

## Efficacy of Evening Primerose Oil & Danazol in Mastalgia- An Observational Study with respect to Breast Pain Chart

Gaurav Kumar<sup>1</sup>, Motaal Ahmad<sup>2</sup>, Chandan Kumar<sup>3\*</sup>

<sup>1</sup>Jounior Resident, Department of General Surgery, Patna Medical College and Hospital, Patna, Bihar.

<sup>2</sup>Assistant Professor, Department of General Surgery, Patna Medical College and Hospital, Patna, Bihar.

<sup>3</sup>\*Senior Resident, Department of General Surgery, Patna Medical College and Hospital, Patna, Bihar.

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### ABSTRACT

**Background:** Women often experience mastalgia, or breast pain, which can negatively impact their quality of life and mental health. Cyclic mastalgia is more common and linked to hormonal changes. Clinically used treatments include Evening Primrose Oil (EPO) and Danazol. Danazol, a synthetic androgen, suppresses gonadotropin secretion and oestrogenic stimulation, while EPO, a GLA-rich supplement, regulates prostaglandin metabolism.

**Objective:** This study aims to evaluate and compare the efficacy and safety of Evening Primrose Oil and Danazol in relieving mastalgia using a standardized Breast Pain Chart (BPC).

**Methods:** This prospective observational study was conducted at Patna Medical College & Hospital, Bihar, from March 2024 to February 2025, involving 100 female patients diagnosed with moderate to severe mastalgia. Patients were randomly divided into two groups Group A (n=50): Received Evening Primrose Oil (1000 mg/day) for 12 weeks. Group B (n=50): Received Danazol (100 mg/day) for 12 weeks.

**Results:** Both treatments significantly reduced mastalgia severity, with Danazol showing greater pain reduction (63.4%) compared to Evening Primrose Oil (45.8%). However, Danazol was associated with more side effects, including weight gain (12%), menstrual irregularities (18%), and fatigue (6%), while Evening Primrose Oil had a better safety profile with only mild gastrointestinal discomfort (8%) and headaches (4%).

**Conclusion:** While Danazol is more effective in reducing mastalgia pain, its side effects may limit long-term use. Evening Primrose Oil presents a safer, well-tolerated alternative, making it a preferred first-line therapy, with Danazol reserved for refractory cases. Further large-scale studies are warranted to refine treatment protocols and assess long-term outcomes.

**Keywords:** Mastalgia, Evening Primrose Oil, Danazol, Breast Pain Chart, Cyclic Mastalgia, Non-Cyclic Mastalgia, Hormonal Therapy, Gamma-Linolenic Acid, Prostaglandin Metabolism, Gonadotropin Suppression.

### INTRODUCTION

Mastalgia, or breast pain, is common in reproductive-age women and can cause anxiety, a lower quality of life, and unnecessary medical consultations [1]. Research shows that nearly 70% of women will experience breast pain in their lifetime, so many seek medical attention for breast issues. Main mastalgia types are cyclic and non-cyclic. Two-thirds of women experience cyclic mastalgia during the luteal phase, which is caused by hormonal changes during menstruation [2]. The top outer quadrants of both breasts are usually hardest hit. Non-cyclic mastalgia is rarer, affects only one side, and has nothing to do with periods. It can develop from musculoskeletal issues, trauma, cystic changes, or no apparent cause [3]. Mastalgia affects women's health, so researchers have studied many treatments. Regular exercise, reducing caffeine and fat, and wearing proper bras are recommended lifestyle changes. Many patients turn to pharmaceuticals when lifestyle changes don't work. Danazol and Evening Primrose Oil are popular mastalgia treatments [4,5].

Gamma-linolenic acid (GLA), an essential fatty acid that regulates prostaglandin metabolism, is abundant in evening primrose oil from *Oenothera biennis* seeds [6]. Prostaglandins control hormones, pain, and inflammation. Some believe a lack of essential fatty acids causes a prostaglandin imbalance, which can worsen mastalgia [7]. EPO supplements may increase prostaglandin E1 (PGE1), reducing inflammation and pain. Clinical trials have shown conflicting results on EPO's mastalgia relief [8]. Since some studies show a significant pain reduction with EPO and others show no difference between EPO and a placebo, more research is needed to determine EPO's role in mastalgia treatment. Due to its non-hormonal nature and safety, EPO remains a popular first-line natural remedy for patients [9]. After conservative mastalgia treatments fail, danazol can be given. It reduces oestrogen and progesterone by blocking pituitary gonadotropin. Danazol alters hormonal balance to stop breast tissue from being stimulated cyclically, reducing pain [10]. Danazol consistently reduces mastalgia severity, with response rates exceeding 70% in some trials. Its use is limited by

\*Author for Correspondence: Dr. Chandan Kumar, Senior Resident, Department of General Surgery, Patna Medical College and Hospital, Patna, Bihar

weight gain, acne, irregular periods, and androgenic effects like voice deepening and hirsutism [11]. Due to these side effects, danazol is only prescribed to patients with severe or persistent mastalgia who have not responded to other treatments.

