

The Effect of Vitamin E on Ameliorating Primary Dysmenorrhea: A Systematic Review and Meta-analysis

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ABSTRACT

Dysmenorrhea or painful menstruation is one of the most common problems of women. Using systematic review and meta-analysis, this study aimed to determine the effect of vitamin E on ameliorating the intensity of pain of primary dysmenorrhea. Available databases comprising PubMed, Google Scholar, ISI, Science Direct, SID, Iran Medex, and Magiran were searched to find relevant papers. Clinical trials with the aim of the effect of vitamin E on pain reduction of primary dysmenorrhea were selected. Two independent reviewers assessed the quality of studies and extracted the necessary data. Three studies were eligible for meta-analysis. The meta-analysis of these studies showed that vitamin E (with or without mefenamic acid), could reduce the intensity of pain about 7% (95% CI: 2-30%). Based on these studies, vitamin E can reduce the intensity of primary dysmenorrhea.

KEY WORDS: Complimentary medicine, dysmenorrhea, vitamin E

INTRODUCTION

Normal menstruation is the periodic shedding of the uterine endometrial layer as a result of falling estrogen and progesterone levels, which occurs due to corpus luteum regression.^[1] Almost 50% of women experience dysmenorrhea and 1% of reproductive age women take a leave from their jobs about 1-3 days in a month because of dysmenorrhea.^[2] However, dysmenorrhea does not threaten women's lives; it can influence their quality of life and even cause their inability when the pain intensity is high.^[3,4]

Dysmenorrhea is the most common cyclic pain in women and based on its cause, it can be divided into two types.^[1] Primary dysmenorrhea is painful menstruation without any pelvic diseases, and secondary dysmenorrhea is painful menstruation as a result of pelvic pathologic problems such as endometrioses and pelvic inflammatory disease (PID). The most common age of primary dysmenorrhea occurrence is about 15-25 years.^[5] Wong and Khoo indicated that more

than half of the Asian girls who have dysmenorrhea had limited concentration in the classroom and restricted social activities; 21.5% of these girls missed school; and 12.0% had poor performance in school.^[6] Kordi *et al.* showed that dysmenorrhea is positively correlated with occupational stress.^[7] The prevalence of dysmenorrhea has been reported to be between 16.8-81% by the World Health Organization (WHO).^[8] In Iran, the incidence of primary dysmenorrhea has been reported to be 74-81.6%.^[9]

The high prevalence and medical, social, and economic complications of primary dysmenorrhea has led to several studies for finding its treatment. The actual reason of dysmenorrhea is unknown; however, the accepted theory is the high production of endometrial prostaglandins. Therefore, the aim of the treatment should be reduction of prostaglandins.^[10] There are various alternatives for treatment of primary dysmenorrhea such as non-steroidal anti-inflammatory drugs (NSAIDs), oral contraceptive pills (OCPs), psychotherapy, vitamins, and several vegetative medications.^[11,12] The first choice for treatment of primary dysmenorrhea is anti-prostaglandin medications such as Ibuprofen^[13] whose side effects include nausea, stomach

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ache, reflux, diarrhea, and constipation.^[14] Because of these side effects of this group of medications, some other methods such as vitamins have been considered. Vitamin E is an antioxidant without any side effects; it prevents pre-oxidation of phospholipids, releasing arachidonic acid, and converting it to prostaglandins.^[15,16] Many studies have shown the effect of vitamin E on ameliorating primary dysmenorrhea. In some of these studies, the effect of vitamin E is compared with placebo and in some of the others with mefenamic acid, Ibuprofen, etc., Therefore, the aim of this study was to investigate the effect of vitamin E on ameliorating primary dysmenorrhea from aspects of pain intensity with systematic review and meta-analysis. All participants were women of reproductive age with dysmenorrhea; the intervention was the effect of vitamin E in comparison with placebo, and the outcome was pain intensity.

