Original Article

Efficacy Of Vitamin E For Alleviating The Symptoms Of Primary Dysmenorrhea: A Review Of Randomized Clinical Trials And Quasi Experimental Studies

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Abstract

Myometrial contractions generated by prostaglandins cause primary dysmenorrhea. The uterine ischemia and sensitivity of afferent nerve fibres to painful stimuli are additional effects of prostaglandins. Nonsteroidal anti-inflammatories are useful medications, however some women should not take them and many women only see a slight improvement in their symptoms. Prostaglandin synthesis inhibitors, or NSAIDs (like Ibuprofen), work well for treating primary dysmenorrhea, although they may not be appropriate for people who have stomach ulcers or bronchospastic hypersensitivity to aspirin. Nausea, dyspepsia, diarrhoea, and occasionally exhaustion are moderate side effects that can occur. Today, vitamins are crucial in the management of dysmenorrhea. Primary dysmenorrhea is relieved by vitamin E, and its antioxidant properties may also prevent arachidonic acid from being oxidised, which would reduce the amount of prostaglandin produced. The safety of vitamin E supplementation, especially in large doses, has been questioned. People who use blood thinners or have a vitamin K deficiency may have a higher risk of bleeding. When used in healthy adults at dosages typically found in food and in healthy people over 65 at doses up to 800 IU taken orally daily for up to four months, vitamin E is probably safe. This brief review aims to demonstrate Vitamin E's effectiveness in treating primary dysmenorrhea.

Key words: Pain,Vitamin E, menstrual pain, primary dysmenorrhea, adolescents, treatment of dysmenorrhea

Introduction

Menarche is a turning point and a symbol of feminization for girls. Dysmenorrhea is just one of the issues that can arise throughout the menstrual cycle.[1] The most typical symptom that prompts someone to seek medical attention is pain. Most of the time, it is a sickness symptom that can be treated to help it go away. Since it indicates life quality and the potential for reintegrating the person into his career and social activities, pain control becomes even more crucial.[2] Dysmenorrhea is the most prevalent menstrual condition, affecting 50% of women of childbearing age, and 10% of these women feel incapacitating pain for 1-3 days per month[1,2]. Among 60–90% of adolescents in India, dysmenorrhea is a significant factor in college absences

or restrictions on activities and social engagement. [1,2,3]

PGF2a concentrations in menstrual fluid are often higher in women with dysmenorrhea, and suppression of PG production has taken over as the primary therapy. Through an effect on the enzymes phospholipase A2 and cyclooxygenase, vitamin E prevents the release of arachidonic acid and the conversion of arachidonic acid to PG. Protein kinase C and the rise in intracellular calcium concentration are thought to control the activation of phospholipase A2.. [4,5]

In 1992, Evans and Bishop conducted research on the connection between diet and fertility and made the first discovery of vitamin E. It was discovered that this vitamin might prevent the release of arachidonic acid and its conversion to prostaglandin. Additionally, it might enhance internal opioids and relieve pain.[19] New therapeutic modalities have been presented by complementary and alternative medicine (CAM), such as the use of vitamin E supplements.[6]

A cross-sectional study conducted at Dumlupinar University and Kutahya Health High School in Western Turkey sought to determine the prevalence of dysmenorrhea and how it affected the health-related quality of life of 623 female university students (HRQoL). The severity of dysmenorrhea was evaluated using a 10-point visual analogue scale. The Short Questionnaire-36 (SF-36) form was used to assess HRQoL. The prevalence of dysmenorrhea was found to be 72.7%, and it was significantly higher in those who drank coffee, had periods that lasted fewer than seven days, and had relatives who had the condition (P 0.05 for each of these categories). With the exception of the social functioning, role-emotional, and mental categories, the SF-36 points acquired by the females with dysmenorrhea were higher. Except for the social functioning, role-emotional, and mental health domains, the females with dysmenorrhea scored higher on the SF-36 in all other categories (for each one, P 0.05). With the exception of the physical functioning and role-emotional dimensions, the scores from the remaining SF-36 scale categories showed deterioration with increasing severity of dysmenorrhea (P 0.05 for each). The study's findings indicate that dysmenorrhea is a common health problem that has a detrimental effect on female pupils. HRQoL. [7]

