly assigned into two equal groups. Randomization was accomplished using cards. Sixty sequentially numbered cards were used containing 30 card labeled as placebo and 30 cards labeled as *E. platyloba* extract. All of the cards were mixed together randomly and placed in the box. The first group received *E. platyloba* extract and the placebo group received sterile water. The amount of the given extract and the placebo was 30 drops, every 8 hours three days before and in 3 first days of menstruation. None of participants didn't take oral contraceptive pills. The Barriage Essence Company in prepared the extracts and placebo. For preparing the extract of *E. platyloba*, the leaves, flowers, and stem of the herb were used. After collecting and drying the herb, extracting was done in procolation way. Placebo was also prepared by using sterile water and its appearance was similar to *E. platyloba* extract. The students were blind about the kind of drugs throughout the study and at the end of first and second cycles after the intervention; the severity of PMS was evaluated again. Both groups were given written instructions as well as regular phone calls for proper use of extract and placebo and they were required to take medication for a period of two cycles and the effects of *E. platyloba* and placebo were evaluated at the end of each cycle and compared with before the intervention. Data were analyzed with Mann-Whitney *U*, Wilcoxon and Pearson correlation tests, through SPSS-11 software. The data were shown as Mean±SD, $p<0.05$ is considered statistically significant.

Results

In *E. platyloba* group, 4 and in placebo group, 3 of participants excluded the study due to the incomplete use of medications. Information on individual characteristics is presented in table 1, displaying no significant difference in age, body mass index (BMI), age at menarche, age at dysmenorrhea, and duration of menstruation between the two groups. The family history of PMS, amount of bleeding, and medication use for dysmenorrhea were found be similar in both groups. It was noted that ibuprofen was commonly taken for relieving of dysmenorrhea, by both groups. Two groups were also similar in terms of menstrual irregularity and presence of disease. The intensity of PMS is presented in table 2. As shown, there was no significant difference in

Table 1. Characteristics of students in two groups

Characteristics (Mean±SD) / Treatment Groups	Age (year)	BMI (kg/M^2)	Duration of menstruation (day)	Age at dysmenorrhea (year)	Age at menarche (year)
Placebo (N=27)	20.4±2	19.7±4	6.9±1.3	15.3±1.4	14.1±1.2
E. platyloba (N=26)	20.3±1.6	20.7±2.7	6.2±1.2	14.4±1.9	13.5±1.5
p-Value	0.471	0.621	0.058	0.063	0.147

Table 2. The intensity of PMS scores in E. platyloba and placebo groups

The intensity of PMS (Based on the intervention) / Treatment groups		Placebo	E. platyloba	*p*-Value
Anxiety symptoms	Before	23.9±6	24.3±5.1	0.72
	After	23.4±5.5	12.0±4.3	<0.001
	Reduction	0.4±3.1	12.3±4.7	<0.001
Depressive symptoms	Before	28.8±6.7	28.9±6.8	0.95
	After	21.2±6.7	14.0±6.1	0.04
	Reduction	8.9±8.6	15.9±5.9	0.029
Emotional symptoms	Before	21.8±6	18.4±6.3	0.06
	After	14.2±8	10.3±6.3	0.23
	Reduction	5.4±7.5	9.3±5.9	0.29
Fluid retention symptoms	Before	20.1±7.2	19±7	0.71
	After	13±6.1	9.5±6.5	0.06
	Reduction	8.2±6.7	10.5±6.4	0.15
Somatic symptoms	Before	9.7±3.8	10.1±4.4	0.73
	After	6.4±5.6	4.2±4.5	0.20
	Reduction	2.8±4.9	6.0±4.2	0.10
Total	Before	104.3±19.5	100.8±22.1	0.58
	After	79.1±28	49.7±23.1	0.009
	Reduction	25.5±22.4	55.3±18.5	<0.001

