# Role of Essential Fatty Acids In Cyclic Mastalgia

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**Abstract**

There is a strong relation between essential Fatty acids( EFA) levels in plasma phospholipids and cyclic mastalgia. In this study essential fatty acids levels of 40 patients with cyclic mastalgia were measured. Concentrations of the main dietary linoleic acid were found to be consistently normal or slightly elevated, whereas levels of linoleic acid metabolites were consistently low. This suggests that these patients have an abnormality in EFA metabolism, probably involving reduced conversion of linoleic acid to its EFA products. This deficiency of essential fatty acids metabolites was improved after supplementation of essential fatty acids in the form of evening primrose oil capsules in a dose of 3 grams per day; also the degree of pain was improved with a response rate of about 65% after 6 months of treatment.

**Keywords:** cyclicmastalgia- essential fatty acids

**Introduction:**

Breast pain or mastalgia, is the commonest symptom in patients attending a breast clinic **[1]**, and most of the attempts to understand it have occurred only very recently. Previously it was regarded as a part of a psychosomatic disorder and therefore it was greatly under reported. The recognition of two types of mastalgia, cyclical and noncyclical, was known as early as 1970s ,and confirmed later **[2,3].**

Cyclic mastalgia is a common condition in women seen in primary care practice **[4].** The prevalence of mastalgia reported in the medical literature ranges from 4-69%. The clinical presentation is often described as premenstrual breast pain and tenderness associated with swelling, regular occurrence during the luteal phase of the menstrual cycle, about seven days duration, and resolution of symptoms with menstruation **[5].**

An estimated 70 percent of premenopausal women are affected by breast pain at some point in their life. For most women the symptoms are effectively managed with physician reassurance and conservative measures **[4].**

It is clearly a disorder precipitated by ovarian hormones since any method of disruption of ovarian functions, whether by drugs, surgery or a natural menopause, almost always leads to relief of the pain. Yet no consistent abnormalities of circulating ovarian hormone levels have ever been detected. It must therefore be concluded that women with breast pain have breast tissue which is unduly sensitive to normal amounts of ovarian hormones **[6].**

Boyd et al. in 2005 have drawn attention to the cause of this sensitivity based on the fact that breast pain is associated with a high consumption of saturated fats and that a very low fat diet can often relieve such pain **[7].**

It was found that in women with breast pain , the plasma and red cell membranes have unusually low concentrations of gamma linolenic acid (GLA) metabolites, and especially of arachidonic acid (AA) **[8].** Linoleic acid (LA) levels may be normal or slightly reduced, but the reduction in AA is always proportionately greater than the reduction in LA. This indicates either a deficit in the formation of GLA and its metabolites, or an increased rate of consumption which cannot be compensated by the rate limiting delta-6 desaturation of LA **[9].**

The aim of this study is to review and assess the relationship between essential fatty acids and cyclic mastalgia, and effect of evening primrose oil supplementation on fatty acid level and cyclic mastalgia.

**Materials and Methods**

This prospective study was carried out on 40 female patients presenting with mild to severe breast pain at the surgical outpatient department of kasr el ainy hospital, from April 2012 to December 2012.

Female patients with ages ranging between 17 and 45 years were included in the study. Cyclic mastalgia was defined as pain that occurs within 2 weeks of menses onset, partially or completely relieved with menses and that had occurred for at least 3 consecutive cycles. Written informed consent from patients was taken before starting treatment.

Exclusion criteria included women with previous breast surgery, suspicious or malignant breast masses, pregnant women or those aiming for conception in the near future, breast abscess, mastitis or nipple discharge. Also patients under treatment with anticonvulsants, phenothiazines lithium, estrogen therapy, digoxin, or anticoagulation were all excluded.

During the first visit, a detailed clinical history was taken regarding the onset of mastalgia days prior to menses, wearing a well fitting brassiere, smoking habit, caffeine intake, and previous medications taken to relief symptoms. However, in order not to disturb the patients' lifestyles, they were not asked to alter their habits.

Proper Physical examination was done to confirm the diagnosis and exclude any clinically palpable masses. Mammography was ordered for all patients over 25 years old and US for patients less than 25 years old, to exclude any clinically non palpable masses and to rule out malignancy.