MATERIALS AND METHODS

Search method

In this study, available literature searched in databases of SID, Science Direct, Google Scholar, ISI, PubMed, Magiran, Iran Medex with the purpose of finding the related sources. This search included the period from database inception until the end of 2013. Reference list of all articles and related reports accessed from electronic search was investigated manually with the purpose of finding the other probable sources. In order to reach maximum sensitivity in primary search, the English and Persian keywords of dysmenorrhea and ("Vitamin E" or Tocopherol or Alpha Tocopherol) were used. After preparing the primary table of content, two of the study authors, investigated the titles and abstracts (in case of accessibility) independently and identified the articles related to the topic.

Quality assessment

The related studies were evaluated based on Jadad scale to determine minimum quality. This scale assesses studies according to probability of errors in randomization, follow up of patients, and blinding. In this scale, the maximum score is five.^[17] The studies that gained a score of three or more were included in this study. The clinical trials related to pain were assessed further with the Oxford Pain Validity Scale (OPVS) qualitatively. This instrument examines studies based on blinding, groups' size, outcome measures, baseline pain and internal sensitivity, and statistical analysis items. The maximum score in this scale is 16 and the minimum accepted score is 12.^[18] Clinical trials that were more effective had more chance of publication; therefore, the risk of publication bias may exist.

Data summarizing method

The data were entered to special sheets and final records table. The meta-analysis was carried out based on the records table and mean and standard deviation

of pain intensity. Articles in which participants had consumed vitamin E two days before and three days after menstruation with outcome assessment after two months using the Visual Analogue Scale (VAS) were entered to meta-analysis.

RESULTS

After quality assessment among 15 selected studies, the studies of Butler and McKnight^[19] and Moslemi *et al.*^[20] because of different period of treatment (10 days and 2 months, respectively, against 2-3 days), the study of Akhlaghi *et al.*^[21], because of lack of control group (comparison of pain before and after intervention), the studies of Zakeri Hamidi *et al.*^[22] and Farahmand *et al.*^[23] because of different study outcomes (reduction in gastrointestinal disorders and amount and duration and interval of menstrual bleeding), and the studies of Sehati *et al.*^[24] and Nasehi *et al.*^[25] because of different intervention method (the combination of fennel extract and vitamin E), were excluded from Meta-Analysis. In addition, two related studies with crossover design^[26,27] and two studies with another intervention (acupressure in SanYinJiao points^[28] and Omega 3^[29]) instead of placebo were also excluded from meta-analysis. However, the results of excluded studies were assessed and discussed.

Finally, among four clinical trials eligible for meta-analysis based on criteria,^[9,30-32] one study was excluded because it did not have any information about mean and standard deviation.^[9] The characteristics of included studies in meta-analysis are shown in Table 1.

Figure 1 shows the diagram of the effect of vitamin E in comparison with placebo on pain reduction of dysmenorrhea. As can be seen in the diagram, among three studies participating in meta-analysis, the study of Ziaei *et al.* did not show statically significant effect of vitamin E on reducing pain intensity of primary dysmenorrhea.^[30] However, two other studies showed the effect of vitamin E on pain reduction.^[31,32] The meta-analysis of these studies showed that consuming vitamin E had a statically significant effect on pain reduction. Accordingly, regardless of pain intensity scale (10 points or 100 points), using vitamin E (with or without mefenamic acid) caused about 7% (95% CI: 2-30%) pain intensity reduction in participants.

DISCUSSION

Systematic review and meta-analysis of clinical studies showed that vitamin E is effective in pain intensity reduction of dysmenorrhea.

