

## Original Article

# Effectiveness of Evening Primrose Oil (EPO) versus Tamoxifen in the Treatment of Mastalgia

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Mastalgia, also called Mastodynia, is the most common breast symptom in patients attending a breast clinic. Up to 70% of women are believed to develop pain in their breasts in their life time<sup>1</sup>. Despite its commonness, however, it is believed to be under reported due to social factors, partly due to reluctance of both, the patients to disclose it and of the Health Care Workers to ask about it<sup>2</sup>. Breast pain in childbearing age with or without a lump, is a common complaint and a cause of anxiety and fear of breast cancer<sup>3</sup>. Various modalities of management and treatment are suggested and employed. Herein, we present the results of a prospective study conducted on patients of breast pain, using two drugs ie, Evening Primrose Oil (EPO) and Tamoxifen, from among a spectrum of them.

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**Key words :** Mastalgia, Cyclical Mastalgia, Non-cyclical Mastalgia, Evening Primrose Oil (EPO), Tamoxifen.

The two most common causes of patients presenting with mastalgia are the fear of breast cancer and the presence of severe pain affecting the Quality of Life. The most important responsibility of the breast specialist is to consciously rule out cancer and reassure the patients. Mastalgia may be cyclical (worse before a period) or non-cyclical (with no relation with periods). Cyclical breast pain resolves spontaneously in 20-30% of women but tends to recur in 60% of them. Non-cyclical pain responds poorly to treatment but tends to resolve spontaneously in half of women. Non-breast pain can mimic mastalgia; chest wall pain mimicking mastalgia includes costochondritis (Tietze's disease), referred nerve root pain as in cervical spondylitis and herpes zoster before eruption of vesicles. Non-chest wall pain can arise from diverse causes such as ischemic heart disease, biliary pain, and peptic ulcer disease<sup>4</sup>.

Mastalgia has been linked to a variety of conditions such as high levels of stress, anxiety, depression, chronic myalgia, irritable bowel syndrome, chronic pelvic pain and some psychiatric disorders suggesting multifactorial pathogenesis<sup>5</sup>, yet it is emphasized that majority of these patients may have either physiological or pathological cause which needs to be addressed. Some factors such as caffeine, cigarettes smoking, high plasma fatty acids, prolactin and acute stress have been demonstrated as other possibilities<sup>6</sup>.

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### Editor's Comment :

- Mastalgia is the most common breast symptom in women.
- Various treatment modalities have been tried with varied response.
- Clinically evaluated the effectiveness of EPO and tamoxifen and found both to be effective, the latter being a better choice in the long run.

Management is multipronged. However, the first line of management remain life style changes<sup>7</sup>. The most important first step is reassurance after exclusion of cancer. A low-fat diet, high carbohydrates, regular exercise, well-fitting bra, a breast support and explanation with cancer reassurance, is suggested. This is the first line (conservative) treatment and may also include the "over the counter" analgesics as well. If not responding, the treatment will be upgraded to the second line therapy ie, medicines like Tamoxifen, GLA etc<sup>8</sup>.

Evening Primrose Oil (EPO), a plant derivative, is obtained from the seed of *Oenotherablennis*. EPO is an Essential Fatty Acid (EFA) used empirically by many to reduce cyclical mastalgia. EPO is a rich source of EFA's and contains 7-14% Gamma Linolenic Acid (GLA). Its mechanism of action is thought to involve inhibition of prostaglandins, which potentially contribute to breast pain. Usual dose of EPO is 1000mg per day.

Tamoxifen is a synthetic anti-estrogen that, since its introduction for the treatment of patients with breast cancer in the early 1970's, has come to have a major role in the management of all stages of the disease. It is used in the treatment of mastalgia as it reduces estrogen levels. It acts as a Selective Estrogen Receptor Modulator (SERM). In the breast tissue, it

antagonistically competes with oestrogen for binding sites and causes antioestrogenic, as well as anti-tumour effect<sup>9</sup>. The dose of the tamoxifen used for management of breast pain ranges from 10 to 20mg per day.

### MATERIALS AND METHODS

The study was conducted in the Postgraduate Department of Surgery, Government Medical College, Jammu, J&K, over a period of one year, from 1<sup>st</sup> November, 2020 to 31<sup>st</sup> October, 2021. The study aimed at comparing the efficacy of Evening Primrose Oil (EPO) *versus* Tamoxifen in the treatment of Mastalgia.

In this study, sixty patients who fit the inclusion criteria were placed into two groups, comprising of 30 each, (Group A and Group B), on basis of Random sampling method after taking proper consent.

