

## The Impact of Nutritional Supplement on Reducing the Symptoms of Primary Dysmenorrhea in Comparison to the Classical Anti-Inflammatory Treatment; A Sequential Self Case-Controlled Study

Maryam Rezaeyan, Parichehr Khedri and Ashraf Direkvand-Moghadam\*

Faculty of Nursing and Midwifery Ilam University of Medical Sciences, Ilam, Iran

This article was published in the following Scient Open Access Journal:

Women's Health & Gynecology

Received December 25, 2016; Accepted February 14, 2017; Published February 21, 2017

### Abstract

**Objective:** Primary dysmenorrhea occurs as a result of release of prostaglandins due to the destruction of the endometrial cells in the uterus. The present study aimed to compare the effect of a nutritional supplement with classical anti-inflammatory treatment in reducing the symptoms of primary dysmenorrhea.

**Design:** A sequential self case-controlled study was conducted among 60 single university students who suffered from primary dysmenorrhea accommodated on the campus of Islamic Azad University Branch of Boroujerd, Iran from January- November 2011. Each participant was randomly assigned to A or B group. The A group received 25 cc of Extra Virgin Olive Oil (EVOO) daily for 2 months during two weeks before the start of the menstrual cycle. After 4-week washout period, they received Ibuprofen three times, as soon as the onset of menstrual cycle for 2-3 days. The B group included classical treatment treated basically similarly, except that they received Ibuprofen during the two first cycles, then 4-week washout period and EVOO during the two cycles. A P value of 0.05 was considered statistically significant.

**Results:** Classical and nutritional supplement interventions reduced the extent of pain, but the difference between two types of intervention was not statistically significant. The pain grade was decreased among classical and nutritional supplement interventions. The dysmenorrhea symptoms decreased after both interventions.

**Conclusions:** Since the classic treatments have significant side effects in some consumers, we recommend the use of nutritional supplements to reduce the symptoms of primary dysmenorrhea and promote overall health.

**Keywords:** Cox Menstrual Symptom Scale, Dysmenorrhea, Extra Virgin Olive Oil, Verbal Multidimensional Scoring

### Introduction

Dysmenorrhea is a common condition among women in reproductive age [1]. Based on the absence or presence of a basic reason, the dysmenorrhea is classified into two groups of primary and secondary dysmenorrhea. Primary dysmenorrhea is a physiological condition that occurs as a result of release of prostaglandins due to the destruction of the endometrial cells in the uterus and subsequent uterine contractions. These contractions, and the resulting temporary oxygen deprivation to nearby tissues, are responsible for the pain and cramps experienced during the primary dysmenorrhea [2]. While, secondary dysmenorrhea represents a pathological condition that requires further investigation and treatment [3].

However, the pelvis or lower abdomen are the most common symptoms of dysmenorrhea, but also, some women experience other primary dysmenorrhea symptoms including nausea, vomiting, diarrhea or constipation, headache, dizziness, disorientation. In the most cases, symptoms start with menstruation begins and last less than three days [1,4].

Due to the annoying symptoms and the individuals demand there are a variety of pharmacological and non-pharmacological therapies for the treatment of primary dysmenorrhea. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are the most common treatments for primary dysmenorrhea [5]. But it should be noted that NSAIDs have

\*Corresponding Author: : Ashraf Direkvand-Moghadam, Psychosocial Injuries Research Center, Faculty of Nursing and Midwifery Ilam University of Medical Sciences, Ilam, Iran, Tel: +98 8432240404, Fax: +98 8432240404, Email: [direkvand-a@medilam.ac.ir](mailto:direkvand-a@medilam.ac.ir)

several side effects included; nausea, dyspepsia, peptic ulcer, and diarrhea [4].

However, in cases where individuals are unable to take NSAIDs medications, the COX-2 inhibitor are recommended as other effective therapies in the treatment of primary dysmenorrhea [6].

The uses of nutritional supplements are recommended methods in the treatment of primary dysmenorrhea. Thiamine and vitamin E are recommended as effective nutritional supplements on primary dysmenorrhea [7]. Vitamin B1 and Magnesium are other potential supplement for treatment of primary dysmenorrhea [8].

Today, Extra Virgin Olive Oil (EVOO) is taken into consideration for its anti-inflammatory properties. Virgin olive oil is an essential component of a Mediterranean diet. Also the nutritional, medical, and cosmetic benefits of Virgin olive oil are widely recognized and accepted [9]. A study exposed significant antioxidant and anti-inflammatory effects of EVOO [10]. Several studies have been confirmed the anti-inflammatory properties of olive oil [11-13].

