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The Effect of Evening Primrose Oil on the Intensity of Postpartum Blues Among Primiparous Females: A Double-blind, Randomized, Controlled Clinical Trial

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Abstract

Background: The most vulnerable time to develop mood disorders such as sadness, depression, and psychosis is the postpartum period. Postpartum blues is the most common mood disorder and can endanger the relationships between mother, child, and family, and in case of lack of appropriate treatment can cause irreparable damages.
Objectives: The current study aimed at investigating the effect of evening primrose oil on the intensity of postpartum blues among primiparous females.
Methods: The current double-blind, randomized, controlled clinical trial was conducted from December 2012 to November 2013 on 132 primigravida females referred to health centers of Ahvaz, Iran. They were randomly divided into two groups of 66 to receive a daily dose of 1 g of evening primrose oil capsules (intervention group) or similar placebo capsules (control group) from the beginning of the 37 weeks of pregnancy up to 2-weeks postpartum. Females in both groups were asked to complete the Edinburg questionnaire on the days 4, 10, and 14 postpartum. Data were analyzed using the t-test, Chi-square test, and repeated measures, and $P < 0.05$ was considered significant.
Results: There was a statistically significant difference ($P = 0.0001$) between the two groups regarding the severity of the postpartum blues (the severity in the intervention group was less than that of the placebo group, $P = 0.0001$). The score of Edinburgh questionnaire was significantly less in the intervention group compared with that of the control group on the days 4, 10 ($P = 0.0001$), and 14of postpartum ($P = 0.01$) ($P = 0.014$). The averages of Edinburgh score in the intervention group was significantly less compared with those of the control group on the days 4 (10.5 ± 0.57 vs. 13.3 ± 3.28; $P = 0.0001$), 10 (11.2 ± 1.22 vs. 14.9 ± 3.6; $P = 0.001$), and 14 postpartum (11.7 ± 1.3 vs. 13.05 ± 2.6; $P = 0.08$).
Conclusions: The use of evening primrose oil effectively reduced the severity of postpartum blues.

Keywords: Blues, Depression, Disorder, Evening Primrose, Female, Mood, Oil, Postpartum

1. Background

Postpartum blues is the most common mood disorder in the postpartum period under different names including postpartum blues, mother's sadness, and postpartum temporary depression (1).

The postpartum blues is a disorder that occurs with symptoms of depression including insomnia, down mood, the desire to cry, fatigue, irritability, and emotional instability. Females with postpartum blues may weep a few hours and feel completely relaxed and cry the next day again (2).

The prevalence of depression in females is almost twice more than that of males, with the highest risk of its occurrence during their reproductive years and pregnancy (3). The prevalence of the disorder is reported 30% to 85% worldwide (4).

Postpartum blues is a disturbing disease, mostly occurs 10 days postpartum, and almost happens in 50% of females who experience a natural childbirth (5).

The cause of the disorder is unknown and researchers linked it with the rapidly changing hormonal level, postpartum physical and psychological stress such as health problems, mental instability after delivery, the anxiety of

increasing responsibility for baby care, fatigue, sleep disturbance, and concern for the care of other children as well as the spouse (6). However, this condition is usually transient and self-limiting and can be observed only during the first few days after childbirth (7).

Postpartum blues can have two significant impacts on the postpartum health, the first one, associated with postpartum depression and the other with its debilitating effect on the relationship between mother and baby (8). Unfortunately, since in most cases, the problem resolves on its own and usually uncomfortable symptoms do not have a negative impact on the ability of mothers in the care of newborns, specific treatments for these problems are not assessed and treatments are mainly supportive (9). The treatment includes taking enough rest, having a healthy diet with plenty of fluids, exercise and light daily activities, and in most cases, medication is not applied (10).

In the past 2 or 3 decades, extensive researches are conducted on herbal antidepressants, sedatives, and analgesics, and some effective herbal medicines with minimal side effects are supplied to world markets, which in many cases can replace chemical antidepressant medications (11). Evening primrose (*Oenothera biennis*) is a plant belonged to the family of Willowherb and its seeds contain 2 essential fatty acids (70% linoleic acid (Omega-3) and 8% - 14% gamma-linolenic acid) (12).