**Group A :** Patients receiving Evening Primrose Oil (EPO) 1000mg per day, single dose, orally.

**Group B :** Patients receiving Tamoxifen 20mg per day, single dose, orally.

Initial assessment of pain, at the time of presentation, was recorded, according to Visual Analogue Score (VAS). A detailed physical examination of the patient was done followed by relevant investigations. All patients were subjected to ultrasound examination of both breasts, abdomen and pelvic organs. Bilateral mammography was performed, wherever indicated.

The patients in both the groups were followed up for re-assessment later for improvement in symptoms at the end of four and eight weeks. They were again followed up at 16 weeks for assessment of recurrence of pain. A relief of pain was considered when the VAS score was equal to or less than 3 on subsequent follow ups.

All the findings were noted down for statistical evaluation. Statistical analysis was performed using IBM SPSS 21. The data was tested for normality and then analysis was done using student-t test and Mann Whitney –U test for continuous data. Categorical variables were compared, using Chi-Square test and Fisher's Exact test.

### OBSERVATIONS AND RESULTS

The following observations were made: The maximum number of patients (45%) belonged to 28-37 age group. The youngest patient was 18 years old and the oldest was 45 years old. This was in contrast to some authors reporting age group of 41-50 years to be affected most by mastalgia<sup>10</sup>. Bilateral pain was seen to occur in 27 patients (45%) followed by left

sided pain in 21 patients (35%) and right sided pain in 12 patients (20%).

The association with menstrual cycle (Cyclical Mastalgia) was seen in 34 patients (56.66%). The associated history included co-morbidities (like hypertension, diabetes mellitus, hypothyroidism) in 12 patients (20%), dysmenorrhea in 19 patients (31.66%), OCP's use in 5 patients (8.33%), and alcohol history in 2 patients (3.33%). There was no history of smoking in any patient. Majority of the patient were married (71.76%). Examination was normal in 51 patients (85%) at the first visit to hospital followed by breast tenderness in 4 (6.67%) patients, lumpiness in 3 patients, and nipple discharge in 1 patient. On USG examination of right breast, 50% were categorized by BIRADS 1, 46.67% as BIRADS 2 and 3.33% as BIRADS 3. On the other hand, left breast USG examination showed BIRADS 1 in 55%, BIRADS 2 in 41.67% and BIRADS 3 in 3.33%.

Ultrasound examination of the breasts at the time of presentations was normal grossly, with most (96%) having BIRADS 1 and 2 changes in both breasts. By and large it is suggested that without abnormal findings on physical examination, pre-menopausal women presenting with cyclical breast pain, do not require radiographic imaging routinely<sup>11</sup>.

In general, in the present study, better relief in Mastalgia was seen to be obtained with EPO than with Tamoxifen ( $p=0.035$ ) at the end of 4 weeks' treatment (Fig 1). However, at 8 weeks' treatment both drugs were observed to be equally effective with no statistical difference in their effectivity ( $p=0.11$ ) (Fig 2). Impliedly continuation of treatment for longer period than 4 weeks' increased effectiveness. Individually also, both EPO and Tamoxifen were more effective at 8 weeks' treatment than at 4 weeks' treatment ( $p=0.0001$ ) (Table 1). The pattern of relief of pain persisted with

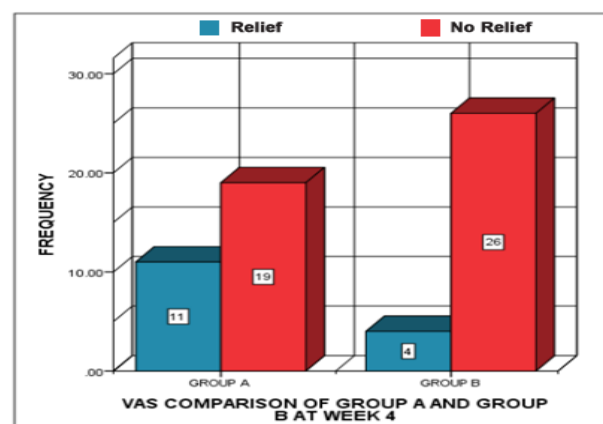


Fig 1 — Pain Relief at 4 weeks Group A (EPO) *versus* Group B (Tamoxifen)

