

## Comparing the Effects of Echinophora-platyloba, Fennel and Placebo on Pre-menstrual Syndrome

Masoumeh Delaram<sup>1\*</sup>, Soleiman Kheiri<sup>2</sup>, Mohammad Reza Hodjati<sup>3</sup>

1- Department of Midwifery, Shahrekord University of Medical Sciences, Shahrekord, Iran

2- Department of Biostatistics and Epidemiology, Shahrekord University of Medical Sciences, Shahrekord, Iran

3- Department of Physiology, Shahrekord University of Medical Sciences, Shahrekord, Iran

### Abstract

**Introduction:** Premenstrual syndrome (PMS) is a condition characterized by a number of behavioral, psychological and physical symptoms recurring cyclically during the luteal phase of the menstrual cycle. The uncertainty in the pathogenesis of PMS has led to many treatment protocols being suggested as possible therapies. The present study was carried out to compare the effects of echinophora-platyloba and fennel extracts on the PMS against placebo in students of Shahrekord University of Medical Sciences in 2008.

**Methods:** In this single-blind randomized clinical trial, 90 students with moderate to severe PMS enrolled in the study and were randomly divided into three equal groups. The first group received echinophora-platyloba extract, the second group received fennel extracts and the third group received placebo. The severity of PMS was measured by Daily Record of Severity of Problems (DRSP) questionnaire at the end of the first and second menstrual cycles before the intervention and the results were compared with them after the intervention. Data was analyzed using Dunn, Kruskal Wallis, and Pearson correlation tests by SPSS (v. 11.5) and  $p < 0.05$  was considered statistically significant.

**Results:** There were not any significant differences in the means of premenstrual syndrome scores before the intervention among the three groups ( $100.8 \pm 22.1$  in echinophora-platyloba group,  $101.3 \pm 27.1$  in fennel group and  $104.3 \pm 19.5$  in placebo group,  $p > 0.05$ ), but the differences were significant after the intervention ( $49.7 \pm 23.2$  in echinophora-platyloba group,  $64.4 \pm 27.5$  in fennel group and  $79.1 \pm 28.1$  in placebo group, respectively,  $p < 0.001$ ). No significant differences were seen between the echinophora-platyloba and fennel groups.

**Conclusion:** The echinophora-platyloba and fennel extracts could reduce the severity of PMS. The effects of echinophora-platyloba and fennel were similar and greater than the placebo. Administration of the extracts of these herbs is suggested for relieving the signs and symptoms of PMS.

**Keywords:** Echinophora-platyloba, Fennel, Placebo, Premenstrual syndrome.

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\* Corresponding Author:  
Masoumeh Delaram,  
Midwifery Department,  
Shahrekord University of  
Medical Sciences,  
Shahrekord, Iran  
E-mail:  
masoumehdelaram@  
yahoo.com

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### Introduction

Premenstrual syndrome (PMS) is characterized by a number of behavioral, psychological and physical symptoms recurring cyclically during the luteal phase of the menstrual cycle and they disappearing in the first days of menstruation (1).

More than fifty symptoms have been found which are contributed to PMS. The most common symptoms of PMS are irritability, mood swings, anxiety, depression, breast tenderness, bloating and headache (2, 3). Due to the variety and sever-

ity of the symptoms, it is difficult to estimate the exact prevalence of PMS, but previous studies have reported a 20-90% estimate (4). With the limited diagnostic criteria, the prevalence of PMS reaches to 2-6% in reproductive age (1). Sometimes premenstrual syndrome and related behavioral symptoms are legally important and are considered as a defense against criminal acts and sometimes they can lead to murder (5 - 7). A study reported that PMS caused a 27.5% reduction in women's work efficacy and 22% had problems in working relationship. This study also demonstrated that PMS led to problems with husband (83%), problems with children (61%) and social relationships disorders (41.5%) (8).

The etiology of PMS is largely unclear and different theories have been suggested, including hormone imbalances, hypoglycemia, hyperprolactinaemia, psychological causes, reduced endorphins release, ovary infections, deficiency of essential fatty acids, dysfunction in acid and base balance, imbalances in prostaglandins, vitamin and mineral deficiencies (9 - 12).

Pathophysiology of PMS is unknown and different therapeutic protocols have been suggested for its treatment. Non-pharmacological treatments include changes in dietary habits, reduction in salt intake, reduction in animal fat consumption, exercise, stress reduction and availability of support systems. Pharmacological treatments include GnRH analogues, spironolactone, danazol, alprazolam, mephenamic acid, gamalinoleic acid, and fluoxetine (13 - 15).

