

Role of Vitamin E in Improving Pain Severity in Cyclical Mastalgia in Adolescent Women: A Prospective Study.

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Abstract

Aims: To study the efficacy of vitamin E in improving pain severity in cyclical mastalgia in adolescent women.

Materials and Methods: In a prospective trial of 194 patients suffering from cyclic mastalgia were advised 400 IU of vitamin E daily for 2 month. Written informed consent was obtained from all participants. Severity of breast pain was evaluated by the Cardiff breast pain score during one menstrual cycle before and two menstrual cycle after the intervention

Results: There was significant difference in the mean severity of cyclic mastalgia during one menstrual cycle before the intervention vitamin E (9.1 ± 2.1), but the difference was significant during the first cycle (4.9 ± 1.5) and second cycle (1.5 ± 1.1) after the intervention. There was decreasing trend in pain severity score and remarkable improvement in the second cycle.

Conclusions: From the results of this study, regimens containing vitamin E has an excellent improvement in reducing breast pain severity in cyclic mastalgia.

I. Introduction:

The most prevalent breast disorder which makes women consult with an informed individual is breast pain or mastalgia. Mastalgia is in fact the reason for 30–47% of the referrals for clinical breast examination [1, 2]. Severe mastalgia is present in 10–30% of the cases, and causes disturbances in normal life; thus, it requires frequent evaluation and treatment [3]. Mastalgia may also leads to disorders in sexual, physical, and social activities in 48%, 37%, and 12% of the cases, respectively [1].

Mastalgia may be cyclical, noncyclical, and extramammary (nonbreast). Cyclical mastalgia is related to menstrual cycles and starts in luteal phase. The symptoms of cyclical mastalgia include congestion of breast, soreness, and feeling of heaviness and tenderness [4, 5]. Cyclical mastalgia might last for more than 7 days in 11% of women [2].

The etiology of cyclical mastalgia is not known; however, since it starts in luteal phase, hormonal stimulation might be the cause. High level of estrogen, low level of progesterone, and imbalance in estrogen to progesterone ratio are assumed among its causes, as well [3, 4, 6]. Bromocriptine and tamoxifen are considered as two effective drugs in treatment of cyclical mastalgia. Yet, bromocriptine is accompanied by some side effects, such as nausea, vomiting, and dizziness and the common side effects of Tamoxifen are hot flashes and vaginal dryness [4, 7]. These side effects have reduced the popularity of these drugs for treatment of cyclical mastalgia.

The main etiologies of cyclic mastalgia remain unknown. However, various physiological conditions, inflammatory processes, and even underlying psychological disturbances have been postulated in affected patients.[8] Among pathophysiological aspects, increased water retention in breast and ductal ectasia have been suggested to be the causes in these patients.[9] Also, regarding the role of inflammatory mechanisms, increased level of some inflammatory biomarkers such as some interleukins (IL-6 and IL-1 α) and tissue necrotizing factor (TNF- α) has been reported following the appearance of cyclic mastalgia.[10] Recently, perceived stress and anxiety has been found to be associated with cyclic mastalgia. Cyclic mastalgia is one of the major causes of breast pain for women visiting primary care clinics.[11] Due to the multifactorial features of this phenomenon, its management using single drug regimens seems not to be proper.

Recent attempts have been focused on employing chemical and natural supplemental agents for treatment of cyclic mastalgia. Among synthetic agents, the potential effects of some drugs such as Danazol as a gonadotrophin release inhibitor,[12,13] Bromocriptine as a dopamine agonist,[14,15,16] Tamoxifen as an anti-estrogen,[17,18]and Goserline as a luteinizing Hormone-Releasing Hormone (LHRH) analog [19] have been examined and their benefits have been proved. However, the low response rate along with their serious side effects have limited their prescription and continued usage. In order to overcome these limitations, some approaches have started using agents of natural origin.

Evening primrose (*Oenothera biennis*) is a North American wild flower that has escaped cultivation and is a precursor of prostaglandin E₁, which is one of the anti-inflammatory prostaglandins.[20,21] Because of the underlying abnormal metabolism of fatty acids in cyclic mastalgia and as this oil is rich in essential fatty acids, the use of this agent has been also considered as a first-line treatment for cyclic mastalgia.[22]

Recently, it has been recommended to add an antioxidant agent or co-factors in the proposed metabolic pathway for enhancing the therapeutic efficacy of other drugs.[23] In fact, these agents may be considered as safe alternatives to hormonal therapies or may be used in combination with hormonal drugs as they result in lesser drug-related side effects. Even these co-factor supplements may be employed for treatment of cyclic mastalgia. In the present study, we examined the efficacy of vitamin E in improving pain severity in cyclic mastalgia.

II. Materials And Methods

In this prospective trial, We included 198 patients of adolescent age who attended General Surgery out patient department at Dr R M L Combined Hospital Lucknow during May 2014 to October 2015 for cyclical mastalgia after ethical clearance and written informed consent. Four patients did not turn up for follow up so our study was confined to

Inclusion criteria:

- 1) Diagnosis of cyclic mastalgia,
- 2) No previous history of breast malignancies,
- 3) Not having consumed other vitamin supplements within 2 months of the study period.