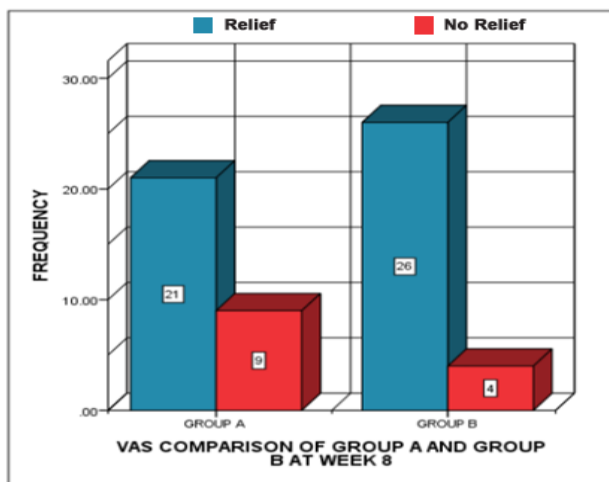


Fig 2 — Pain Relief at 8 weeks Group A (EPO) versus Group B (Tamoxifen)

both drugs after usage for 16 weeks. The pain recurrence at this stage was statistically insignificant in both the drug groups (p=0.60) (Table 2).

In Cyclical Mastalgia, while there was no difference between two drugs affecting a pain relief at 4 weeks' treatment (p=0.07) (Table 3), Tamoxifen was seen to be comparatively more effective than EPO, at the end of 8 weeks' treatment (p=0.046) (Table 4).

VAS Score	Group A		Group B		P-value
	Mean	SD	Mean	SD	
0wks	7.53	1.33	7.53	1.27	0.98
4wks	4.26	1.50	4.97	1.88	0.93
8wks	2.73	1.53	2.73	0.98	0.99
P-value (4 weeks versus 8 weeks)	0.0001		0.0001		

Recurrence Pain at 16 Weeks	Group A	Group B	P-value
Present	3	1	0.60
Absent	27	29	
Total	30	30	

	Relief	No Relief	Total	P-value
Group A	6	10	16	0.07
Group B	2	16	18	
Total	8	26	34	

	Relief	No Relief	Total	P-value
Group A	12	4	16	0.046
Group B	14	4	18	
Total	26	8	34	

## DISCUSSION

The cause of mastalgia is not clear but there are several theories. Hormonal theory, especially in cyclical pain, is suggested by the onset at the age of menarche, its relationship with the menstrual cycle and its resolution with the menopause. There is some evidence that suggests that women with mastalgia have increased levels of saturated fatty acids and reduced levels of essential fatty acids, especially Gamma Linoleic Acid (GLA). This makes the cell membrane more sensitive to nociceptive depolarization and allows the estrogen receptor to be more available.

The initial management of Mastalgia includes non-medicinal therapy, reassurance and a good external breast support. The condition is usually benign but has a major impact on the work activities. Ozturk, *et al*<sup>12</sup> described mastalgia as a debilitating disorder, which has effects on one's daily life and causes significant medical costs. While the chances of mastalgia being a symptom of breast cancer is quite low, Dave, *et al*<sup>13</sup> emphasized that most breast cancers do not cause pain. Yet, at the same time it is important to screen women who are at risk. Upto 85% of women will show alleviation of pain episodes after getting reassurance of not having breast cancer<sup>14</sup>.

Cyclical mastalgia, which occurs in two third of patients with mastalgia occurs one to two weeks before menstruation and is relieved by the onset of menstrual flow. Pain in the breast in the reproductive age is usually experienced either in the center, spreading to other parts of the breasts or to the other breast. It may be caused by normal cyclical changes in the hormones, and therefore responds very well to hormonal therapies.

Non-cyclical mastalgia is characterized by constant or intermittent breast pain and is not associated with menstrual cycle. Its etiology is unclear, occurs in older age and responds less to hormonal modulation and therefore more challenging to treat. Extramammary pain is linked to skeletal disorders like costochondritis etc.

In general, 92% of patients with cyclical mastalgia and 64% of non-cyclical mastalgia can obtain pain relief with conservative treatment<sup>15</sup>. Yet in approximately 8% of patients pain will be severe and will require medication after initial detailed assessment<sup>16</sup>.

## CONCLUSION

This study suggested that EPO and Tamoxifen both were effective in providing pain relief in mastalgia. EPO showed quick relief at 4 weeks. At the end of 8 weeks of treatment both drugs were equally effective.

For cyclical mastalgia both EPO and Tamoxifen were effective drugs, yet the results seemed to be better with Tamoxifen. However, considering the small sample size of the study, this finding may not be held absolutely. The Pattern of pain relief in Mastalgia persisted till the end of 16 weeks after the start of treatment with no significant recurrence with either of the drugs.

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