Today, vitamins are crucial in the management of dysmenorrhea. Primary dysmenorrhea is relieved by vitamin E, and its antioxidant properties may also prevent arachidonic acid from being oxidised, which would reduce the amount of prostaglandin produced. [8,9,10] According to Iaghmaii et al., a combination of vitamin E and mefenamic acid reduced pain more effectively than mefenamic acid alone. [11]

100 young women who complained of substantial menstrual pain were given 500 IU of vitamin E or a placebo for 5 days as part of a double-blind, placebo-controlled experiment. Treatment started 2 days prior to the anticipated start of menstruation and lasted for 3 days afterwards. Despite the fact that both groups had a considerable decrease in pain over the course of the study's two months (a result of the placebo effect), the treatment group experienced a higher pain reduction than the placebo group. [12] In a separate Iranian trial, 278 teenagers with dysmenorrhea were given 400 IU of vitamin E twice day, on the same schedule as above, or a placebo. Once more, vitamin E outperformed the placebo. [13]

A fat-soluble vitamin having antioxidant properties is vitamin E. Alpha, beta, gamma, and delta tocopherol and alpha, beta, gamma, and delta tocotrienol are the eight distinct forms of vitamin E. In people, alpha-tocopherol has the highest level of activity. Vitamin E dosage is frequently stated as alpha-tocopherol equivalents (ATEs). This explains why different types of vitamin E have varied physiological effects. 1.5 international units are equal to one milligramme of an ATE (IU). Both natural and synthetic supplements for vitamin E are readily available. Natural forms are typically identified by the letter "d" (for instance, d-gamma-tocopherol), while synthesised forms are identified by the letter "dl" (for example, dl-alpha-tocopherol). Numerous health issues have been examined in relation to the prevention or treatment of vitamin E. With the exception of vitamin E insufficiency, there isn't enough solid data to yet to support its usage for any diseases.[14]

The safety of vitamin E supplementation, especially in large doses, has been questioned. People who use blood thinners or have a vitamin K deficiency may have a higher risk of bleeding. Evidence suggests that using high-dose vitamin E supplements on a daily basis may slightly raise your risk of dying from any cause, but the science is mixed on this. The word of caution. Adults over the age of 14 should consume 15 milligrammes (or 22.5 IU) per day, pregnant women of any age should

consume the same amount, and nursing mothers of any age should consume 19 milligrammes per day (or 28.5 IU). The maximum daily dose for people older than 18, pregnant women, and nursing mothers is 1,000 milligrammes (or 1,500 IU).[12,13,14]

When used in healthy adults at dosages typically found in food and in healthy people over 65 at doses up to 800 IU taken orally daily for up to four months, vitamin E is probably safe. [9,10,11] Since vitamins are frequently used to treat dysmenorrhea and are widely available and sold without a prescription, it is crucial to establish some practical and thorough evidence on their effective dose, effectiveness, and drug interactions. Dymenorrhea is considered to be one of the major problems that women face throughout their lives. Additionally, there is no review study available in this area.

MATERIAL AND METHODS

1. Search Strategies

Using sources including PubMed, Scopus, Web of Science, Google Scholar, and the Cochrane Library, this study assesses published articles in English (clinical trials) from 2000 to 2022 in order to conduct a mini-review of randomised controlled trials (RCTs). The keywords "Dysmenorrhea OR Menstrual Pain OR Painful Menstruation" AND "Vitamin A OR Retinol OR vitamin D3 OR Cholecalciferol OR Vitamin E OR Tocopherol" were used to conduct the search. 160 of the 640 articles that were found during the initial study were carefully chosen. Replication of the database led to the deletion of 120 articles. There were no duplicates, and it was decided if 40 papers qualified. Due to the absence of the whole text, 34 papers were rejected. As a consequence, 6 papers—including their full texts and abstracts—were carefully reviewed. According to the inclusion criteria, 713 people in total were included in the study. There are randomised clinical trials in the literature (RCTs). Among the keywords cited were "Vitamin E" AND "dysmenorrhea," "primary dysmenorrhea," "randomised controlled study," "non-pharmacology methods," and menstrual discomfort.