The intensity of mastalgia was self assessed with a numeric rating scale **[10]** by the participants as following in figure (1):

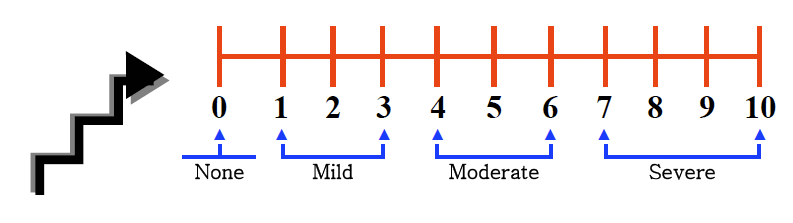


Figure 1: Numeric rating scale

Fig (12) Numeric rating scale for pain.

1. The patient was asked any one of the following questions:

* What number would you give your pain right now?
* What number on a 0 to 10 scale would you give your pain when it is the worst that it gets and when it is the best that it gets?
* At what number is the pain at an acceptable level for you?

2. When the explanation suggested in #1 above was not sufficient for the patient, it was sometimes helpful to further explain or conceptualize the Numeric Rating Scale in the following manner:

* 0 = No Pain
* 1-3 = Mild Pain (nagging, annoying, interfering little with adult life style) (ADLs).
* 4–6 = Moderate Pain (interferes significantly with ADLs).
* 7-10 = Severe Pain (disabling; unable to perform ADLs).

The breast pain scale was recorded for each patient twice,at the baseline cycle and after 6 months of starting treatment.

Essential fatty acids levels were measured using gas chromatography before and after 6 months of starting treatment.

The serum samples for fatty acids were taken after overnight fasting. Samples were analyzed for essential fatty acids levels in total plasma phospholipids, and expressed as (milligrams per 100 milligrams).

Treatment was initiated after complete assessment, by reassurance, advice for low fat diet and dietary supplementation with Evening Primrose oil capsules 3000mg/day for 6 months. The Cardiff breast pain score was used to asses degree of satisfaction **[11]** as follows:

|  |
| --- |
| **CARDIFF BREAST PAIN SCORE (CBS)** |

**CBS 1**

An excellent response with no residual pain

**CBS 2**

A substantial response but with some residual pain, Considered by the patient to be bearable

**CBS 3**

A poor response with substantial residual pain

**CBS 4**

No beneficial response at all

All collected data were revised for completeness and consistency.All data were then transferred to the Statistical Package of Social Science Software program, version 21 (SPSS) to be statistically analyzed.

Data was summarized using mean and standard deviation or Median and percentiles for quantitative variables and frequency and percentage for qualitative variables.

Relative percent change was calculated to all repeated measures as follow:

Relative % change = [(post measure - pre measure) / pre measure] \* 100

Comparison between groups was done using independent sample t-test for quantitative variables and chi square test or Fisher’s exact test for qualitative variables.

Repeated measures were analyzed using paired t test for quantitative variables& marginal homogeneity test for qualitative variables.

Spearman correlation coefficient was calculated to test the association between the quantitative & ordinal variables

P values equal to or less than 0.05 were considered statistically significant. Graphs were used to illustrate some information.

**Results:**

A total of 40 patients were included with their ages ranging from 17 years to 46 years with mean age 30.2 (± 10.1) years . Figure (2) shows the distribution of patients according to age groups which shows two peaks (16-20) 32.5% and (41-45) 25%. Mastalgia presented bilaterally in 70% of cases

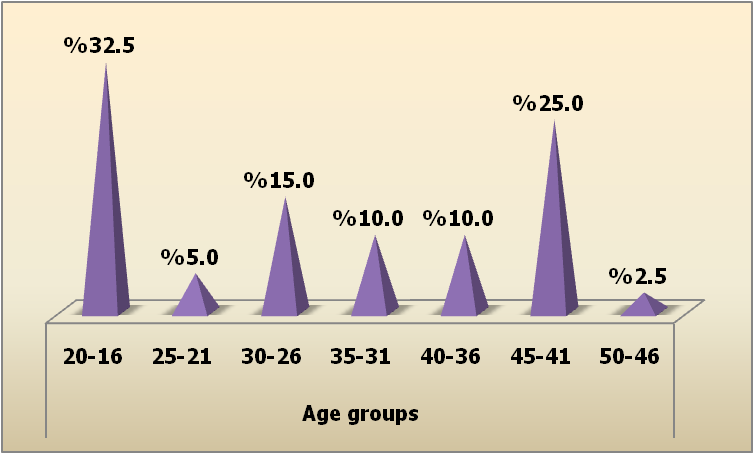
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Figure 2: Age group distribution

Assessment of associated risk factors for mastalgia revealed that 47.5% of the patients were not wearing well fitting bra, and 17.5% were drinking coffee while none of the patients included were smokers. **(Figure 3)**



**Figure 3: Distribution of patients according to factors that may affect mastalgia.**

Before starting treatment, the pain was moderate in 25 patients (62.5%), mild in 8 patients (20%), and severe in 7 patients (17.5%) **(Figure 4)** .