Exclusion criteria:

- 1 Allergy to drug, pregnancy
- 2 Unwillingness to continue in the research..

All appropriate information was noted by interviewing, including demographic characteristics, marital state, occupation, educational level, characteristics related to cyclic mastalgia such as its time and duration, characteristics related to menstrual cycles, results of diagnostic interventions (breast sonography and mammography), and also, previous history of psychological disorders including depression or anxiety. Cyclical mastalgia was defined as a bilateral painful breast swelling lasting for >4 days and up to 3 weeks, premenstrually and always preceding menses, and subsiding progressively during menstruation.[24] After initial evaluation, patients with cyclic mastalgia were randomly assigned to receive 400 IU vitamin E daily for 2 months. Severity of cyclic mastalgia was determined by the Cardiff breast pain score during one cycle before and two cycles after the intervention. Cardiff breast pain score was finally classified as one of the following levels: None, mild, moderate, or severe breast pain. Cyclical mastalgia characterized by a swelling and minor discomfort lasting 1–4 days premenstrually is considered mild and the symptoms lasting for 5–14 days or more every month is considered moderate to severe.[24,25]

The Cardiff breast pain chart has been utilized and it is a daily chart for monitoring breast pain, as shown in Figure 1.

III. Results

There was significant difference in the mean severity of cyclic mastalgia during one menstrual cycle before the intervention vitamin E (9.1 ± 2.1), but the difference was significant during the first cycle (4.9 ± 1.5) and second cycle (1.5 ± 1.1) after the intervention. There was decreasing trend in pain severity score and remarkable improvement in the second cycle

IV. Discussion

Adding an antioxidant agent to first-line therapeutic regimes for treatment of cyclical mastalgia has been shown to be an effective schedule. Recently, direct attention has been paid toward using vitamins to facilitate pain relief in these patients. It has been suggested that use of adequate levels of vitamins as co-factors in the proposed metabolic pathways involving this complaint may be fully beneficial.[26] Although some controlled trials could demonstrate the effects of vitamins in relieving cyclical mastalgia pain, some others failed to support the efficacy. Thus, previous studies gave questionable results with conflicting evidence. [27,28,29] In a similar randomized trial of Iranian women suffering from mastalgia, administration of 200 mg twice daily could effectively reduce pain severity both 2 and 4 months after treatment, compared with the placebo group.[30] In another trial, daily doses of 1200 IU vitamin E alone or in combination with evening primrose oil taken for 6 months decreased the severity of cyclical mastalgia.[31] Also, a study similar to the present trial was conducted in the United Kingdom by Goyal and Mansel, who used a combination treatment arm of antioxidants and minerals which included beta-carotene, vitamin C, vitamin B6, zinc, niacin, and

selenium in a coconut oil base and essential fatty acids. The investigators obtained equivocal results in the reduction of breast pain symptoms.[32] Three clinical trials have been performed, and all have shown vitamin E to be no better than placebo in the treatment of benign breast disease. In the first trial, 50 patients were asked whether their breast pain was better, worse, or unchanged after 2–3 months of therapy. In each group, 40% reported improvement.[33] The second trial did not assess breast pain, but found no reduction in nodularity.[34] The third trial found no reduction in nodularity or mammographic density, and although a larger proportion of women in the vitamin E group reported reduction in breast tenderness, this was statistically not significant.[35] Contrarily, some studies could not find beneficial effects of supplemental vitamins on mastalgia, probably because of small sample size or inappropriate nature of the study designs including ignoring adequate inclusion criteria or incorrect adjusting for confounders.[36,37,38] Considering the key role of oxidation and inflammation processes in the appearance and expansion of cyclical mastalgia, it is believed that the use of vitamin supplements, especially of our studied vitamins, can successfully decrease the pain severity related to this phenomenon. However, it seems that the dosages of vitamins, duration of administration, as well as using them concurrently with other standard therapeutic regimens can all potentially influence the clinical results of these regimens, and thus, examining different regimens containing vitamin E in different doses and durations should be considered.

V. Conclusion

Regimens containing vitamin E have an excellent improvement in reducing breast pain severity in cyclic mastalgia. It seems that using vitamin E concurrently with other standard therapeutic regimens can potentially influence the clinical outcomes, and thus, examining different regimens containing vitamin E in different doses and durations need to be looked into.

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Table #1- Base Line Characteristics-N=194

On l ^s t V i s i t	
M i l d	1 5 (7 . 7 %)
M o d e r a t e	1 4 4 (7 4 . 2 %)
S e v e r e	3 5 (1 8 . 1 %)
One Month Later(Cycle#1)	
M i l d	9 5 (4 8 . 9 %)
M o d e r a t e	8 2 (4 2 . 3 %)
S e v e r e	1 7 (8 . 8 %)
Two Months Later(Cycle#2)	
N o n e	5 2 (2 6 . 8 %)
M i l d	1 2 5 (6 4 . 4 %)
M o d e r a t e	1 2 (6 . 2 %)
S e v e r e	0 5 (2 . 6 %)

Table#2-Level Of Pain Severity