

# Vitamin E and Omega-3, 6 and 9 Combinations Versus Vitamin E in the Treatment of Mastodynia

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**Received:** March 4, 2014; **Revised:** July 15, 2014; **Accepted:** September 23, 2014

**Background:** Breast pain or mastodynia is moderate to severe pain, which affects around 22 - 41% of women. If no anomaly is found and other causes, like nutritional changes, are excluded, many drugs, including herbal supplements, are recommended for the treatment of mastodynia.

**Objectives:** This study was performed to evaluate the effects of vitamin E and omega-3, 6 and 9 free fatty acids combinations versus Vitamin E in women with mastodynia.

**Patients and Methods:** A double blind, randomized clinical trial was conducted in Shohada Ashayer Hospital in Khorramabad Lorestan province, in the vest of Iran. A total of 88 women with symptoms of mastodynia, aged between 20 - 55 years old, were divided to two groups. The patients were randomly assigned to receive vitamin E (400 U/day) and vitamin E (400 U/day) plus omega-3, 6 and 9 (1200 mg/day) orally, for 3 months.

**Results:** Vitamin E plus omega free fatty acids are more effective than the use of vitamin E alone in decreasing mastodynia. Significant difference was seen between the Cardiff Breast Score (CBS) of the vitamin E group compared to vitamin E - omega group ( $P < 0.05$ ) at the end of the first, second and third months after treatment.

**Conclusions:** Our results showed that vitamin E plus omega free fatty acids decrease the severity of mastodynia better than vitamin E alone.

**Keywords:** Mastodynia; Vitamin E; Omega-3 Fatty Acids; Omega-6 Fatty Acids

## 1. Background

Breast pain or mastodynia is moderate to severe pain, which affects around 22 - 41% of women and persists for more than 5 days (1, 2). The fear of cancer and presence of severe pain are two major concerns of patients and, in several patients, severe pain may disrupt daily activities and require medication (3). If no anomaly is found then, based on possible causes, multiple drugs, such as anties-trogens, topical nonsteroidal anti-inflammatory drugs (NSAIDs), diuretics, vitamins and herbal supplements are recommended for treatment of mastodynia (1-5). The side effects associated with hormonal drugs preclude their use as first-line agents (3).

Based on including nutritional changes, drugs such as vitamin E and herbal supplements have been used. There are results showing that vitamin E alone and in combination with other drugs can be considered as a safe drug to control mastodynia (6-10). On the other hand, essential free fatty acids and primrose oil are used for reducing mastodynia (11-14).

## 2. Objectives

Based on this hypothesis that the effects of vitamin E and omega-3, 6, 9 free fatty acids can work synergistically, this study was done to compare vitamin E combined with omega-3, 6 and 9 fatty acids and vitamin E alone, in the treatment of mastodynia.

## 3. Patients and Methods

This randomized controlled trial was performed in Lorestan University of Medical Sciences, Khorramabad, Iran, with approval of the Board of Ethics of the University. The consent form was obtained from the participants. Totally, 88 women with symptoms of cyclic mastodynia (aged 20 - 55 years) were enrolled in our study. They were divided into two groups of case and control, randomly, each group containing 44 patients. Blocked randomization method was used in this study. Participants with palpable mass, recent breast abscess, breast drainage and breastfeeding women were excluded from this study by

a surgeon. A questionnaire, containing women demographics and history of familial cancer, BMI (Body Mass Index), history of drug consumption, breast biopsy and asthma and also duration, intensity and site of symptoms, was completed.

The patients were randomly assigned to receive vitamin E (400 U/day) and vitamin E (400 U/day) plus omega (1200 mg/day) orally, for 3 months. Both groups were visited 4, 8 and 12 weeks later and were reassessed for pain relief according to the Cardiff Breast Pain Score (CBS), as follows: CBS1 = excellent response with no pain; CBS2 = good response with slight tolerable pain, CBS3 = weak response with pain, CBS4 = no response. When the pain was CBS1 or CBS2, the response was defined as satisfactory.

Statistical analysis was performed using Fisher exact test and Mann-Whitney test, with the SPSS software version 11.5 (SPSS Inc., Chicago, IL, USA). A  $P < 0.05$  was considered to be statistically significant.

#### 4. Results

Totally, 87 patients participated to this study. The mean  $\pm$  SD of the age for the vitamin E group was  $40.1 \pm 7.4$  years and for the vitamin E + omega was  $35.2 \pm 9.8$  years. Table 1 shows the demographics and history of each group, including age, marriage, types of pain, BMI and drug consumption. Most of the women were married. Medical history included aspirin or aspirin-like medication use. Unilateral mastodynia was present in 55% and 52% of

patients in the vitamin E and vitamin E + omega groups, respectively. Because of side effects, one patient was lost to follow-up after 4 weeks in the control group, although she had a good response to the drugs.