**Figure (4): distribution of patients according to degree of pain before starting treatment**

As shown in table (1) the duration of pain ranged from 4 to 30 months with a mean duration of 11.2 (±5.7)) month.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **MIN** | **MAX** | **Mean** | **SD** | **Percentiles** | | |
|  |  |  |  |  | **25th** | **50th** | **75th** |
| **Duration of cyclic mastalgia** | 4.0 | 30.0 | 11.2 | 5.7 | 7.3 | 10.5 | 12.0 |

Table (1): distribution of patients according to duration of pain per months

Pain reassessment after 6 month of treatment showed that 11 patients (27.5%) had no pain after 6 months of treatment while 15 patients (37.5%) had mild pain, 13 patients (32.5%) had moderate pain and 1 patient (2.5%) still have severe pain.figure (5).



**Figure (5) :the degree of pain after 6 months of treatment**

Statistical analysis showed a significant decline of the degree of pain (P value < 0.05) after receiving treatment for six months (table 2 and figure 6). There was complete relieve of pain in 6 patients out of the 8 patients with mild pain and 5 patients of those presenting with moderate pain but none on those presenting with severe pain .

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | | **Post** | | | | **Total** | **P value** |
| **No** | **Mild** | **Moderate** | **Severe** |  |
| **Pre** | **Mild** | 6 | 2 | 0 | 0 | 8 | **<0.001** |
| **Moderate** | 5 | 9 | 11 | 0 | 25 | **HS** |
| **Severe** | 0 | 4 | 2 | 1 | 7 |  |
|  | **Total** | 11 | 15 | 13 | 1 | 40 |  |

**Table (2): Improvement of degree of pain after receiving treatment for six months**



**Figure (6) Improvement of degree of pain after receiving treatment for six months**

The Cardiff breast pain scale revealed an overall good response in about 65% of patients as 27.5% of patients have excellent response while 37.5% of patients have substantial response. On the other hand 22.5% of patients have poor response and 12.5% of patients have no response to treatment. (table 3 and figure 7),

**Table (3) distribution of patients according to degree of satisfaction measured by CBS (Cardiff breast pain scale)**

|  |  |  |
| --- | --- | --- |
| **CBS** |  |  |
| Excellent response | 11 | 27.5 |
| Substantial response | 15 | 37.5 |
| Poor response | 9 | 22.5 |
| No response | 5 | 12.5 |



**Figure (7) distribution of patients according to degree of satisfaction**

After 6 months of treatment with primrose, the serum levels of Linoleic acid, GLA , Arachidonic acid and Dihommo gamma linolenic acid were significantly increased. While the alpha linolenic acid levels showed no significant changes (table 4 and 5).

**Table (4) changes in essential fatty acids levels after treatment:**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Pre** | **Post** | **P value** |
| **Linoleic** | 23.2 ± 3.1 | 24.9 ± 2.1 | **<0.002** |
|  |  |  | **HS** |
| **GLA(Gammalinlinolenic)** Acid | 0.12 ± 0.09 | 0.33 ± 0.2 | **<0.001** |
|  |  |  | **HS** |
| **Alpha linolenic** | 0.7 ± 0.08 | 0.7 ± 0.08 | 0.3 |
|  |  |  | NS |
| **Arachidonic** | 5.7 ± 0.6 | 6.9 ± 0.6 | **<0.001** |
|  |  |  | **HS** |
| **Dihommo** | 1.5 ± 0.2 | 3.0 ± 0.6 | **<0.001** |
|  |  |  | **HS** |

Results are expressed as the mean ± SD. Fatty acids are measured as mg/100mg of total fatty acids present.

**Table (5) relative% change regarding each fatty acid level after treatment**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **MIN** | **MAX** | **Mean** | **SD** | **Percentiles** | | |
|  |  |  |  |  | **25th** | **50th** | **75th** |
| **Relative Linoleic change %** | -2.0 | 19.7 | 7.5 | 6.6 | 1.9 | 5.4 | 14.0 |
| **Relative GLA change %** | 85.7 | 786.7 | 225.0 | 148.2 | 127.4 | 182.5 | 269.6 |
| **Relative Alpha Linolenic change %** | -8.6 | 14.1 | 1.0 | 5.4 | -3.4 | 1.4 | 4.6 |
| **Relative Arachedonic change %** | 6.0 | 48.8 | 21.1 | 10.0 | 13.2 | 20.9 | 27.0 |
| **Relative Dihommo Change %** | 30.0 | 206.7 | 109.5 | 47.6 | 66.0 | 110.8 | 150.6 |

As shown in table (5) there is significant change in Relative GLA, Arachedonic and Dihommo change% ,but on the other hand there is little or no change in Relative Linoleic acid and Alpha Linolenic acid change% .