There is visible evidence suggesting Omega-3's effect on reducing the levels of serotonin in cell membranes and cerebrospinal fluid and plasma of patients with depressive disorders (13). Researchers observed a significant correlation between abnormal metabolism of fatty acids and depression; in addition, reduction of the amount of omega-3 may cause a depressed mood, a negative attitude towards life and an impulsive and suicidal behavior (14).

So far, no serious side effects are observed in taking these supplements during pregnancy and lactation. The impact of primrose oil consumption during pregnancy to prevent preeclampsia and eclampsia (15-17) and labor induction through the production of prostaglandin and cervical ripening (15, 16) was studied. Evening primrose oil was effective according to some researches on depression (18). It can reduce symptoms of menopause such as hot flashes, breast pain, inflammation, fluid retention, depression and irritability, symptoms of premenstrual syndrome such as allergy and painful breasts, fatigue, and mood disorders (15, 16).

Saki et al., in a study on the effect of evening primrose oil supplements on the treatment of patients with depression showed that this supplement caused a significant reduction in depression and improved function in patients (19). Due to the high prevalence of postpartum blues, especially in primiparous females, and to create a healthy relationship between mother and baby as a necessity to continue breastfeeding, there is a need to find less risky methods to treat this disorder. Also to the authors' best knowledge, no study measured the effect of primrose oil on postpartum blues. Therefore, the current study aimed at evaluating the effect of evening primrose on postpartum blues in primiparous females.

2. Objectives

The current study aimed at investigating the effect of evening primrose oil on the intensity of postpartum blues among primigravida females.

3. Methods

3.1. Participants

The current double-blind, randomized, controlled trial was conducted from December 2012 to November 2013 on 132 primigravida females referred to health centers of Ahvaz, Iran.

Inclusion criteria included: gestational age $\geq$ 36 weeks and monogamous females. Exclusion criteria included: any unusual event in the time of childbearing such as a cesarean section, induction or instrumental delivery, delivering an alive baby with Apgar score of < 10, required hospitalization, family problems such as a dispute with the husband and relatives, history of infertility and systemic diseases (diabetes, heart disease, kidney failure, and so on), taking supplements similar to primrose family in the 3rd trimester of pregnancy, unwanted pregnancy, and getting a score more than 23 in the public health test.

For sample size calculation, a pilot study was conducted on 10 participants with the review of Edinburgh test scores on the day ten postpartum, and the sample size was calculated 66 females in each group ($\alpha = 0.05$, $\beta = 0.2$), based on the following formula:

$$N = \frac{\left(z_{1-\frac{\alpha}{2}} + z_{1-\beta}\right)^2 \left(s_1^2 + s_2^2\right)}{-\left(\overline{x}_1 - \overline{x}_2\right)^2} \quad (1)$$

3.2. Randomization

To select the participants, researchers first attended the health centers of Ahvaz and found eligible cases. After explaining the objectives of the study to eligible females, the written informed consent was obtained from each subject. Females were allocated to the intervention or control groups using permuted-block randomization with the block size 2 and ratio of 1:1.

3.3. Measures

To determine the mental health of participants and the inclusion criteria, a test was conducted by measuring 25-item Afghan symptom checklist (25-ASCL) and general health questionnaire (GHQ). The 25-ASCL is a 25-item questionnaire to measure psychological symptoms derived from the symptom checklist-90-revised (SCL-90-R) and its primary version was developed by Deragotis, Lipman, and Covi in 1973 and was revised for the 1st time in 1983 by Deragotis (20). The 25-ASCL was validated in Iran by Najarian and Davoudi in 2001 (21). The questionnaire contains 25 short-answer questions and the 5-option Likert scale was used for scoring (none, a little, somewhat, high, very high).