2. Study Selection

We chose trials in which oral Vitamin E was administered to female adolescents between the ages of 13 and 30 and was compared to a placebo or active treatment. We only took into account randomised controlled studies. The degree and duration of self-reported menstrual discomfort were evaluated using a patient-reported rating method. All three writers reviewed and extracted the data. Two reviewers separately gathered the data from the included trials; the first author evaluated all of the studies, while the second and third researchers each looked at 50% of them. Disagreements were settled by discussion and agreement with the assistance of the third reviewer. A study or work of literature that was authored in English, had a sample size of more than 30, and was published between 2000 and 2022 was considered. Observational studies, non-human or in vitro research, and trials of non-oral vitamin E use (such as essential oil massage) were also disregarded.

Only published studies that met the following PICO criteria between 2000 and 2022 were considered for inclusion in this study; studies that did not met these criteria were disqualified. We took the following data from each study: authors, publication year, study location, sample size, study design, and conclusions. To reduce the likelihood of errors, the authors reviewed the extracted data for discrepancies after extraction. Study selection criteria used in this review:

Selection of studies:

- **Participants' types:** all clinical trials that require healthy adolescent girls or women with primary dysmenorrhea as entry criterion.
- **Types of interventions:** all clinical trials comparing the effects of vitamin E treatment on primary dysmenorrhea to placebo, no treatment, or any treatment.
- **Examples of comparator/controls** include non-pharmacological treatments, placebos, and other standard treatments.

- **Primary dysmenorrhea** pain is one type of outcome measure, and it is assessed using standardised scales such the visual analogue scale, the numeric rating scale, the multi-dimensional speech criterion, and pain rating scales. The adverse impacts that studies reported were noted.
- **Primary outcome:** according to a conventional pain measurement scale, the severity, duration, or alleviation of menstrual pain**.**
- **Secondary outcome:**not included

RESULTS

Figure 1 displays a PRISMA flow chart that shows how studies are reported, screened, rejected, and included. The narrative analysis includes six of the trials that met the criteria.