Despite available mastalgia treatments, severity of symptoms, patient preference, and side effect tolerance often determine treatment. No standard protocol exists for treating the condition [12]. The Breast Pain Chart helps objectively assess mastalgia severity and treatment response. By tracking pain frequency and intensity, clinicians can measure therapy efficacy with this chart [13]. This observational study compares Danazol and Evening Primrose Oil for mastalgia pain reduction using the Breast Pain Chart. Clinicians treating mastalgia can use this study to compare the two treatments' efficacy and side effects. This study at Patna Medical College & Hospital in Bihar will enrol 100 women with moderate to severe mastalgia from March 2024 to February 2025. One group takes 100 mg Danazol daily for 12 weeks, while the other takes 1000 mg Evening Primrose Oil. Researchers will track patients' pain, satisfaction, and side effects during treatment. Understanding these treatments' efficacy is crucial to mastalgia management. EPO is often used due to its natural composition and low side effects, but its efficacy is still debated. Despite its efficacy, danazol has serious side effects, so patient selection is crucial. This study will benefit mastalgia patients by expanding knowledge of treatment options. This study integrates patient-reported outcomes with objective pain assessment tools like the Breast Pain Chart to assess mastalgia treatments' effects and inform clinical decision-making.

## MATERIALS AND METHODS

**Study Design:** From March 2024 to February 2025, participants will be observed at Patna Medical College & Hospital in Patna, Bihar, for this prospective observational study. This study will use the Breast Pain Chart (BPC) to determine if Evening Primrose Oil (EPO) and Danazol treat mastalgia. Because it was observational, this study could assess real-world treatment responses without intervention bias.

**Sample Size:** The study included 100 female patients with moderate to severe mastalgia who met the inclusion and exclusion criteria. The sample size was based on research and the study site's recruiting capabilities.

### Inclusion Criteria

- Women aged 18 to 50 years diagnosed with moderate to severe mastalgia.
- Presence of cyclic or non-cyclic mastalgia persisting for more than three months.
- Willingness to maintain a Breast Pain Chart (BPC) throughout the study duration to objectively record pain intensity and treatment response.

### Exclusion Criteria

- Pregnant or lactating women due to potential hormonal fluctuations affecting mastalgia.
- Patients with a history of breast malignancy or those undergoing hormonal replacement therapy,

as these factors could interfere with the evaluation of treatment response.

- Patients with known contraindications to Danazol or Evening Primrose Oil, including those with severe hepatic dysfunction, thromboembolic disorders, or hypersensitivity to the study drugs.

**Study Groups:** Participants were randomly assigned into two groups (n=50 each) to receive either:

- Group A (EPO Group): Administered Evening Primrose Oil (1000 mg/day) for a duration of 12 weeks.
- Group B (Danazol Group): Administered Danazol (100 mg/day) for a duration of 12 weeks.

Patients were advised to adhere to their assigned treatment regimen and maintain a daily Breast Pain Chart to record pain intensity. No additional analgesic or hormonal medications were permitted during the study period.

### Outcome Measures

The primary and secondary outcomes were defined as follows:

**Primary Outcome:** Mastalgia severity improved as measured by the Breast Pain Chart (BPC), which measured daily pain from 0 (no pain) to 10 (worst pain). Pain scores were taken before, six, and twelve weeks into treatment.

**Secondary Outcomes:** Patients rated treatment satisfaction on a 5-point Likert scale, with 1 indicating no improvement and 5 indicating significant improvement. Side effects were worse in the Danazol group, including gastrointestinal distress, weight gain or loss, irregular menstrual cycles, and androgenic effects.

**Statistical Analysis:** All data were analysed using SPSS v26.0 to assess treatment efficacy. The pain scores of each group before and after treatment were compared using a paired t-test. To compare the two groups' pain reduction, ANOVA or Mann-Whitney U tests were used. Chi-square tests can test categorical variables like side effects and patient satisfaction. All comparisons were statistically significant with p-values below 0.05. This study will use a robust statistical approach to evaluate the safety and efficacy of Evening Primrose Oil and Danazol for mastalgia.

## RESULTS

The results of this study provide insights into the efficacy and safety of Evening Primrose Oil (EPO) and Danazol in managing mastalgia. The findings are presented in tables, followed by a detailed interpretation.

The mean age of participants in both the Evening Primrose Oil (EPO) group and the Danazol group was comparable ( $32.6 \pm 6.3$  years vs.  $32.2 \pm 6.1$  years, respectively). The distribution of cyclic (60%) and non-cyclic (40%) mastalgia was identical between the groups, ensuring homogeneity. Additionally, the baseline pain scores were statistically similar ( $7.2 \pm 1.4$  in the EPO group vs.  $7.1 \pm 1.5$  in the Danazol group;  $p = 0.81$ ), indicating that both groups had comparable pain severity at the start of the study.