Our results showed that vitamin E + omega is more effective than the use of vitamin E alone in decreasing mastodynia (Table 2). A significant difference was seen between the CBS score of the vitamin E group compared to vitamin E + omega group ( $P < 0.05$ ) at the end of the first, second and third months after treatment.

**Table 1.** Demographic Data of the Vitamin E and Vitamin E + Omega Groups <sup>a, b</sup>

Variable	Vitamin E	Vitamin E + Omega
Age, y	40.8 $\pm$ 8.2	35.3 $\pm$ 8
<b>Marital status</b>		
Married	88.10	73.30
Single	11.90	22.20
<b>Cyclic pain</b>	57.10	48.90
<b>Noncyclic pain</b>	42.90	51.10
<b>BMI, kg/m<sup>2</sup></b>	25.81 $\pm$ 4.82	25.9 $\pm$ 3.2
<b>Drug history</b>		
Yes	12.00	60.00
No	88.00	40.00

<sup>a</sup> Data are presented as mean  $\pm$  SD or %.

<sup>b</sup> Abbreviation: BMI, body-mass index.

**Table 2.** The CBS Scores of the Vitamin E and Vitamin E + Omega Groups <sup>a, b</sup>

Variables	First Month	Second Month	Third Month
<b>CBS1</b>			
Vitamin E	19	19	35.7
Vitamin E + omega	88.9	90.9	90.9
P value	0.01	0.13	0.12
<b>CBS2</b>			
Vitamin E	21.4	50.9	21.4
Vitamin E + omega	2.2	0	0
P value	0.01	0.001	0.001
<b>CBS3</b>			
Vitamin E	16.7	15.9	0
Vitamin E + omega	0	9.1	9.1
P value	0.001	0.11	0.001
<b>CBS4</b>			
Vitamin E	42.9	14.2	42.9
Vitamin E + omega	8.9	0	0
P value	0.14	0.001	0.001

<sup>a</sup> Data are presented as %.

<sup>b</sup> Abbreviation: CBS, cardiff breast pain score.

## 5. Discussion

In this study, we compared the effect of vitamin E and vitamin E plus omega on patients with mastodynia. Our data showed that omega usage with vitamin E is more effective than vitamin E alone in the decrease of mastodynia pain among the patients. Vitamin E is the most commonly used supplements as a treatment for breast pain (4), with minimal side effects, although there are several controversies. Our results confirm previous studies that showed that vitamin E can reduce the cyclic mastodynia, individually (1, 2). In addition vitamin E plus other supplements, such as Evening Primrose oil (EPO) and fish oil were more effective against mastodynia, individually (2, 3). The EPO (2, 3) and Flax seed oil (4) have a number of effects on mastodynia (5). Flax seed oil is a source of omega-3 fatty acid (4) and EPO is rich in omega-6 fatty acids and contains 9% gamma-linolenic acid (GLA), by weight (6). The GLA is believed to restore the saturated/unsaturated fatty acid balance and decrease sensitivity to steroidal hormones (7). In addition, it has been showed that in women with cyclic mastodynia who have low plasma levels of GLA, the replacement treatment was effective (15, 16).

Three previous studies have evaluated vitamin E supplementation as a potential treatment for breast pain. These studies had a treatment duration ranging around 2 - 3 months and a vitamin E daily dose ranging from 15 - 600 IU. They showed no benefit of these regimens in the management of breast pain or benign breast disease. A more recent, 4 months randomized, double-blind clinical trial of 150 premenopausal Iranian women assessed the therapeutic effects of 200 mg vitamin E twice daily or placebo, for the treatment of cyclical mastodynia.

A study similar to the present trial was conducted in the United Kingdom and used a combination treatment arm of antioxidants and minerals (which included beta-carotene, vitamin C, vitamin B, zinc, niacin, and selenium in a coconut oil base) and essential fatty acids. The investigators found equivocal results in the reduction of breast pain symptoms.

The present study was conducted with a small sample size because large randomized trials are expensive. This kind of studies, with small sample sizes, are important as an initial step in determining whether there is preliminary evidence to justify a larger, potentially costly study.

Our results showed that the combination of vitamin E and omega is better than vitamin E alone. Although the main mechanism of action of vitamin E may be due to its antioxidant activity, however, the mechanisms of combination effects are need to be investigated more closely.

## Acknowledgements

The authors wish to thank the Lorestan University of Medical Sciences, Khorramabad, Iran, for supporting this study.

## Authors' Contributions

Developed the original idea and designed the project: Bahram Delfan and Farshad Zarei. Analyzed the data and performed the project: Somayeh Irvani and Farzad Ebrahimzadeh. Wrote the manuscript: Ahmad Adineh, Reza Sepahvand and Mohsen Asadbaigi.

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