Original article

The effect of primrose oil on the premenstrual syndrome among the female students in Lorestan University of Medical Sciences: A triple blind study

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Abstract

Background and Purpose: The premenstrual syndrome is the emergence of a set of symptoms before menstrual which results in imbalance in individual's life and daily activities. Today the prescription of herbals is recommended for the treatment of the illnesses. The present study aimto pinpoint the effect of primrose oil on the premenstrual syndrome.

Methods: The study was a triple blind clinical-trial which was conducted with 80 female university students residing in Lorestan Medical University hostels. The samples were selected based on the DSMIV-TR criterion for the premenstrual syndrome. Using block-randomization method, they were categorized into two groups (each 40), one treated with primrose oil and the other with placebo. The dose of the primrose oil is 1500 mg per day for the first group. The total score for sever symptom (for each from 0 to 10) was assigned at first monthly and then for three months. For the data analysis $\chi 2$ and repeated measures were deployed.

Results: The score for symptom severity before the intervention for the primrose group was 53.20 ± 14.31 at the beginning. At the end of the third month, it got 33.62 ± 16.94 therewas a significant difference in the reduction of symptom severity in the follow-up periods $(p < 0.001)$. In the Placebo group, the score for sever it ysymptom before the intervention was 53.38 ± 13.93. At the end of the third month after treatment, it was 50.27 ± 16.94. This didn't show any significant difference in the decrease of the symptom severity in the follow-up period. There was a significant difference for the symptom severity in both primrose and Placebo group $(p < 0.001)$.

Conclusion: Taking the effect of primrose oil on premenstrual syndrome reduction and the harmlessness of hessrb medicals into account,bioresearches recommend primrose oil for the treatment of premenstrual syndrome.

Keywords: Primrose Oil, Premenstrual Syndrome, Gammalinoleic Acid

Introduction

The premenstrual syndrome (PMS) is the emergence of a period with one or more symptoms before the menstrual period which makes imbalance in individual's life style and daily activities (1). This syndrome starts with average age of 19-20. About 30%-80% of the females experience this moderately and 10% - 20% experiences it severely (2). As it was reported the epidemics of this disorder among women in moderate form reaches to 72% and in severe form it reaches to 12.2% (3). Based on the studies done in Iran, the prevalence of this disorder among high school girls hit 40% - 66.5% (4,5). The symptoms of the disease appear as changes in mood such as depression mode, feeling of hopelessness,

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anxiety, mental tension, emotional disturbance, violence and face blushing. The behavioral symptoms of this disease include low desire to routine jobs, distraction, reduction of energy, rapid fatigue, changes in diet, and sleep disturbances. The physical symptoms appear as pains in breasts, headache, pain in muscles and weight gain. The wide scope of behavioral changes in the premenstrual period increases. These changes involve isolation, work absentees, distraction, criminal behaviors and suicide. These symptoms at the end of luteal phase of menstrual period increase severely in such a way that they create irregularity in personal functions in individual's job, education as well as family and personal affairs (6-13). The findings of Diegoli's study on the 100 women with PMS showed reduction in the following items: 27.5% job efficiency, 22.1% job miscomm unication, 82.2% clashes with spouse, 61% sibling misunderstanding and 41.5% social relation. (14). The causes for this syndrome are unknown (1,9,15,16). Although some different theories like hormone changes, neurotransmitters, prostaglan dins, the imbalance of estrogens and progesterone, zinc reduction, magnesium and B6 vitamin reduction, central Dopamine and Serotonin were mentioned (17,18,15, 9). Since the central Dopamine and Serotonin supposition is more feasible than other cases. Scholars in the field proposed the anti-depressants like Venlafaxine, Fluoxetine and other specific Serotonin reuptake inhibitor for the treatment of this disorder (10,16).

Also the anti-prostaglandin medicines were proposed in the syndrome treatment (17,9). Today, herbal medicines are the most common treatment methods for any disease. As it is economical and has fewer side effects than chemical drugs. There are evidences that proved the efficiency of primrose oil on premenstrual syndrome (21,19,17).