Because the role of inflammatory factors approved in the creation of primary dysmenorrhea, seems logical the use of uncomplicated nutritional supplements to control symptoms of dysmenorrhea. In the present study compared the effect of EVOO as a nutritional supplement with Ibuprofen as a classical anti-inflammatory treatment in reducing the symptoms of primary dysmenorrhea.

## Methods

A sequential self case-controlled study was conducted among 60 single university students who suffered from primary dysmenorrhea accommodated on the campus of Islamic Azad University Branch of Boroujerd, Iran from January- November 2011. The sample size was computed using  $\alpha=5\%$  and power by 80%. However, 54 eligible participants were estimated as the study sample size, considering the possibility of sample loss 30 eligible participants were allocated in each group and finally 60 eligible participants were enrolled in the study.

The inclusion criteria included age 18-30, regular menstrual cycles, moderate primary dysmenorrhea. The exclusion criteria were all cases with known abnormalities affecting pelvic pain and dysmenorrhea, use of OCP contraceptive, medicines or plant allergy and mild dysmenorrhea, everyone who taking any medication for reduce the symptoms of dysmenorrhea before the interventions due to possibility of correct compared before and after intervention .After getting written permission from of Islamic Azad University Branch of Boroujerd researcher visited the students of the dormitories and objectives of the study were explained to them.

In order to identify and follow up of eligible participants, both questionnaire and checklist was used. The questioner was included the demographic data, menstrual history, smoking, diet, exercise and past medical and reproductive history that was completed before the intervention of the trial. The checklist was designed to cover the severity and duration of pain and the accompanying symptoms was completed during the months follow up of the study. Then the eligible and interested participants fulfilled the self-completed questionnaire and were visited physically by a licensed gynecologist before randomization. Randomization was determined on a 1:1 basis using random number tables.

The primary outcome was the extent and duration of menstrual pain. However, the secondary outcomes were the intensity of menstrual symptoms including fatigue, vomiting, headache, diarrhea and menstrual bleeding volume. The first section of checklist was the extent of pain that determined by a Cox Menstrual Symptom Scale. The second section of checklist was designed to cover the intensity of menstrual pain and the accompanying symptoms. These checklists were completed during the all months follow up of the study. The intensity of menstrual symptoms was determined using the Verbal Multidimensional Scoring System (VMS) (Andersch and Milsom, 1982) [14]. The VMS grading system ranges from grade 0 to 3 for evaluating the working ability, the systemic symptoms and analgesia required (Table 1).

A Higham chart was use to assessment of menstrual blood loss [15]. The grade 0 means the mild menstrual volume and equal 1 cc or spotting, grade 1 means the moderate and equal 5 cc menstrual volume and grade 2 means sever and equal 20 cc menstrual volume.

An Iranian product of Extra Virgin olive oil was used which is made simply by crushing olives and extracting the juice by Razi Herbal Medicine Center, Lorestan University of Medical Sciences, Iran. Each 100 ml of EVOO containing: saturated fat: 13.8%, monounsaturated fat: 73% (most of it the 18 carbon long oleic acid), omega-6: 9.7%, omega-3: 0.76%, vitamin E: 72% of the RDA and vitamin K: 75% of the RDA.

Each participant was randomly assigned to A or B group (30 participants in each group). The A group received a nutritional supplement included 25 cc of EVOO daily for 2 months during two weeks before the start of the menstrual cycle and completed a checklist containing items on Cox Menstrual Symptom Scale and VMS grading for two consecutive cycles. After 4-week washout period, they received Ibuprofen (400mg) orally three times, as soon as the onset of menstrual cycle for 2-3 days. The B group included classical treatment treated basically similarly, except that they received Ibuprofen during the two first cycles, then 4-week washout period and EVOO during the two cycles. All participants were permitted to take another drug that they

| Grade   | Working ability     | Systemic symptoms | Analgesia       |
|---|---------------------|-------------------|-----------------|
| Grade 0: Menstruation is not painful and daily activity is unaffected   | Unaffected          | None              | Not required    |
| Grade 1: Menstruation is painful but seldom inhibits the woman's normal activity. Analgesics are seldom required. Mild pain                               | Rarely affected     | None              | Rarely required |
| Grade 2: Daily activity affected. Analgesics required and give relief so that absence from work or school is unusual. Moderate pain                       | Moderately affected | Few               | Required        |
| Grade 3: Activity clearly inhibited. Poor effect of analgesics. Vegetative symptoms, e.g. headache, tiredness, nausea, vomiting and diarrhea. Severe pain | Clearly inhibited   | Apparent          | Poor effect     |

**Table 1:** The verbal multidimensional scoring system (VMS)

usually took for their pain relief, in addition to the allocated treatment in case of continued pain. However, at the end of the trial, these participants were excluded in data analysis. Changes in the menstrual symptom and the duration of the pain of participants were compared in both groups.

