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Original Research Article

Vitamin E in the treatment of primary dysmenorrhoea

Vilvapriya S., Vinodhini S.*

Department of Obstetrics and Gynecology, Government Kilpauk Medical College Hospital, Kilpauk, Chennai, Tamil Nadu, India

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***Correspondence:**

Dr. Vinodhini S.,

E-mail: vinodhini.nature@gmail.com

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ABSTRACT

Background: The objective of this study is to determine the efficacy of Vitamin E in the treatment of primary dysmenorrhoea compared to the placebo.

Methods: Sixty women, aged 17-25 years old who suffered from primary dysmenorrhoea, among 1000 Women attending the gynec OPD in Kilpauk Medical College. 30 women were given 200 units of vitamin E (each tablet twice daily) and 30 were given a placebo tablets (each tablet twice daily). The treatment began two days before the beginning of menstruation and continued through the first three days of bleeding. The severity of pain and duration of pain before and after the treatment was studied. Treatment in both groups was carried out in three consecutive menstrual periods.

Results: As to the findings, the mean age of the participants was 22.6 years. There was a significant difference between the pre- and post-treatment periods in terms of pain severity ($P=0.72$ and $P=0.002$, respectively) and pain duration ($P=0.514$ and $P=0.027$, respectively) in Vitamin E group. There was a significant difference observed between the Vitamin E group and placebo group regarding the mean of pain severity and duration ($P=0.002$ and $p=0.027$ respectively).

Conclusions: Vitamin E helps to relieve pain in primary dysmenorrhoea. As this is a relatively easier method for control of pain with lesser amount of side effects and as it is cost effective, it can be considered as a universal drug in the treatment of primary dysmenorrhoea.

Keywords: Dysmenorrhoea, Placebo, Vitamin E

INTRODUCTION

Dysmenorrhoea means cramping pain accompanying menstruation. Primary dysmenorrhoea refers to one that is not associated with any identifiable pelvic pathology.^{1,2} Its incidence has been estimated between 50-90% in different communities.² Primary dysmenorrhoea usually starts 1-2 years after menarche and is associated with normal ovulatory cycles.

Many young women reported limitations on daily activities, such as missing school, sporting events, and other social activities, because of dysmenorrhoea. However, only 15 percent of females seek medical advice

for menstrual pain, signifying the importance of screening.

The pain is due to myometrial contractions induced by prostaglandins originating in the secretory endometrium that occurs mostly in the first 48 hours of menstruation.³⁻⁵

Women with dysmenorrhoea have a relatively high concentration of PGF_{2a} in menstrual fluid and suppression of PG synthesis has become the main treatment. Vitamin E inhibits the release of arachidonic acid and the conversion of arachidonic acid to PG via an action on the enzymes phospholipase A₂ and cyclooxygenase.⁶ Activation of phospholipase A₂ is

considered to be regulated by protein kinase c and the increase in the concentration of intracellular calcium.

Vitamin E was found to inhibit protein kinase c in bovine brain.³

Complementary and alternative medicine (CAM) has proposed new treatment approaches such as administration of vitamin E and vitamin B1 supplements.

Vitamin E was discovered for the first time in 1992 during a research on the relationship between nutrition and fertility by Evans and Bishop. As it was revealed, this vitamin could inhibit arachidonic acid release and its conversion to prostaglandin. It could also increase internal opioids and cause pain relief.

Our study aimed to determine the efficacy of vitamin E on pain severity in the women suffering from primary dysmenorrhoea as compared to the placebo.

This vitamin can be administered as an alternative for the complicated drugs, in case they are shown to be useful.

Objective

The objective of this study is to determine the efficacy of Vitamin E in the treatment of primary dysmenorrhoea compared to the placebo.

METHODS

A randomized placebo-controlled trial was conducted in women who attended the gynaec OPD in Kilpauk Medical College in the period July 2017 to November 2017.

The sample size was calculated as 60.

The study was approved by the ethical committee.

After selecting the sample, written informed consent was obtained.

Inclusion criteria

Inclusion criteria were within the age group of 17-25 years; being single; regular menstrual cycles; no urogenital disorders; no previous history of abdominal or pelvic surgery.

The participants were given a form to fill about their menstrual cycle.

Visual Analog Scale (VAS) was used for grading the severity of pain and Cox Menstrual Symptom Scale (CMSS) was used for grading the duration of pain. Pain duration was measured from the onset of uterine cramps until they ended.

Based on Cox regression, pain duration was categorized as follows: score 0: no pain; score 1: ≤0-5 hours of pain; score 2: 0.5-1 hours of pain; score 3: >1 hour of pain; score 4: >1 day of pain. The subjects were asked to record the longest duration of menstrual pain in the first three days of menstruation on special forms, based on CMSS score.