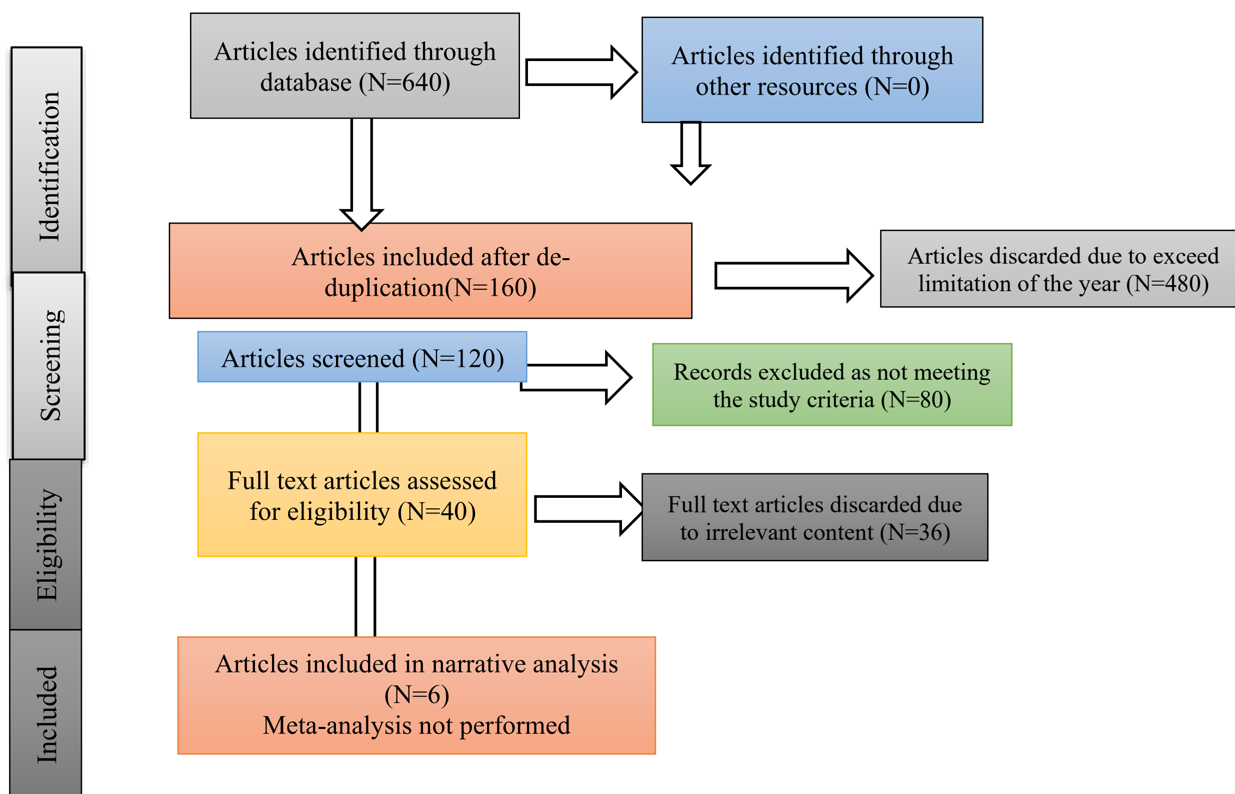

Fig. 1. Prisma flow diagram for Mini Review

Discussion:

There are studies that support the impact of vitamin E on pain reduction in dysmenorrhea in addition to those in the systematic review. In a quasi-experimental study including 200 students from Mashhad Medical University, Akhlaghi et al. found that vitamin E reduced pain intensity from 5.18 prior to intervention to 3.40 following treatment.[15]Fennel extract and vitamin E together have been shown to lessen uncomfortable menstruation.[16] In addition, vitamin E performed better in SanYinJiao locations than acupressure.[3] In women with primary dysmenorrhea, vitamin E, ibuprofen, or mefenamic acid reduced pain, amount, length, and interval of monthly bleeding, according to studies by Safari et al. and Farahmand et al. [2]

Regarding vitamin E's negative effects in typical amounts, there are no reports. High vitamin E dosages, however, may result in a greater mortality risk. [13,14] Vitamin E is useful in alleviating stomach issues associated with primary dysmenorrhea in the

fourth month, however Zakeri Hamidi et al. [17] found that it is ineffective in the second month. Compared to ibuprofen and mefenamic acid, vitamin E has fewer gastrointestinal side effects.[2]

The study's intriguing finding is that although extensive searches were made using English-language scientific databases, the majority of studies in this area were conducted in Iran. Iranian scholars appear to be interested in this area. This topic can benefit from further research into the mineral content of micronutrients like vitamin E in Iranian women's plasma and the rate of consumption. Since vitamin E has no negative side effects and advantageous properties including antioxidation and anti-prostaglandins, it can be recommended for additional clinical research to determine vitamin E's impact on various gynecologic conditions.Although we agree that the systematic review only covered a small number of studies, we nevertheless think the result can serve as a starting point for additional study on this subject.