GHQ consisting of 28 questions was used to measure the health status of people. The questionnaire was developed by Goldberg and Hillier in 1979 (22) with four subscales including physical symptoms and anxiety, insomnia, social dysfunction, and symptoms of depression. Validity and reliability of this questionnaire was approved in Iran (23).

By the application of the Edinburgh test, the mood changes after delivery were examined. Edinburgh test was developed by Cox, Holden, and R. Sagovsky (24). The scale consists of 10 multiple-choice questions, and participants should choose the closest option to the emotional state of themselves in the recent days. Scoring was based on the severity of symptoms as 0 - 1 - 2 - 3 in different questions. A score of 13 and above was considered a sign of postpartum blues.

3.4. Intervention

The current study lasted 13 months. The evening primrose capsules included 500 mg evening primrose oil purchased from a pharmaceutical company in Iran and originally developed by Webber Naturals of Canada. The placebo capsules were prepared by Zahravi Pharmaceutical company and were similar to the interventional capsules in shape and color. A member of the division of pharmacognosy, department of pharmacy, Ahvaz Jundishapur University of Medical Sciences, checked the ingredients of primrose oil and placebo. All primrose and placebo were coded by a 3rd party that was not aware of the purpose of the current study. In the 1st stage, 14 capsules were given to each participant to consume weekly from the beginning of the week 37 of gestation to delivery, and they were asked to consume a daily dose of 1 g equivalent to two capsules at the same time, and if they missed doses for a week or refrained from consumption and informed the researcher, they were considered as drop-outs.

One of the researchers made a phone call once a week to each participant to ensure correct usage. Phone calls to participants were scheduled in order to control drug consumption, problems, and possible complications, once every week or more often as needed until delivery were determined. Also, by providing the phone number of the researcher, the participants were asked to contact the researcher at the time of admission for delivery so that the 2nd phase of supplements consisted of 28 capsules, started after the childbirth and participants were requested to take capsules for two-weeks after delivery. By application of the Edinburgh test, the mood changes after delivery were examined. Edinburgh test was completed four days after birth and at the days 10 and 14 after delivery. Thus, the participants were studied based on the severity of symptoms of postpartum blues. Finally, 66 subjects in each group completed the study.

3.5. Statistical Analysis

Data were analyzed using SPSS Statistics for Windows, version 20.0 (IBM Corp., Armork, N.Y., USA). The normal distribution of data was assessed by the Kolmogorov-Smirnov test. For comparison between the groups, Chi-square test, t-test, and repeated measures test were used. The P values < 0.05 were considered significant.

3.6. Ethical Consideration

The current study was approved by the ethics committee of Ahvaz Jundishapur University of Medical Sciences (Ethical code: E505). The study was registered in the Iranian registry for randomized controlled trial (Ref No: IRCT2013052513452N1). The goals of the study were explained to mothers and informed written consent was signed by each participant. They could withdraw at any time during the research.

4. Results

The age range of females participating in the study was 18 - 30 years. The mean age of the females in the intervention and the control groups was 23.8 ± 3 and 23.5 ± 2.3 years, respectively.

In terms of educational level, the most frequent degree in the two groups was high school diploma 48.5% and 50% in the control and intervention groups, respectively.

Most of the participants (90.9%) were housemakers, and the rest (9.1%) were employed. The most frequent subjects in the context of the economic situation were moderate 74.2%, and 77.3% in the intervention and control groups, respectively. In the current study, there was no significant difference between the two groups regarding demographic characteristics ($P > 0.05$) (Table 1).