This study was undertaken with the approval of the ethics committee of Azad University Branch of Boroujerd. This study was registered in IRCT with NO; IRCT2013051110804N2. Participation in the study was voluntary and the participants were free to withdraw from the study whenever they wished. Informed consents were obtained from all participants before their enrollment into the study. All collected data were analyzed using SPSS version 16 (IBM, Armonk, NY, USA). Comparisons of means were done by t-test and t paired test, A P value of 0.05 was considered statistically significant. Statistical comparisons were made using the Mann-Whitney U test and Chi-square test.

## Results

The Mean (SD) age was 21.86 (2.35) and 22.86 (2.35) years in A and B groups, respectively. The pain grades were similar in both groups before the intervention. No significant difference was observed for the matched characteristics studied, including age start of dysmenorrhea, duration of menstruation and pain duration between the two groups. All symptoms associated with dysmenorrhea were similar among study participants before the interventions ( $p > 0.594$ ).

The result showed that although both interventions reduced the extent of pain determined by a Cox Menstrual Symptom Scale in compared with before interventions ( $P < 0.001$ ), but the difference between two types of intervention was not statistically significant ( $P > 0.08$ ) (Table 2).

On the first day of the 2th month of intervention, the Mean (SD) of pain grade was decreased amongst classical and nutritional supplement interventions from 2.2 (0.2) to 1.23 (0.4) and 2.1 (0.3) to 1.7 (0.33), respectively, using the given dose explained at method section. These differences were statistically significant ( $P < 0.05$ ).

The result showed that the Mean (SD) of dysmenorrhea symptoms, including fatigue, vomiting, headache and bleeding, decreased after both interventions in compared with before interventions ( $P < 0.05$ ), but these differences was not statistically significant between two types of intervention ( $P > 0.05$ ) (Table 3). However, the differences between Mean  $\pm$  SD of diarrhea before and after intervention was not significant ( $P = 0.211$ ).

## Discussion

Although the chemical medicines are used widely for the treatment of primary dysmenorrhea, due to concerns regarding the side effects of using these drugs [4,5,8], this study compared

| Pain extent     | Interventions    |                               | P- value |
|-----------------|------------------|-------------------------------|----------|
|                 | Classical, N (%) | Nutritional supplement, N (%) |          |
| Less than 0.5 h | 3 ( 10)          | 2 ( 6.7)                      | 0.08     |
| 0.5-1 h         | 6( 20)           | 7(23.3)                       |          |
| Several h       | 18 (60)          | 19 (63.3)                     |          |
| Several days    | 3 (10)           | 2 (6.7)                       |          |

**Table 2:** The comparison of the pain extent using a Cox Menstrual Symptom Scale among study participants in 2nd months of interventions

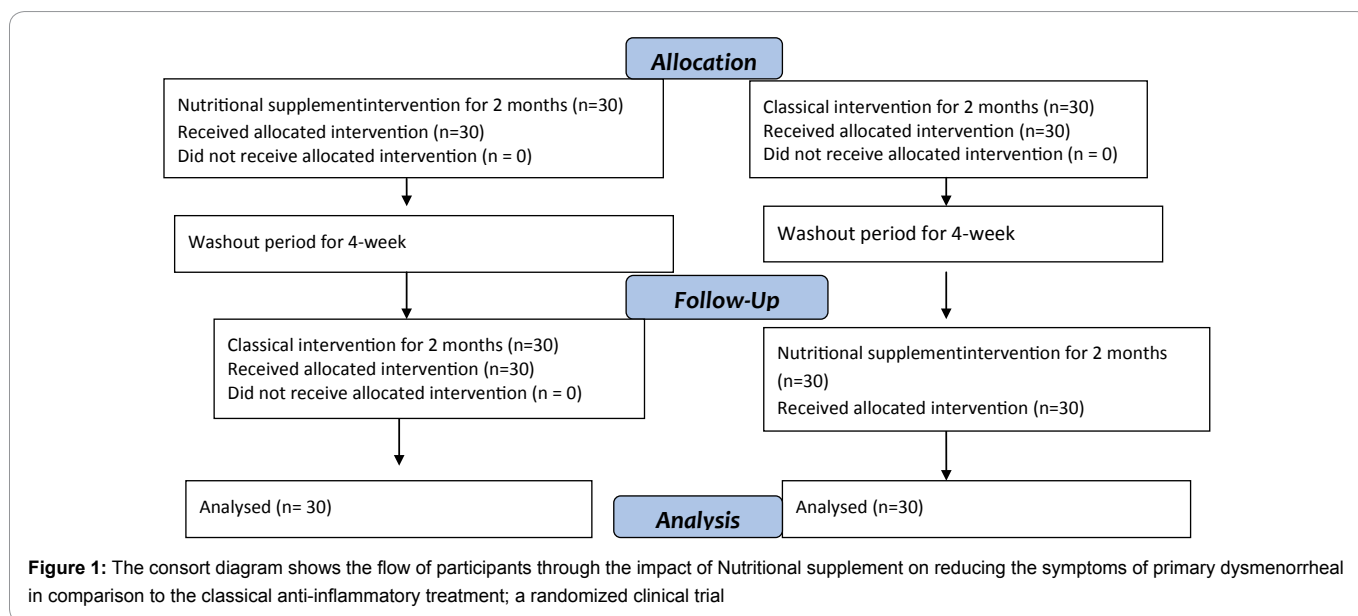
the efficacy of nutritional supplements and classic medication to reduce symptoms of primary dysmenorrhea.