Table 1: The characterize of included studies

Details from the 6 articles selected for the review were summarized in the form of a table containing the following information: Author, Method, Subjects, Intervention Measure, Outcome and Adverse effects**.**

Author	Method	Subjects	Intervention	Measure	Outcome	Side effects
Vilvapriya S., Vinodhini S[19]	Randomized placebo-controlled trial	60 single women aged 17-25 years	Vitamin E 400 units/day in two divided doses was given to the experimental group beginning two days before the start of menstruation and continuing for the first three days of bleeding. Controlling factor: Placebo	Cox Menstrual Symptom Scale (CMSS) and Visual Analogue Scale (VAS) are used to rate pain duration and severity, respectively.	Between the pre- and post-treatment periods, there was a statistically significant difference in the vitamin E group's pain severity and duration (P=0.72 and 0.002, respectively). There was a statistically significant difference between the Vitamin E group and the placebo group in terms of the mean of pain severity and duration (P=0.002 and p=0.027, respectively).	Was not reported
Ziaei et al.,[7]	Double-Blind Placebo-Controlled Randomized Clinical Trials	278 girls aged 15–17 years	Vitamin E 200 units twice day for the experimental group, starting two days before to the start of menstruation and continuing for the first three days of bleeding Controlling factor: Placebo	Visual Analogue Scale	At 2 and 4 months, there were statistically significant decreases in pain score in both groups, although the vitamin E group experienced a much larger decrease than the other group (P<0.001). Menstrual blood loss and discomfort duration were both reduced in the intervention group substantially more than in the control group (P <0.05).	Without adverse effects
Ziaei et al.,20	Randomized placebo-controlled trial	100 girls aged 16–18 years	100 IU of a placebo vitamin E. (5 tablets a day for 5days; two days before and 3 days after the beginning of menstruation) Controlling factor: Placebo	Visual Analogue Scale	After treatment, both the treatment and control groups' levels of pain decreased, although the reduction was larger in the vitamin E-treated group (P <0.05).	Was not reported

Kashania et al.,21	Double-Blind Placebo-Controlled Randomized Clinical Trials	94 women 18-25years	For two cycles in a row, a dose of 400 IU/day of vitamin E was recommended beginning two days before to the start of menstruation and continuing for a total of five days. Controlling factor: Placebo	Visual Analogue Scale	The amount of discomfort experienced throughout the first and second months of therapy with vitamin E and a placebo was less than it had been (P <0.05). In comparison to other groups, the study group experienced less discomfort in the second month.	Was not reported
Moslemi et al.,22	Single blind placebo-controlled trial	65 single female students who suffered from primary dysmenorrhea	The 100-unit vitamin E capsules were taken every 6 hours for 3 days following the onset of their menstruation for 2 consecutive cycles. 46 mg fennel Controlling factor: Placebo	MDSC (multi-dimensional speech criteria)	Pain intensity was reduced compared to before treatment in the vitamin E and fennel extract groups (P<0.001), with the fennel extract group experiencing a higher reduction (P<0.019).	Was not reported
Wagito et al[23],	Randomized, double-blind controlled trial	116 females aged 12 to 18 years, with primary dysmenorrhea,	From two days prior to menstruation to the third day of menstruation, 58 patients received 200 units of vitamin E twice daily. for three rounds of menstruation Controlling factor: Placebo	pain rating scales	There were statistically significant variations in pain intensity and duration between the 2 groups after receiving therapy for 2 months and 3 months.	Adverse event not reported

*DBRCT stands for Double-Blind Placebo-Controlled Randomized Clinical Trials; VAS stands for Visual Analogue Scale; NRS stands for Numeric Rating Scale; PVAS stands for Pain Visual Analogue Scale; MDSC stands for Multi-dimensional Speech Criteria.

Conclusion

Despite the scant evidence, the research looked at in this review article suggest that vitamin E may have some effects on lowering the intensity of primary dysmenorrhea pain. However, additional research is required to discover the ideal dose of vitamin E as well as to confirm the security and efficacy of different kinds of micronutrients.

Recommendations: Therefore, the author suggests that Vitamin E may aid in the pain relief of primary dysmenorrhea. It can be regarded as a universal medicine in the treatment of primary dysmenorrhea since it is a very simple way for pain control with fewer side effects and is cost-effective.

Limitations of the short review: Only five research from a small number of nations were considered, and no works produced in languages other than English were included.

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Conflict of Interest: There is no conflict of interest to be declared.

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