In recent years, use of herbs has been considered in the treatment of premenstrual syndrome (16 - 19). *Echinophora platyloba* (*E. platyloba*) and *Foeniculum vulgare* (Fennel) are herbs that are traditionally used for menstrual disorders. *Echinophora platyloba* belongs to Umbelliferae family and consists of four species including *E. cinerea*, *E. platyloba*, *E. orientalis* and *E. sibthorpiana*. The two aforesaid herb species are exclusive of Iran (20). *E. platyloba* species is known by different local names of Khoshariz, Tigh Touragh, Tigh Masti, Khoshandar, Kouzang, Tanghez or Khousharouz. This plant is a pasture plant used for flavoring foods, cheese and yoghurt (20, 21). Sadraei et al (20) reported that *E. platyloba* extract reduced the ileum contractions in rats. Anti-fungal effects of *E. platyloba* has been depicted on a

number of common dermatophytes (21). The anti-candida effects of this plant was compared with amphotericin by Mahbobi et al. (22) and it was shown that this plant was effective in the treatment of candida albicans.

Fennel (*Foeniculum vulgare*) has been shown to have anti-inflammatory, anti-spasmodic, analgesic, diuretic, laxative, carminative and expectorant effects. In addition, because of its antioxidative effects, it is also useful for digestive and nervous disorders (23 - 25).

Torke Zahrani, et al (26) reported that fennel extract reduced the severity of dysmenorrhea. The effects of fennel and Mephenamic acid was studied on dysmenorrhea and it was demonstrated that both drugs reduced dysmenorrhea compared to placebo (27). Fennel essence can reduce the frequency and intensity of contractions in rat uterus (28). To the best of our knowledge, the effects of *echinophora-platyloba* and fennel extracts on premenstrual syndrome (PMS) has not been reported yet. The purpose of the present study was to compare the effects of *echinophora-platyloba* and fennel against placebo on premenstrual syndrome in the students of Shahrekord University of Medical Sciences in Iran.

### Methods

This single-blind randomized clinical trial study was done on 250 female university students aged 18-25 years in Shahrekord University of Medical Sciences in Iran. The Ethics Committee approved the study (No. 352.87-1-3 on 12.5.2008) and the study was registered at the Iranian Registry of Clinical Trials and the identifier being IRCT 138810263078N1.

The participants were requested to fill the Daily Record of Severity of Problem (DRSP) two cycles before the intervention and then the severity of premenstrual syndrome was evaluated for all subjects. The daily record of severity of problem form is a standard tool for detecting the intensity of PMS and its validity and reliability have been approved by Borenstein and et al (29). This form determines the severity of PMS 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, isolation and loss of interest to

daily activities), emotional symptoms (headache, sweating, hot-flushes, increased appetite, heart palpitation, fatigue, reduced energy, and inability to do the daily activities), fluid and electrolyte retention symptoms (increases 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)] (29). 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 individual seldom has problems in daily activities), 2: moderate (the individual has problems in maintaining daily activities, but can go to work or school), 3: severe symptoms (the individual is not able to do daily activities) and 4: very intense (the individual is confined to bed). Considering the purpose of the present study, the students with moderate and severe PMS were selected for the intervention.

All the students were also asked about their menstrual patterns; such as duration of menstruation, menstrual interval, dysmenorrhea, familial history of PMS and use of drugs for the reduction of PMS. Students with pelvic inflammatory disease (PID), any chronic diseases, drug use or with any stressor factors were excluded from the study. Finally, ninety students with the highest PMS scores, were selected and they were randomly assigned into three equal groups. The first group received echinophora-platyloba extract, the second group received fennel extract and the placebo group received sterile water. The amount of the given extracts and the placebo was 30 drops, every 8 hours, 3 days before until 3 days after the onset of menstrual bleeding. The subjects completed the DRSP form at the end of their first and

second menstrual cycles. After the interventions, the severity of PMS was evaluated again. The students were blind about the kind of drug throughout the study. Data was analyzed by Dunn, Kruskal-Wallis and Pearson correlation tests, using SPSS and a  $p < 0.05$  was considered significant.

### Results

From the total number students who participated in the study, 4 persons in the echinophora-platyloba group, 2 persons in the fennel group and 3 persons in the placebo group did not complete the study. The demographic data of the students have been presented in Table 1. As shown in the table, no significant differences were observed for age, body mass index, age at menarche, age at dysmenorrhea onset and duration of menstruation between the three groups. In addition, menstrual cycle intervals and family histories of PMS were similar among the groups.

As shown in Table 2, there were no significant differences regarding the total PMS scores among three groups before the intervention ( $P=0.58$ ), but differences were significant after the intervention ( $P=0.009$ ). Statistical analysis demonstrated that the total premenstrual syndrome scores has been reduced upon the treatments in three groups ( $P < 0.001$ ). It means that echinophora-platyloba, fennel and placebo reduced the severity of PMS, but the effects of echinophora-platyloba was more significant (Table 2). When the effects of echinophora-platyloba was compared with fennel extract, there was no significant differences between the two extracts ( $P=0.08$ ). There were no significant correlations between the age and body mass index of the individuals with symptoms of PMS before and after the intervention ( $P > 0.05$ ).