Primrose is a herb from the Oenotherabennie's family. The seeds of the herb contain two essential fatty acids: linoleic acid (LA) and Gamma linoleic acid (GLA) which facilitate the prostaglandin EI synthesis (21,20,19, 17). Gamma – linoleic acid (GLA) is one of the rare fatty acids which are found in a few plant species. Primrose is regarded as the main source of (GLA) (21,19, 17, 14). In most sources, as it is reported, the degree of linoleic acid (Omega-3) reaches to 72%. Some studies have emphasized the impact of Omega-3 on the treatment of many diseases, specially, diseases related to Serotonin reduction such as depression, mood symptoms, premenstrual symptom, menopause and menstrual disturbance (27,19). The findings from Atanabe's study (2005) indicated that the rate of (GLA) in women with premenstrual syndrome was significantly lower as compared to the placebo group. ($p<0.00\%$). Also, the results of the study suggested that the herbs with the GLA acid could significantly reduce the PMS symptoms in the patients (20). Contrary to these findings, there are other studies which did not confirm the above findings. It seems that there exist contradictory results about the effect of primrose oil on the premenstrual syndrome.

Dante in a systematic survey related to efficient herbal treatment in the reduction of premenstrual symptoms found that (in a 17 qualified articles out 0f 102 on clinical trial published in (1980-2010) in all clinical trials, Vitagnos (5 finger) and saffron as compared to semi drugs could reduce premenstrual syndrome well, while Primrose and Hypericum perforatum (John's wort) did not show any significant difference in reduction of premenstrual syndrome (28). As the application of herbal products is widely increasing in the world, most women would like to treat their disease symptomsby using natural and complementary medicines (13).

Some researchers in this field believed that more chemical studies are required to prove the curing effect of herbal medicines on the premenstrual syndrome (19,12).

With regard to the effect of premenstrual syndrome in creation of disorders in family, social,

And vocational affairs of the individuals and the need for efficient treatment interventions, in spite of the contradictory findings, the present study was conducted to manifest the effect of primrose oil on the premenstrual syndrome.

Materials and Methods

The study was a triple blind clinical trial. The sample contained Lorestan university female students residing in the hostels. The measure for inclusion was 18-30 years of age having regular menstrual period with the 24-35 intervals, without any other physical, Illness, the record of pacifier's intake, mental disorder specially depression, and anti depressants intake and hormone drugs. No special diet and no experience of terrifying event three months before the study and during the study were considered as well.

The samples were divided into two groups (each 40, total 80) based on the entry measure and assigning sample size formula. Mean and standard deviation were fixed on the formula on basis of pilot studies.

$$N=\frac{\left(Z_{1-\frac{a}{2}}+Z_{1-\beta/2}\right)^2}{(\mu_1-\mu_2)^2}=\frac{(1.96+.86)^2(14^2+17^2)}{(10)^2}\cong 40$$

All the participants took part in the study with complete awareness and satisfaction. For sample selection in the first phase, the DSMIV–TR standard questionnaire for the premenstrual syndrome (2) was provided and purposefully was given to the cases with at least 5 symptoms of premenstrual syndrome. The questionnaire assessed the following symptoms:

1. Feeling of hopelessness and depressed mode.
2. feeling of anxiety tension and worry.
3. Emotional disturbance, violence or face blushing.
4. reluctance toward usual jobs.
5. Reduction of concentration
6. Drowsiness and fatigue
7. appetite change.
8. Drowsiness and sleeplessness.
9. Lack of self-manipulation.
10. Physical symptom as pain in breasts, muscles and joints pain.

The severity score for any symptom was assigned from 0 to 10, then the total score was computed. The reliability and validly of the questionnaire with the correlation coefficient above 87 was confirmed in Zeaei's (2001), Baksheesh (2009), and Islamloo (2013) studies (30-32). According to these studies, having at least 5 symptoms and getting the score 35 or more of severity symptoms were the criterion for entering the study.