**Table (6) Correlation between relative fatty acids changes with other variables**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Age** | **days of pain before menses** | **Duration of pain** | **degree of pain before treatment** | **degree of pain after treatment** | **CBS** |
| **Relative Linoleic change %** | **rho** | 0.19 | -0.14 | **0.38** | **0.38** | 0.10 | 0.14 |
|  | **P** | 0.25 | 0.40 | **0.02** | **0.02** | 0.55 | 0.41 |
| **Relative GLA change %** | **rho** | -0.19 | 0.04 | 0.01 | 0.21 | 0.01 | -0.05 |
|  | **P** | 0.25 | 0.80 | 0.98 | 0.19 | 0.93 | 0.78 |
| **Relative Alpha Linolenic change %** | **rho** | -0.06 | -0.07 | 0.12 | -0.02 | 0.04 | -0.03 |
|  | **P** | 0.72 | 0.66 | 0.46 | 0.91 | 0.82 | 0.87 |
| **Relative Arachedonic change %** | **rho** | 0.20 | 0.11 | 0.17 | 0.29 | 0.07 | 0.03 |
|  | **P** | 0.23 | 0.50 | 0.30 | 0.07 | 0.67 | 0.86 |
| **Relative Dihommo Change %** | **rho** | 0.09 | 0.04 | 0.20 | **0.50** | 0.31 | 0.24 |
|  | **P** | 0.60 | 0.81 | 0.21 | **0.00** | 0.06 | 0.14 |

rho= Spearman correlation coefficient, P = P value

The statistical analysis proved that patients with high degree of pain before treatment were associated with a significant positive strong correlation with Dihommo change % & significant positive moderate correlation with linoleic change% after 6 month treatment. Also,patients with longer duration of pain before treatment showed a significant positive moderate correlation with linoleic change%. Otherwise there is no other significant correlation.(Table 6)

**Table (7) Correlation between relative fatty acids changes with other factors that may affect mastalgia**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Relative Linoleic change %** | **P value** | **Relative GLA change %** | **P value** | **Relative Arachedonic change %** | **P value** | **Relative Dihommo Change %** | **P value** |
| **Side** |  |  |  |  |  |  |  |  |
| Unilateral | 9.2 ± 7.5 | 0.3 | 161.2 ± 61.1 | 0.08 | 22.3 ± 10.1 | 0.6 | 104.3 ± 44.5 | 0.7 |
| Bilateral | 6.9 ± 6.1 | NS | 252.3 ± 166.2 | NS | 20.6 ± 10.1 | NS | 111.7 ± 49.5 | NS |
| **Coffee drinking** |  |  |  |  |  |  |  |  |
| Yes | 7.2 ± 5.4 | 0.9 | 223.6 ± 110.8 | 1.0 | 19.1 ± 5.0 | 0.6 | 114.5 ± 49.8 | 0.8 |
| No | 7.6 ± 6.9 | NS | 225.3 ± 156.4 | NS | 21.5 ± 10.8 | NS | 108.4 ± 47.9 | NS |
| **Well-fitting bra** |  |  |  |  |  |  |  |  |
| Yes | 7.3 ± 6.8 | 0.8 | 217.9 ± 122.2 | 0.8 | 22.8 ± 10.9 | 0.3 | 104.3 ± 49.2 | 0.5 |
| No | 7.8 ± 6.5 | NS | 231.4 ± 171.1 | NS | 19.6 ± 9.1 | NS | 114.2 ± 46.8 | NS |

As presented in table (7), % changes were not different regarding laterality of pain, Coffee drinking & not wearing well fitting bra.

**Discussion:**

Analysis of the results obtained from our study showed that the mean age of the patients was 30.2 with a standard deviation (SD) of (± 10.1) years, ranging from 17 to 46 years. Mastalgia was most common in the age groups of 16-20 years and 41-45 years (32.5% and 27.5% respectively) .The incidence then declined in the age groups of 26-30 years (15%), 31-35 years (10%) and 36-40 years (10%).The incidence of mastalgia was least in both age groups of 21-25 (5%) and 46-50 years (2.5%).