Table 1: Characteristics of clinical trials included into meta-analysis of the effect of vitamin E on pain intensity of primary dysmenorrhea

Author, year	OPVS score	Age	Intervention	Dose (IU)	Statistics are presented for comparison	No. in intervention group	No. in control group	Intervention group				Control group			
								Mean pain intensity score		SD of the mean pain intensity score		Mean pain intensity score		SD of the mean pain intensity score	
								Baseline	2 months	Baseline	2 months	Baseline	2 months	Baseline	2 months
Ziaei et al. 2001	15	16-18	Vitamin E	500	Mean of pain score (VAS 10 point)	50	50	5.5	3.5	3.7-5	0.5	5.4	4.3	3.7	2-6.5
Yaghmaei et al. 2005	14	Less than 30	Vitamin E and mefenamic acid compared with mefenamic acid and placebo	400	Mean of pain score (VAS 100 point)	34	32	67.5	17.5	17.3	16.2	66.0	41.5	17.4	21.6
Kashanian et al. 2010	15	18-25	Vitamin E	400	Mean of pain score (VAS 10 point)	42	52	7.4	4.7	1.8	1.8	7.1	5.3	1.7	2.0

VAS: Visual analogue scale; OPVS: Oxford pain validity scale

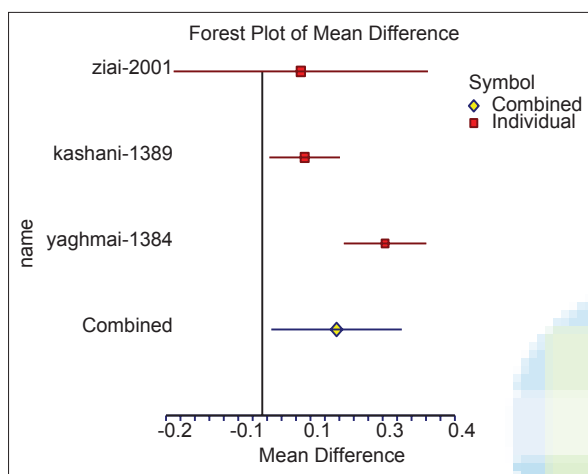


Figure 1: The effect of vitamin E on ameliorating pain intensity of primary dysmenorrhea

The interesting result in this study is that comprehensive searching was done in various scientific databases with English and Persian languages but most studies in this field had been implemented in Iran. It seems that Iranian researchers are interested in this field. Investigation of mineral amount of micronutrients such as vitamin E in Iranian women’s plasma and rate of consumption of them can provide valuable information about this field. Vitamin E has no side effects and has beneficial characteristics such as antioxidation and anti-prostaglandins; therefore, it can be suggested for other clinical trials to assess the effect of vitamin E on the other gynecologic diseases.

We acknowledge that the number of studies included in the meta-analysis is small, however we still believe that the conclusion can form a basis for further research in this topic.

In addition to studies included in the meta-analysis, there are studies that support the effect of vitamin E on pain reduction of dysmenorrhea. Akhlaghi *et al.* in a quasi experimental study in 200 Mashhad Medical University students showed that vitamin E decreased pain intensity from 5.18 before to 3.40 after intervention.^[21]

The combination of fennel extract and vitamin E was also effective on decreasing painful menstruation.^[24] Moreover, vitamin E was more effective in comparison with acupressure in SanYinJiao points.^[28] The studies of Safari *et al.* (2006) and Farahmand *et al.* (2005 and 2009) showed that vitamin E as well as Ibuprofen or mefenamic acid decreased pain, amount, duration, and interval of menstrual bleeding in women with primary dysmenorrhea.^[23,26,27] There is no report regarding the side effects of vitamin E in common doses. However, high doses of vitamin E may cause higher mortality rate.^[33,34] Zakeri Hamidi *et al.*^[22] showed that vitamin E is not effective in reducing digestive problems with primary dysmenorrhea in second month but it is effective in fourth month. Vitamin E has less gastrointestinal complications in comparison with ibuprofen and mefenamic acid.^[23]

CONCLUSIONS

The systematic review and meta-analysis of clinical trials indicated that vitamin E is effective in pain intensity reduction of primary dysmenorrhea.

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