Table 1. Demographic Characteristics of the Subjects in the Study Groups (N = 66)[a]

Variable	Placebo Group	Evening Primrose Oil Group	P Value
Age, y	23.5 ± 3.25	23.8 ± 3.05	0.7[b]
Husband's age, y	26.34 ± 1.94	26.72 ± 2.6	0.34[b]
Marriage age, y	22.04 ± 3.35	21.9 ± 2.6	0.7[b]
Occupation			0.069[c]
Housemaker	63 (95.5)	55 (86.4)	
Employed	3 (4.5)	9 (13.6)	
Husband's occupation			0.65[c]
State	11 (16.7)	13 (19.7)	
Self-employed	55 (83.3)	53 (80.3)	
Education			0.67[c]
Primary school	23 (34.8)	23 (19.7)	
Diploma	32 (48.5)	33 (50)	
Higher education	11 (16.7)	20 (30.3)	
Husband's education			0.48[c]
Primary school	18 (27.3)	15 (22.7)	
Diploma	34 (51.5)	31 (47)	
Higher education	14 (21.2)	20 (30.3)	
Economic status			0.68[c]
Good	15 (22.7)	17 (25.8)	
Moderate	51 (77.3)	49 (74.2)	

[a] Values are expressed as SD ± mean or No. (%).
[b] T test.
[c] Chi-square test, P < 0.05 was considered significant.

The average scores of mental health were 12.4 ± 4 and 11.9 ± 6.4 in the intervention and control groups, respectively (P = 0.77).

There was a significant difference between the mean scores of Edinburgh test of the participants in the intervention and control groups on days 4 and 10, but not on the day 14 postpartum (P = 0.0001, P = 0.0001, P = 0.08, respectively). Repeated measure test indicated statistically significant difference between the two groups in total (P = 0.0001) (Table 2).

Totally, 12.1% of the subjects in the intervention group had mild, 12.1% moderate, and 3% severe postpartum blues. In the control group, 16.7% had mild, and 40.9% had severe postpartum blues. There was a significant difference between the two groups in the mean of postpartum blues (P = 0.0001) (Table 3).

5. Discussion

The current study aimed at determining the effect of evening primrose oil on the severity of the postpartum blues in primigravida females. Results of the current study showed that the postpartum blues reduced significantly in the intervention group compared with that of the control group. Prime rose oil is rich in Omega-3 (19). The high levels of Omega-3 in brain tissue can be considered the most important brain structure after water. Omega-3 with the mechanism of action on the nervous system by depressing phospholipids of the nerve cell walls and the proper functioning and the secretion of neurotransmitters may be appropriate to reduce psychological symptoms including anxiety and depression (25). Also, by reducing cytokines, it can cause the proper functioning of the hypothalamus, pituitary, and nervous system. Another impact is the increase of brain-derived neurotrophic factor polypeptides that is highly effective to increase the growth and survival of nerve cells and their evolution (25).

There is evidence suggesting that Omega-3 has an effect on serotonin cerebrospinal fluid and can reduce the levels of that in cell membranes and plasma of patients with depressive disorders (13). Some researchers found a significant correlation between abnormal metabolism of fatty

Table 2. Comparison of Edinburgh Scores Three Times After Delivery Between the Evening Primrose Oil and Placebo Groups (N = 66)[a]

Edinburgh Average Score, (Mean ± SD)	Placebo Group	Evening Primrose Oil Group	P Value
The day, y 4	13.3 ± 3.28	10.5 ± 0.57	0.0001[b]
The day 10	14.9 ± 3.6	11.2 ± 1.22	0.001[b]
The day 14	13.05 ± 2.6	11.7 ± 1.3	0.08[b]

[a]Values are expressed as SD ± mean.
[b]Repeated measures, P < 0.05 was considered significant.

Table 3. The severity of Developing Postpartum Blues in the Study Groups (N = 66)

Severity of Postpartum Blues, N. (%)	Placebo Group	Evening Primrose Oil Group	P Value
Mild	11 (16.7)	8 (12.1)	0.0001[a]
Moderate	0 (0)	8 (12.1)	
Severe	27 (40.9)	2 (3)	

[a]Chi-square test, P < 0.05 was considered significant.