At first, 142 university students in the hostels with different majors with considering the criteria entered the study and did the ten-item questionnaire, these participants, 80 cases with 5 symptoms and the score of 35 or more for severity symptoms were selected and entered the study willingly. For keeping the balance among participants in each group, we used the block-randomization method.

For the experiment group, primrose oil with the dose of 1500 mg daily or 3 capsules (5oo mg). was given. For the control group, placebo capsules (made in Zahravi Pharmaceutical Factory) were given three times a day for three months. The participants, in a three-month period (totally 3 times) were visited by the Gynecologist for severity symptoms measurement. At last, the patients' recovery was identified based on the symptom score decrease. During the study, 5 participants left the study, so they were replaced with other participants. The data were collected and analyzed using SPSS Software. For the exact analysis, frequency, mean and standard deviation as well as χ^2 and repeated measure were applied. The present study has been registered with the code "IRCT 2010 09214789 N1" in the Iranian Registry of Clinical Trials.

Results

The samples entered in the study included nursing students (20.1%), medical students

(17.6%), health students (16.2%), and the rest were radiology, lab science, operation room and midwifery students. In the experiment group (primrose oil) 77.5% and in the placebo group 72.5% were single. The average age for the primrose oil group was 22.3±3.32 and for the placebo group was 13.73±0.75%. There was no significant difference between marital status (p=0.49) and mean age of both groups (p=0.81).

The research findings indicated that the score of severity symptom in the primrose group before and after the intervention had a significant difference. The repeated measure showed a significant difference in the mean score of severity symptom before the treatment, the first month, the second month and the third month and after the treatment. In the placebo group, there was no significant difference at any time. The research findings showed a significant difference in the mean score of the severity symptom among two groups, primrose and placebo, during the end of the third month of follow up (p<0.001), (table-1).

The results of repeated measure test indicated that the time of effect and the group type were important in this study. This meant that the process of changes in severity symptom during the time in both groups were different (Figure1)

Table 1. The comparison of the mean of the score of severity symptoms before and after the intervention with Primrose oil and Placebo groups

Intervention groups / Follow up	Primrose oil		Placebo		P value
	standard deviation	mean	standard deviation	mean	
Before treatment	14.31	53.20	13.93	53.38	P=0.996
After one month of intervention	15.86	41.27	14.04	52.25	P <0.001
After two months of intervention	16.64	36.92	13.61	51.82	P <0.001
After three months of intervention	16.94	33.62	13.56	50.27	P <0.001

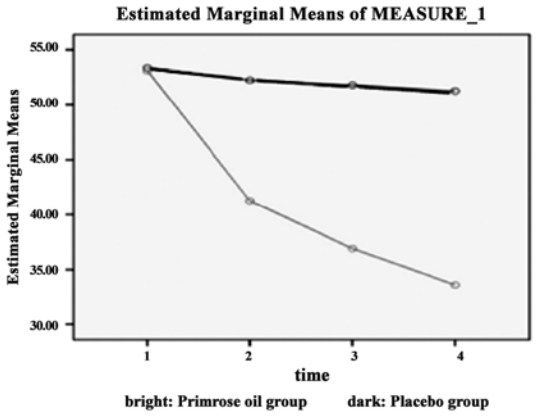

Figure 1. The comparison of testtime interactionand the severity of PMS symptoms in Primrose oil and Placebo groups

Discussion

As it was mentioned, the research findings suggested that there existed a considerable difference in the mean score of severity symptom of premenstrual syndrome in both primrose and placebo groups. Primrose oil is one of the rich sources of two essential fatty acid, linoleic acid and Gamma linoleic acid. This facilitates the prostaglandin synthesis E1with the property of anti–inflammatory and immune regulatory which can reduce the symptoms of premenstrual syndrome. In spite of this, contradictory results were obtained regarding the effect of primrose oil on the premenstrual syndrome (17,19,21). Sampalis et.al got similar results through a study done on the krill oil (of the rich source of fatty acid and gamma linoleic acid) on the reduction of the symptoms of premenstrual syndrome (33). Rochafilho et.al (2011) conducted a study about the effect of essential fatty acid on the premenstrual syndrome with 120 women. They found that the daily intake of 2 grams of essential fatty acid, as compared with placebo, during 3 to 6 months after the start of the study could reduce the unfavorable and teasing symptoms of premenstrual syndrome (27).