For starting the treatment course, the first group was prescribed vitamin E 400 units/day in 2 divided doses (5 days in a month, from two days before the menstruation until the first three days) and the second group received cod liver oil 300 mg twice daily (5 days in a month, from two days before the menstruation until the first three days). Each medication package was placed on a separate box, coded by letters A and B, and was given to each participant.

The subjects were separately treated. As soon as the treatment started, they were asked to record their most severe pain and its duration in the first three days, based on VAS and CMSS, respectively. The participants were also asked if they had taken any analgesics for their pain; if so, the name and dosage of the medication would be recorded in the treatment form.

The treatment course continued for three menstrual cycles, and then all the forms were collected. Finally, two groups of vitamin E and placebo were compared in terms of the mean of pain severity and duration before and after the intervention.

Statistical analysis

The following statistical tests were used for analyzing the data: Mean and standard deviation to describe quantitative data

The reliability of VAS and CMSS was assessed using Cronbach's alpha coefficients. Data were analyzed by t-test, Mann-Whitney, and Kruskal–Wallis tests, using SPSS v22.

RESULTS

In this study, 30 women were given vitamin E and 30 women were given placebo.

Table 1: Age distribution between vitamin E and placebo group.

	Group	N	Mean	Std. Deviation	Std. Error Mean	P value
Age	Vitamin E	30	22.60	2.328	0.425	0.958
	Placebo	30	22.57	2.528	0.462	

Table 2: Pain score at the onset of treatment between vitamin E and placebo group.

	Group	N	Mean	Std. Deviation	Std. Error Mean	P value
Onset of pain score	Vitamin E	30	7.37	0.964	0.176	0.720
	Placebo	30	7.27	1.172	0.214	

The results showed that there was no significant difference between the two groups when age was taken into account (Table 1).

Present study showed that there was no significant difference in pain at the beginning of the study between the Vitamin E and placebo group (7.37±0.94 in vitamin E

group as compared to 7.27±1.172, p=0.72 >0.005) (Table 2).

Present analysis showed that there was no significant reduction in pain at the end of first month between the Vitamin E and placebo group (6.17±1.020 in Vitamin E group as compared to 6.13±1.042, p=0.901 >0.005).

Table 3: Effects of vitamin E and placebo on pain scores.

	Group	N	Mean	Std. Deviation	Std. Error Mean	P value
1st month	Vitamin E	30	6.17	1.020	0.186	0.901
	Placebo	30	6.13	1.042	0.190	
2nd month	Vitamin E	30	4.77	1.357	0.248	0.083
	Placebo	30	5.33	1.124	0.205	
3rd month	Vitamin E	30	3.17	1.840	0.336	0.002
	Placebo	30	4.60	1.522	0.278	

Table 4: Percentage of reduction in pain.

	GROUP	N	Mean	Std. Deviation	Std. Error Mean	P value
% of reduction	Vitamin E	30	57.804233	22.8711105	4.1756744	0.000
	Placebo	30	37.160053	17.4556292	3.1869473	

The results showed that there was no significant reduction in pain at the end of second month between the Vitamin E and placebo group (4.77±1.357 in Vitamin E group as compared to 5.33±1.124, p=0.083 >0.005).

The results showed that there was significant reduction in pain at the end of third month between the Vitamin E and

placebo group (3.17±1.840 in Vitamin E group as compared to 4.60±1.522, p=0.002 <0.005) (Table 3).

The study showed that there was significant difference in % of reduction of pain between the Vitamin E and placebo group (57.8±22.8 in Vitamin E group as compared to 37.1±17.4, p=0.000 <0.005) (Table 4).

Table 5: Duration of pain between vitamin E and placebo group.

	Group	N	Mean	Std. Deviation	Std. Error Mean	P value
Duration of pain	Vitamin E	30	35.00	13.191	2.408	0.514
	Placebo	30	37.20	12.743	2.326	

Table 6: Effects of vitamin E and placebo on pain duration.

	Group	N	Mean	Std. Deviation	Std. Error Mean	P value
1st month	Vitamin E	30	25.00	13.370	2.441	0.259
	Placebo	30	28.97	13.596	2.482	
2nd month	Vitamin E	30	17.77	12.681	2.315	0.049
	Placebo	30	24.97	14.933	2.726	
3rd month	Vitamin E	30	11.33	12.524	2.287	0.027
	Placebo	30	18.97	13.441	2.454	

The results showed that there was no significant reduction in duration of pain at the beginning of the study between the Vitamin E and placebo group (35.0±13.191 in Vitamin E group as compared to 37.20±12.743, p=0.514, >0.005) (Table 5).

The results showed that there was no significant reduction in duration of pain at the end of first month between the Vitamin E and placebo group (25.0±13.37 in Vitamin E group as compared to 28.97±13.596, p=0.259, >0.005).