Based the results of the present study, both Ibuprofen as a classical treatment and EVOO as a nutritional supplement decreased the duration and intensity of symptoms of primary dysmenorrhea.

In general, uterine ischemia, cervical stenosis, increased

| Variable | Interventions          | Intensity of symptoms | Group A, N (%) | Group B, N (%) | P-value |       |
|----------|------------------------|-----------------------|----------------|----------------|---------|-------|
| pain     | Classical              | Grade 0               | 2 ( 6.7)       | 1 ( 3.3)       | 0.734   |       |
|          |                        | Grade 1               | 6( 20)         | 7(23.4)        |         |       |
|          |                        | Grade 2               | 18 (60)        | 19 (63.3)      |         |       |
|          |                        | Grade 3               | 4 (13.3)       | 3 (10)         |         |       |
|          | Nutritional supplement | Grade 0               | 1 (3.3)        | 2 ( 6.7)       |         |       |
|          |                        | Grade 1               | 7(23.4)        | 7(23.4)        |         |       |
|          |                        | Grade 2               | 19 (63.3)      | 18 (60)        |         |       |
|          |                        | Grade 3               | 3 (10)         | 3 (10)         |         |       |
| Fatigue  | Classical              | Grade 0               | 1 ( 3.3)       | 2 ( 6.7)       | 0.999   |       |
|          |                        | Grade 1               | 18 (60)        | 18 (60)        |         |       |
|          |                        | Grade 2               | 9 (30)         | 9 (30)         |         |       |
|          |                        | Grade 3               | 2 (6.7)        | 1 (3.3)        |         |       |
|          | Nutritional supplement | Grade 0               | 26 ( 86.7)     | 23 ( 76.7)     |         | 0.373 |
|          |                        | Grade 1               | 4 (13.3)       | 6 (20)         |         |       |
|          |                        | Grade 2               | 0 (0)          | 1 (3.3)        |         |       |
|          |                        | Grade 3               | 0 (0)          | 0 (0)          |         |       |
| Vomiting | Classical              | Grade 0               | 1( 3.3)        | 1(3.3)         | 0.990   |       |
|          |                        | Grade 1               | 12(40)         | 13 (43.3)      |         |       |
|          |                        | Grade 2               | 7 (23.3)       | 6 (20)         |         |       |
|          |                        | Grade 3               | 10 (33.3)      | 10 (33.3)      |         |       |
|          | Nutritional supplement | Grade 0               | 22( 73.3)      | 27(90)         |         | 0.181 |
|          |                        | Grade 1               | 8(26.7)        | 3 (10)         |         |       |
|          |                        | Grade 2               | 0 (0)          | 0 (0)          |         |       |
|          |                        | Grade 3               | 0 (0)          | 0 (0)          |         |       |
| Diarrhea | Classical              | Grade 0               | 10 (33.3)      | 7 (23.3)       | 0.447   |       |
|          |                        | Grade 1               | 12(40)         | 16 (53.3)      |         |       |
|          |                        | Grade 2               | 7(23.3)        | 7 (23.3)       |         |       |
|          |                        | Grade 3               | 1 (3.3)        | 0 (0)          |         |       |
|          | Nutritional supplement | Grade 0               | 26 (86.7)      | 26 (86.7)      |         | 0.763 |
|          |                        | Grade 1               | 2(6.7)         | 3 (10)         |         |       |
|          |                        | Grade 2               | 2(6.7)         | 1 (3.3)        |         |       |
|          |                        | Grade 3               | 0 (0)          | 0 (0)          |         |       |
| Headache | Classical              | Grade 0               | 3 (10)         | 3 (10)         | 0.993   |       |
|          |                        | Grade 1               | 16 (53.3)      | 15 (50)        |         |       |
|          |                        | Grade 2               | 8 (26.7)       | 9 (30)         |         |       |
|          |                        | Grade 3               | 3 (10)         | 3 (10)         |         |       |
|          | Nutritional supplement | Grade 0               | 23 (76.7)      | 25 (83.3)      | 0.745   |       |
|          |                        | Grade 1               | 5 (16.7)       | 3 (10)         |         |       |
|          |                        | Grade 2               | 2(6.7)         | 2(6.7)         |         |       |
|          |                        | Grade 3               | 0 (0)          | 0 (0)          |         |       |
| Bleeding | Classical              | Grade 0               | 27( 90)        | 24(80)         | 0.247   |       |
|          |                        | Grade 1               | 3 (10)         | 6 (20)         |         |       |
|          | Nutritional supplement | Grade 2               | 0 ( 0)         | 0 ( 0)         |         |       |
|          |                        | Grade 0               | 27( 90)        | 24(80)         |         | 0.427 |
| Grade 1  | 3 (10)                 | 6 (20)                |                |                |         |       |
| Grade 2  | 0 ( 0)                 | 0 ( 0)                |                |                |         |       |