Khoo' sresults suggested that the score of the premenstrual syndrome after three treatment periods in two groups, primrose and placebo showed no significant difference, but with the

treatment continuation after six periods of treatment, there existed a significant difference between the scores in primrose and placebo group. The findings of this study suggested that primrose had the most effect on the mood symptoms, feeling of illness, and breast stimulation (34).

Hardy's findings done with 68 women with premenstrual syndrome also showed that the daily intake of 2 mg primrose in a treatment period of three months could cause the remedy in the symptoms. 61% of the women taking the medicine, primrose oil, got the complete remedy, 23% got the relative remedy. The findings showed that primrose oil could reduce breast stimulation more compared to other symptoms of premenstrual syndrome (35).

Henshaw also believed that although primrose oil could cure the premenstrual illness, it could not cure other symptoms of premenstrual syndrome (6). The results from the Cornish's study indicated that using primrose oil compared to placebo for the women suffering from the premenstrual syndrome (for more than one year) caused a remarkable reduction in agitation ($p<0.001$), fatigue ($p<0.01$) and depression ($p<0.001$) after the first treatment cycle (36).

The results from Tak Falaha's study aiming the effect of primrose oil on premenstrual syndrome also indicated that taking one gram of primrose oil daily three times a day in two successful cycles, as compared to placebo, could reduce the syndrome significantly. In spite of the studies done, the researcher suggested the repetition of the study in a broader extent with the follow-up periods to get the strong evidences to show the effect of primrose oil (22).

On the contrary, there are some results that show the ineffectiveness of primrose on the premenstrual syndrome. Budeiri et.al in a systematic survey on the designation of primrose oil on premenstrual syndrome with 329 women found that no sufficient clinical evidence was evident on the effect of primrose oil on the PMS. Budeiri believed that primrose has little effect on the syndrome, so doing more clinical trials in a broad extend might confirm the effect (29). Dante (2011) also in his systematic survey has investigated the studies done with primrose oil on the premenstrual syndrome and their contradictory results. Based on the Dante's report in randomized double blind clinical trial by Callender, there was no significant difference in the reduction of anxiety and depression scores in both primrose oil and placebo group.

The primrose oil group took 1 grs of the medicine three times a day for 4 months. In the double blind clinical trial conducted by Khoo, the remedy in the symptom in primrose oil group with 6 grs of medicine daily during 10 cycles showed no significant difference ascompared with the placebo group. The results from Colhins's study indicated that 1.5 grs of primrose oil daily during 4 cycles could reduce the symptoms of premenstrual syndrome, but there was no significant deference between score reduction of primrose oil and placebo group. Dante recommended more studies to be done on the def 30 years of age Considering the materials presented on the contradictory results on the impact of primrose oil on the premenstrual syndrome, the results from this study could confirm the effect of primrose oil on the premenstrual syndrome.

There fore, we suggest that primrose oil can be of choices in tradition medicine for reducing the symptoms of premenstrual syndrome. This kind of medicine is accepted in Iran’s culture.

It is concluded from the results obtained from this study and other studies on the impact of primrose oil on premenstrual syndrome that plants containing linoleic acid such as primrose oil which contains considerable amount of this acid, can reduce and pacify the symptoms of premenstrual syndrome. So, primrose oil can be offered as a proper replacement.

Conflict of interest

The author declares his lack of conflict withinterest through this article.

Author's Contributions

M. Saki was involved in conducting the research and collecting the parts together, drafting the article, S. Akbari doing the visits and, following up process with the patients, M. Saki collecting data, MJ Tarrahi doing data analysis, and M. Gholami revising the article critically and S. Pirdadeh collecting data.

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