**Table 1.** The demographic characteristics of the participants

Group	Echinophora-platyloba	Fennel	Placebo	P-Value
Characteristics	M±SD	M±SD	M±SD	
Age (year)	20.3±1.6	19.9±1.01	20.4±1.9	0.471
Body mass index (kg/m <sup>2</sup> )	20.7±2.7	19.8±4.59	19.7±4.1	0.631
Age at menarche (year)	13.50±1.52	14.10±1.19	14.12±1.18	0.147
Age at dysmenorrhea onset (year)	14.42±1.87	15.32±1.38	15.33±1.46	0.063
Duration of menstruation (day)	6.26±1.25	6.21±1.19	6.98±1.34	0.058

The scores related to symptoms of PMS and the total mean of PMS have been presented in Table 2

Table 2. Comparison of PMS scores in echinophora-platyloba, fennel and placebo groups

Treatment group	E-chinophora-platyloba	Fennel	Placebo	P-Value
PMS Symptoms (before and after the intervention)	M±SD	M±SD	M±SD	
<b>Anxiety</b>				
Before	24.3±5.1	22.8±6.2	23.9±6.0	0.72
After	12.00±4.3	14.1±6.1	23.4±5.5	0<0.001
Reduction	12.3±4.7	8.7±4.6	0.4±3.1	0<0.001
<b>Depression</b>				
Before	28.9±6.8	28.8±9.4	28.8±6.7	0.95
After	14.0±6.1	17.8±9.0	21.2±6.7	0.04
Reduction	15.9±5.9*	11.0±5.5	8.9±8.6*	0.029
<b>Emotional</b>				
Before	18.4±6.3	20.0±6.4	21.8±6.0	0.06
After	10.3±6.3	12.7±5.3	14.2±8.0	0.23
Reduction	9.3±5.9*	7.6±4*	5.4±7.5*	0.29
<b>Fluid Retention</b>				
Before	19.0±7.0	20.5±7.0	20.1±7.2	0.71
After	9.5 ±6.5	13.6±5.5	13.0±6.1	0.06
Reduction	10.5±6.4*	6.9±5.7	8.2±6.7*	0.15
<b>Somatic</b>				
Before	10.1±4.4	9.3±4.5	9.7±3.8	0.73
After	4.2±4.5	5.9±3.6	6.4±5.6	0.20
Reduction	6.0±4.2	3.5±3.1	2.8±4.9*	0.10
<b>Total score of PMS</b>				
Before	100.8±22.1	101.0±27.2	104.3±19.5	0.58
After	49.7±23.1	64.4±27.5	79.1±28	0.009
Reduction	55.3±18.5*	38.7±16.1*	25.5±22.4	0<0.001

\* The reason of difference in the reduction mean of premenstrual symptoms with the mean of symptoms before and after the intervention, is that, a number of participants didn't answer to some of questions after the intervention

### Discussion

The findings of this study showed that echinophora-platyloba and fennel extracts, as well as placebo, reduced the intensity of premenstrual syndrome in students and the effects of the two extracts were more significant than these of placebo.

Echinophora-platyloba is one of the four species in Iran (20) which is also used for food. Anti-microbial and anti-fungal effects of echinophora sibthorpiana have been reported before (22, 23). In addition, Sadraei et al. showed that echinophora sibthorpiana extract reduces the rat ileum contractions in vitro (20). A previous study which was carried out on the echinophora platyloba, revealed that this herb contains elements such as

saponins, alkaloids and flavonoids. Saponines are elements with toxic effects (30). As far as we know, the effects of echinophora platyloba and fennel extracts on premenstrual syndrome have not been studied yet. Previous findings from different medicinal plants have shown that use of herbs is effective in the luteal phase of the menstrual cycle and does not need to be used throughout the cycle (31). In the present study, the effects of echinophora platyloba and fennel extracts were investigated in the luteal phase too.

Our findings indicated that during the two cycles before the intervention, the severity of PMS was similar in the three study groups, but after the intervention the differences were significant. It means that, echinophora platyloba had the highest

and placebo had the lowest effects in the reduction of PMS symptoms. Considering the effects of age, BMI, age at menarch, and age at dysmenorrhea on premenstrual syndrome, since the participants were randomly allocated to each group and there was not a significant difference in these variables between the groups, and also the Pearson correlation test did not show a significant correlation between premenstrual syndrome and these variables.

Among the five classifications of PMS symptoms, which include anxiety, depression, emotional, fluid and electrolyte retention and somatic symptoms, the highest effect was seen on anxiety and depressive symptoms. Aghajani and co-workers reported that the *Vit-agnus castus* can reduce somatic and psychological symptoms (32). Other studies reported that medicinal plants could reduce the severity of PMS up to 45%- 70% (8, 32). In comparing the effects of *echinophora platyloba* and fennel extracts, we found that both plants had similar effects in reducing the intensity of PMS. Psychological effects of placebo have been reported by previous studies (33) and the effect attributed to placebo in our study may also be due to these effects.

### Conclusion

*Echinophora platyloba* and fennel extracts, as well as placebo, reduced the severity of premenstrual syndrome. The effects of *Echinophora platyloba* and fennel were similar and both extracts were effective on symptoms of anxiety and depression. More studies with bigger sample sizes are needed for the use of *echinophora platyloba* and fennel essences, instead of their extracts, to be suggested for PMS treatment.

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