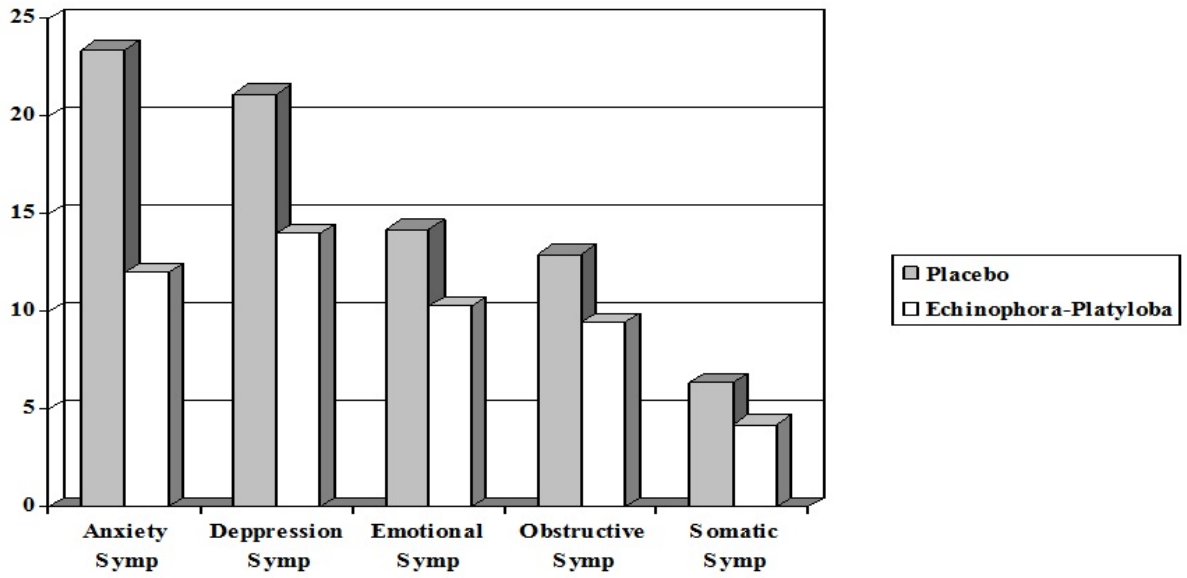

Figure 1. Distribution of participants based on the PMS symptoms and treatment group after the intervention

severity of PMS between two groups before the intervention, with a significant difference after the intervenetion (p=0.002). Distribution of recipients based on the five categories of PMS symptoms and treatment group as shown in figure 1, as indicated the intensity of PMS based on anxiety and depression symptoms after the intervention showed a significant difference between the two groups. The participants in the *E. platyloba* group reported the reduction in the severity of symptoms, with the most reduction in depression and anxiety symptoms. Of those who referred to the physician, two participants complained of an unpleasant taste, nausea and vomiting. Regarding the intensity of PMS symptoms, there was no significant correlation between age or body mass index of recipients in either group before and after the intervention.

Discussion

The findings indicated that the *E. platyloba* extract is probably effective in reducing the severity of premenstrual syndrome. The previous studies have focused on its anti-fungal effect on some common dermatophytes [12], the hydro-alcoholic effects on ileum

contractions in rat [15], its anti-candida effects compared with amphotericin [13], and finally anti-microbial effects on some gram negative and positive bacteria in comparison with some in use antibiotics [17].

Entezari et al. reported that the component of saponin existed in this herb, probably kills the fungal cell by destroying the membrane, however this effect is not considerable in comparison with the revalant chemically anti-fungal drugs [14]. Chemical drugs usually produce by copying herbal drugs formula in laboratory artificially, but recently it is known if some of the components of herbs which are produced purely in laboratory are used with another component of herbs, the side effects of them will be removed and the positive effects will appear [6]. Other studies regarding the effects of other medicinal herbs on premenstrual syndrome have shown that the use of herbs is just effective in luteal phase of menstrual cycle and does not need to be used throughout the cycle [18]. In the present study the effect of *E. platyloba* and placebo were investigated in luteal phase too. The previous studies showed that the herbal components such as saponins, Alkaloids and flavonoids directly affects the pituitary gland, especially the areas that secretes the luteinizing hormone (LH), increases the progesterone level and balances the disorders be resulted of hormone deficiency in the late of menstrual cycle [18].

The findings showed that there is not a significant difference in the mean of PMS scores between two groups prior the intervention, but a significant difference was found after the intervention regarding anxiety, depression and general symptoms. A study reported that the general symptoms of PMS were significantly reduced by using fennel and chamaemelum essences and the most important effect of fennel was upon the fatigue and faintness, and chamaemelum mainly had an influence upon depression, nervousness, abdominal and pelvic pains [9]. Aghajani et al. also reported that the *Vitagnus castus* could reduce physical and psychological symptoms of PMS [19]. In using of *Hypericum perforatum* for reducing the PMS symptoms, physical and psychological symptoms have been reduced [6]. The findings of current study regarding the reduction of psychological symptoms are similar to other studies. Also the findings indicated that besides the positive effects of *E. platyloba* on premenstrual syndrome, placebo also slightly reduced the severity of PMS. A previous study reported that, the placebo may have a psychological positive effect in treating the symptoms of some diseases [20]. Current study recommends that further studies be undertaken on *E. platyloba* as a treatment for PMS symptoms. Finally, due to complaints by some of the study participants regarding the smell and taste of this herb, we recommend that it be pharmacologically modified. Our study had limitations. The number of samples size was finite and duration of treatment was short for the treatment of PMS symptoms, we usually require at least 3 months, but in present study m medications were given for two months. Because the most of students with moderate and severe of PMS, were be educated from the university and follow up the treatment, was not possible. If the sample size was larger and the duration of intervention was longer, probably more comprehensive findings would have been achieved.

E. platyloba extract reduced the severity of premenstrual syndrome. The effects of *E. platyloba* were greater than that of placebo, especially on the anxiety and depression symptoms of PMS. More studies with more sample size and longer duration of treatment are suggested for future researches.

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Conflict of Interest

The author declare no conflict of interest.

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Shahr-e-Kord University of Medical Sciences, Shahr-e-Kord, Iran.

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