**Table 3:** The intensity of symptoms associated with dysmenorrhea among study participants after 2 month of the interventions



vasopressin release, augmented uterine activity, and increased uterine prostanoid production and release have been accepted as main causes of primary dysmenorrhea [16]. Evidence showed that most women whose suffer from primary dysmenorrhea, experience an increasing of endometrial secretion of prostaglandin F2 during their menstrual phase [16].

EVOO contains more than 30 bioactive powerhouses called phenols, with anti-inflammatory and antioxidant properties. A wide range of evidence indicates that phenolic compounds present in EVOO have remarkable anti-inflammatory effect. Oleocanthal is the best-known of these properties. Infect the Oleocanthal component of EVOO inhibits the enzymatic path of pain, similar NSAIDs drugs. Although the chemical structure of the EVOO is different from the NSAIDs drugs [17-19].

The considerable point in the results of the current study is that, Ibuprofen and EVOO intervention have the same effect in reducing symptoms of primary dysmenorrhea. So that in the 2th month of both interventions, there were any cases of severe menstrual bleeding. Despite the fact that the frequency of moderate menstrual bleeding was twice in the Ibuprofen intervention in comparison to EVOO intervention, this difference was not statistically significant.

Anti-inflammatory effect of NSAIDs and Ibuprofen as famous NSAIDs has been confirmed in extensive studies. Ibuprofen inhibits inflammatory reactions and pain because of declining the activity of cyclooxygenase, thereby decreasing prostaglandin synthesis [2,5,20].

A study investigated the anti-inflammatory effects of phenolic compounds from extra virgin olive oil and stating that Oleuropein glycoside can decrease the concentration of interleukin-1beta by 80%. Whereas caffeic acid inhibited production of interleukin-1beta by 40%. As well Kaempferol decreased the concentration of prostaglandin E2 [21].

Actually, the safety and cost-effectiveness should be considered as important elements when choosing therapies and health promotion interventions. Considering to expenses

incurred by primary dysmenorrhea include including 600 million work hours and 2 \$ billion less annually [22], it is necessary to search for treatment options that are reasonably safe and cost-effectiveness. On this line, a study reported that daily consumption of 50 grams (equal to 4 tablespoons) of EVOO will create an anti-inflammatory effect in adults' humans. However, this effect is less than Ibuprofen [23], but also, it should be noted that daily consumption of EVOO is not associated with induced gastrointestinal side effects of long-term use of Ibuprofen.

According to what was said, the cost of consumption of olive oil is less than the cost of preventable diseases by the EVOO.

## Conclusion

Both classical treatment and nutritional supplement have the same effect to decrease the intensity of symptoms of primary dysmenorrhea. Since the classic treatments have significant side effects in some consumers, we recommend the use of nutritional supplements to reduce the symptoms of primary dysmenorrhea and promote overall health.

## Acknowledgment

We thank the participants, coordinators, and data reviewers who assisted in this study.

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