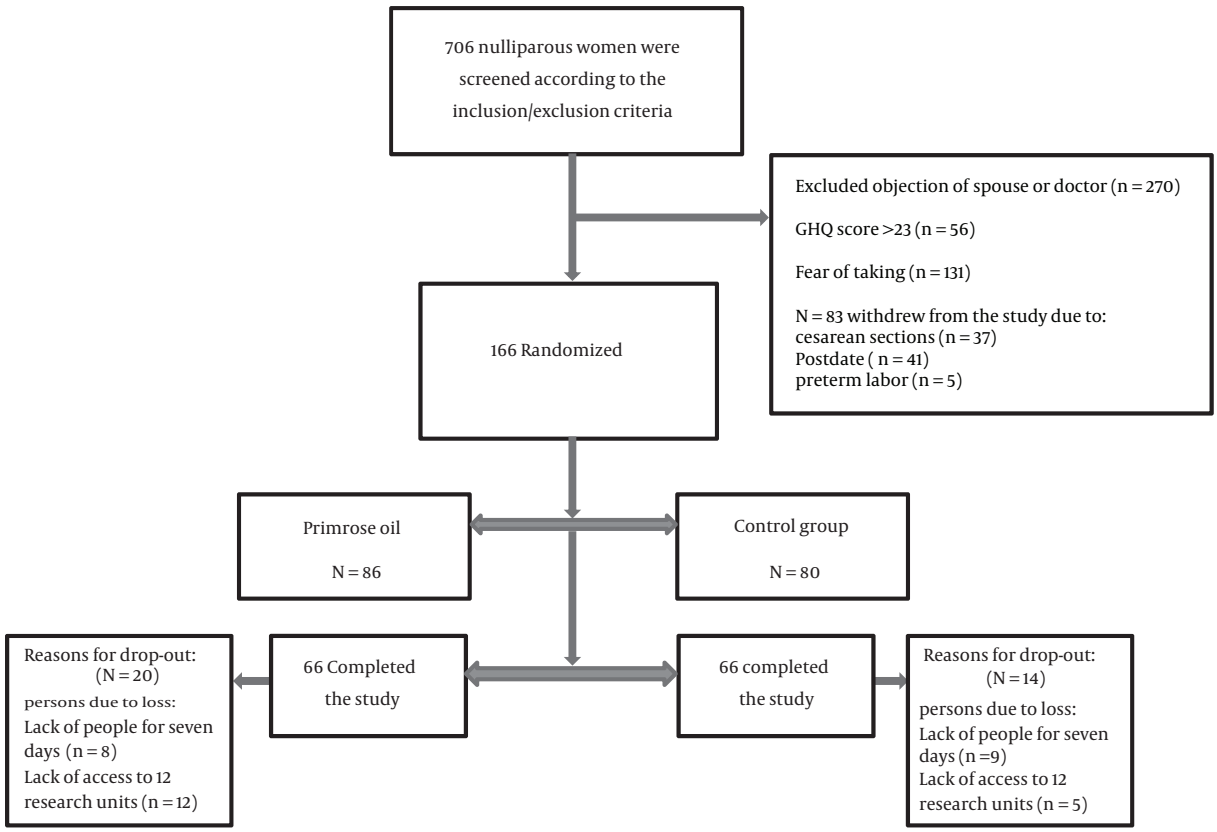

Figure 1. Flowchart of Recruitment and Retention of Participants in the Study

acids and depression, and lower levels of unsaturated fatty acid Omega-3 is effective in causing depressed mood, creating a negative view of life, impulsive behaviors, and suicide (14).

The results of the present study showed that the average Edinburgh score on the day fourth postpartum in the intervention group decreased significantly compared with that of the control group and on the days 10 and 14

postpartum, and increased with a gentle slope. Whereas in the control group, the Edinburgh scores on the day 4 were high, and on the days 10 and 14 had a decreasing mode. Overall, Edinburg test scores on the days 4, 10, and 14 postpartum in the intervention group were significantly lower than that of the control group. This means that over time, both groups, in terms of incidence of postpartum blues, were close to normal psychological situation. Howevere, in an era where there is a risk of postpartum blues, Edinburgh test score that reflects the mental state of the mother, was much lower in the intervention group than the control group. The difference of Edinburgh's score between the two groups was more remarkable on the days 4 and 10 postpartum, since this time is the beginning of the disorder postpartum blues. This reflects the positive effect of evening primrose oil in the intervention group to reduce the severity of postpartum blues.