The results showed that there was significant reduction in duration of pain at the end of second month between the

Vitamin E and placebo group (17.77±12.68 in vitamin E group as compared to 24.9±14.93, p=0.049, <0.005).

The study showed that there was significant reduction in duration of pain at the end of third month between the vitamin E and placebo group (11.3±12.5 in Vitamin E group as compared to 18.9±13.4, p=0.027 <0.005) (Table 6).

Our study showed that there was significant difference in% of reduction in duration of pain between the Vitamin E and placebo group (68.5±28.2 in vitamin E group as compared to 49.3±33.8, p=0.020, <0.005) (Table 7).

Table 7: Percentage of reduction in duration.

	Group	N	Mean	Std. Deviation	Std. Error Mean	P value
% of reduction	Vitamin E	30	68.541667	28.2674453	5.1609058	0.020
	Placebo	30	49.305556	33.8869849	6.1868887	

DISCUSSION

Evans and co-workers isolated Vitamin E in 1936 from wheat germ oil. Eight naturally occurring tocopherols with vitamin E activity are now known. Vitamin E is a fat-soluble antioxidant.^{7,8} The most important vitamin E is considered to be Alpha-tocopherol (5, 7, 8 trimethyltolcol). The peroxidation of unsaturated fatty acids is prevented by this group.^{7,8}

Prostaglandins with the greatest biological activity have two double bonds, derived from arachidonic acid. In the plasma 1% to 2% of the total fatty acid content is free arachidonic acid, the greater part of arachidonic acid being bound up in phospholipids and cholesterol ester.

The rate limiting step in the formation of prostaglandins is the release of free arachidonic acid. A variety of hydrolases may be involved in the release of arachidonic acid, the most important of which is phospholipase A2.

Phospholipases are activated by endotoxin, mechanical stretching, catecholamines, angiotensin and sex steroids. The decline of progesterone levels in the luteal phase of the menstrual cycle triggers lytic enzymatic action, resulting in peroxidation of phospholipids and the release of arachidonic acid, with activation of the cyclooxygenase pathway.

Since dysmenorrhoea is characterised by an increased concentration of prostaglandins in menstrual fluid, suppression of prostaglandin synthesis has become the main treatment of primary dysmenorrhoea.⁹ The antioxidant vitamin E prevents the peroxidation of phospholipids, the release of arachidonic acid and hence its conversion to prostaglandin.⁶

In this study we wanted to find out whether Vitamin E has some role in the reduction of pain during menstruation and in the reduction of duration of pain compared to placebo. In present study authors found that there is significant reduction in pain at the end of third month (p-0.002<0.05)

Ziaei et al in their study reported a significant reduction in severity of pain (p-0.02< 0.05) when 500 units of vitamin E per day was given for 5 days.¹⁰ Ziaei et al in their another study reported a significant reduction in severity of pain (p - 0.001< 0.05) when 200 units of vitamin E twice a day was given for 5 days.¹¹ Nayeban et al in their study reported a significant reduction in severity of pain (p - 0.046< 0.05) when 400 units of vitamin E per day was given for 5 days.¹²

Safari et al showed that vitamin E has a significant effect on dysmenorrhoea, equal to mefenamic acid, which is a well-known medication for the treatment of dysmenorrhoea.¹³ 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.¹⁴

Vitamin E was more effective in comparison with acupuncture in San Yin Jiao points.¹⁵ Kashanian et al showed that vitamin E has a significant effect on dysmenorrhoea when 400 units of vitamin E per day was given for 5 days.¹⁶ There are different pharmacological treatments for primary dysmenorrhoea, such as contraceptives and short-term nonsteroidal anti-inflammatory drugs (NSAIDs). NSAIDs have been shown effective in 80-90% of cases, they are associated with several adverse side effects; therefore, they are contraindicated in many patients.

The combined contraceptive pill (COC) suppresses the progesterone-driven proliferation of the secretory endometrium during the luteal phase, thus resulting in a decrease in PG synthesis and the volume of menstrual fluid. The COC is an accepted treatment for dysmenorrhoea in nonadolescent women, but the efficacy of low dose COC pill in the treatment of adolescent dysmenorrhoea has yet to be determined. Furthermore, prescribing the high dose COC pill from an early age may carry possible long-term risks.

Thus, the use of vitamin E for dysmenorrhoea in women is attractive because of the marked effect we have demonstrated coupled with the absence of significant side effects from vitamin E in therapeutic doses.

CONCLUSION

Here by we conclude from our study that vitamin E has a role in the treatment of dysmenorrhoea and it can replace NSAIDS and COCs as they are cost effective, safe and has lesser amount of side effects.

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