In 2012, Katiyar et al. found that mastalgia is more common in age group 36-45 years (38.5%) followed by age group 26-35 years (37.5%) with less common in age groups 15-25 years (18.5%) and 46-55 years (5%) **[12].**In his study of 232 patients at Welsh national school of medicine, Preece et al. found that most frequent age group complaining of mastalgia was 31-35 years (45%) closely followed by 41-45 years (40%), and 36-40 years (32%) **[2].**

In our study mastalgia was commonly bilateral (70%), and when present unilaterally it is more common in left side (27.5%) while only (2.5%) of patients had right side mastalgia.Those results coinsides with the results of Sabel et al.2007 who reported that mastalgia is commonly bilateral (85%) while only (15%) has unilateral mastalgia **[13].**Also, Thakur et al 2010 reported that (64%) of patients had bilateral mastalgia while (36%) had unilateral mastalgia **[14].**

Several studies were conducted to evaluate the role of evening primrose oil (EPO) capsules for the treatment of cyclic mastalgia Analysis of the results of our study revealed that there is great improvement of essential fatty acids levels towards normal after supplementation of essential fatty acids in the form of evening primrose oil (EPO) capsules with good response in 65% of patients.

The response in our study appeared to be nearly the same as in other studies. In 1982, Preece et al. and in 1990, Mansel et al. reported that patients with cyclic mastalgia had significant improvement in pain after 3 months on EPO but not on placebo **[15,16].**

In addition, In 1992, Gateley et al. reported a slightly lower response rate of 58% to treatment with EPO **[17].** In 2005, Amit et al. reported a 35% response rate to GLA after 4 months treatment and a 58% response rate after 12 months of treatment **[18].** AlsoIn 2005, A study was conducted by Qureshi and Sultan. to evaluate the response of pain to Evening Primrose oil capsules . They observed that 68% had relief with EPO **[19].**

In 2010, Thakur et al. observed in their study a higher response of 75 % to Evening Primrose oil at the end of 6 months treatment **[14].**Again, in 2010, Sandhya et al. reported a benefit in reduction of cyclic mastalgia with vitamin E and EPO individually and in combination **[20].**

Other studies showed a higher response rate. In 1995, Mansel reported a response rate of about 92% to treatment with GLA **[20].** And In 1999, Cheung observed a 97% response rate in oriental women in a pioneer experience of using gamolenic acid in Asia **[21]**.

On the other hand, In 1985, Pye et al. described much lower results as they studied the effect of EPO, Danazol and Bromocryptine in a randomised trial in patients with mastalgia. They observed the following responses in cases with cyclical mastalgia (Danazol 70%,47% response to Bromocryptine, EPO 45% and placebo response was just 19%). **[22].**

In 2009, Rana et al. Reported a low response to EPO, as EPO was given only for a period of 2 months which is in contrast to our study where duration of treatment was 6 months **[23].** And In 2012, Katiyar et al. reported that only 34.6% patients responded to EPO using 3gms/day dose for 2 month **[12].**

In our study there was no relation between improvement in degree of pain or essential fatty acids levels and drinking coffee. Similar results were reported by Marshall et al. in 1982 in their case control comparison of 323 women with benign breast disease and 1,458 controls, no differences were noted in the coffee and tea consumption patterns of the cases and controls **[24].**In 1985, Lubin et al. also reported that there is no association between coffee or methylxanthine consumption **[25].** In 1986, Schairer et al. studied the relation between methylxanthine consumption and mastlgia. Which revealed that there was no evidence of an association between methylxanthine consumption and benign breast disease in the total study population **[26].**

However, In 1981, Minton et al. reported in their study that resolution of signs and symptoms of mastalgia occurred in 85% of patients who abstained from methylxanthines for period of 8 weeks or more **[27].**Also our study found that there was no relation between improvement in degree of pain or essential fatty acids levels and wearing well fitting bra. Although randomized controlled trials (RCTs) are lacking, in 1976, Wilson and Sellwood in their study reported that there is evidence that a well fitting bra may provide relief for mastalgia in 75% of patients **[28].** In 2000, Hadi study revealed that, where women wore an individually fitted bra or a sports bra, an 85% improvement in mastalgia was reported **[29].**

Among our study group there were no smokers, so we couldnot assess the relation between smoking and cyclic mastalgia.

Conclusion:

There is a strong relation between essential fatty acids levels and cyclic mastalgia,patients with cyclic mastalgia has abnormal essential fatty acids metabolism.Evening Primrose oil supplementation can shift essential fatty acids levels towards normal with improvement of degree of mastalgia.

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