Caballero et al., and Lapresti et al., found that increasing the consumption of Omega-6 compared to Omega-3 may lead to mental disorders. They concluded that taking Omega-3 may be considered for patients with depression (26, 27). Evian Bagha et al., compared the effectiveness of Omega-3 fatty acids with placebo to treat mild to moderate postpartum depression in females in Tabriz, Iran. Their results showed that taking Omega-3 capsules at a dose of 1 g per day for eight weeks could significantly reduce postpartum depression ($P < 0.0005$) that was consistent with the results of the current study (28). Also, Kuan-Pin Su et al., conducted a study to examine the effect of Omega-3 fatty acids on postpartum depression. Their results showed that the positive impact of omega-3 on postpartum depression was observed from the week four after starting the treatment (29).

A meta-analysis by Lin et al. was performed on 14 studies to determine the association of Omega-3 and Omega-6 with depression. The results of this study showed that the levels of Omega-3 fatty acids in patients with depression compared with those of the healthy people were significantly lower ($P < 0.001$), while this difference was not observed in the Omega-6 fatty acids. The researchers concluded that Omega-3 fatty acids affected the improvement of depression that was consistent with the results of the current study (30).

However, Einvik et al. concluded that Omega-3 did not affect the improvement of mental health problems that contradicts the results of the current study (31). The reason for this dissimilarity may be due to the difference in nutritional counseling in their study and /or differences in the age and gender of the participants.

Many researches are conducted on the effect of evening primrose oil on the hormonal disorders in females with anxiety and depression including the study by Fathizadeh conducted on 66 women with the pain or tenderness in their breasts. Patients were divided into two groups, one group daily received 3 g of evening primrose oil and the other group received 622 mg of Vitamin E daily. Pain intensity of patients was assessed before and one month after intervention by the Cardiff chart. The results showed that the intensity of periodical pain in both groups showed a significant decline after the treatment ($P < 0.05$). The findings of this research showed that evening primrose oil was more effective than Vitamin E. In this study, none of the participants, in terms of severity of pain, both in the evening primrose and vitamin E groups was pain-free before the intervention, but after the intervention 61.3% of participants in the evening primrose group and 26.7% in the Vitamin E group were pain-free. Comparison of the two groups showed that evening primrose was more effective than Vitamin E (32), which was consistent with the results of the current study.

Freeman et al., reported that Omega-3 was highly effective in reducing the severity of postpartum depression (33), which was consistent with the results of the current study. Gallagher et al., examined the effect of evening primrose oil and reported that the evening primrose could be effective to prevent and reduce the severity of postpartum depression; similar to the results of the current study (34).

Doornbos et al., in the Netherlands found that taking 220 mg docosahexaenoic acid (DHA) started from the week 16 of gestation until three months after delivery was not effective to prevent postpartum depression (35). These results were not in line with the current study findings. The reason for this dissimilarity may be due to the fact that the serum levels of Omega-3 in females in the abovementioned study were reported low, and maybe the participants needed more Omega-3.

5.1. Strengths and Limitations of the Study

According to the authors' best knowledge; it was the first time that a study was conducted on the effects of primrose oil on postpartum blues. The current study recruited females from the week 37 of gestation and intensively followed them until two weeks postpartum. The food intake of participants, especially regarding Omega-3, was not measured. Perhaps with knowing the level of Omega-3, females with lower levels of Omega-3 could be identified. However, the current study results showed that most females in both groups belonged to the same socioeconomic level.

5.2. Conclusion

Evening primrose oil might be an herb effective and devoid of any side effects on reducing the severity of postpartum blues.

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Footnotes

Authors' Contribution: Data collection, Soghra Nikoomazhab; biostatistics analysis, Soghra Nikoomazhab, Parvin Abedi; study design, Parvin Abedi, Soghra Nikoomazhab, Mohammad Reza Haghdoust; final revision and editing the manuscript: Azam Honarmandpour.

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