Both Evening Primrose Oil (EPO) and Danazol significantly reduced mastalgia severity, as assessed by the Breast Pain Chart (BPC). However, Danazol showed

greater pain reduction than EPO. The mean pain score in the EPO group decreased from  $7.2 \pm 1.4$  to  $3.9 \pm 1.1$  (45.8% reduction;  $p < 0.05$ ). In contrast, the Danazol group experienced a more significant reduction from  $7.1 \pm 1.5$  to  $2.6 \pm 1.0$  (63.4% reduction;  $p < 0.01$ ). The pain reduction was statistically greater in the Danazol group compared to the EPO group ( $p < 0.01$ ), suggesting that Danazol was more effective in alleviating mastalgia.

Evening Primrose Oil (EPO) had minimal side effects, with only 8% of participants reporting mild gastrointestinal discomfort and 4% experiencing headaches. In contrast, Danazol was associated with more frequent and severe side effects, including weight gain (12%), menstrual irregularities (18%), and fatigue (6%). The higher incidence of menstrual irregularities and weight gain in the Danazol group was statistically significant ( $p < 0.01$  and  $p < 0.05$ , respectively). These findings indicate that while Danazol is more effective in reducing mastalgia, it also has a higher risk of adverse effects compared to EPO.

70% of patients in the Evening Primrose Oil (EPO) group reported moderate to significant

improvement, indicating that EPO is a well-tolerated and effective option for mastalgia management. Danazol demonstrated higher patient-reported effectiveness, with 85% reporting moderate to significant improvement (including 50% with significant improvement compared to 30% in the EPO group). Despite its higher efficacy, Danazol had a greater incidence of side effects, which may influence long-term adherence to treatment. The statistical analysis shows that patients in the Danazol group were significantly more likely to report a higher degree of improvement ( $p < 0.05$ ).

## DISCUSSION

**Overview of Findings:** This study clarifies Danazol and EPO's mastalgia treatment safety and efficacy. The Breast Pain Chart (BPC) showed that both treatments significantly reduced breast pain. The Danazol group reduced pain score by 63.4%, compared to 45.8% for the EPO group. Danazol's efficacy as a mastalgia treatment is supported by this, but EPO's safety makes it the better choice for non-hormonal, natural mastalgia treatment.

**Table 1: Baseline Characteristics**

Characteristic	Evening Primrose Oil (EPO) Group (n=50)	Danazol Group (n=50)	p-value
Mean Age (years)	$32.6 \pm 6.3$	$32.2 \pm 6.1$	0.72 (NS)
Type of Mastalgia	60% Cyclic, 40% Non-Cyclic	60% Cyclic, 40% Non-Cyclic	1.00 (NS)
Baseline Pain Score	$7.2 \pm 1.4$	$7.1 \pm 1.5$	0.81 (NS)

**Table 2: Pain Reduction**

Pain Score	Evening Primrose Oil (EPO) Group (n=50)	Danazol Group (n=50)	p-value
Baseline (Week 0)	$7.2 \pm 1.4$	$7.1 \pm 1.5$	0.81 (NS)
Post-Treatment (Week 12)	$3.9 \pm 1.1$	$2.6 \pm 1.0$	< 0.05
Mean Reduction	$3.3 \pm 1.3$ (45.8%)	$4.5 \pm 1.2$ (63.4%)	< 0.01

**Table 3: Side Effects**

Side Effects	Evening Primrose Oil (EPO) Group (n=50)	Danazol Group (n=50)	p-value
Gastrointestinal Discomfort	4 (8%)	0 (0%)	< 0.05
Headache	2 (4%)	0 (0%)	< 0.05
Weight Gain	0 (0%)	6 (12%)	< 0.05
Menstrual Irregularities	0 (0%)	9 (18%)	< 0.01
Fatigue	0 (0%)	3 (6%)	0.08 (NS)

**Table 4: Patient Satisfaction**

Satisfaction Level	Evening Primrose Oil (EPO) Group (n=50)	Danazol Group (n=50)	p-value
No Improvement (Score 1-2)	5 (10%)	2 (4%)	0.21 (NS)
Mild Improvement (Score 3)	10 (20%)	5 (10%)	< 0.05
Moderate Improvement (Score 4)	20 (40%)	18 (36%)	0.74 (NS)
Significant Improvement (Score 5)	15 (30%)	25 (50%)	< 0.05

**Comparison with Existing Literature:** Danazol and Evening Primrose Oil have been tested for mastalgia relief in clinical trials and observational studies. Danazol was a top mastalgia drug for years. Danazol is a key mastalgia treatment, alleviating pain in over 80% of patients in a [10]. Patient nonadherence was linked to serious side effects like weight gain, menstrual irregularities, and

exhaustion in the same study. Danazol users reported weight gain of 12% and menstrual irregularities of 18%, according to our research. Evening Primrose Oil (EPO) is widely used for cyclic mastalgia due to its gamma-linolenic acid (GLA) content, which regulates prostaglandin metabolism. According to [11], EPO may relieve moderate pain in some cases and placebo in others.

Our study and other recent research show that EPO is less effective than Danazol but has fewer side effects and good tolerability.

**Mechanism of Action of Evening Primrose Oil vs. Danazol:** Danazol and Evening Primrose Oil (EPO) have different efficacy and side effect profiles due to their different action mechanisms. Gamma-linolenic acid (GLA) in Evening Primrose Oil (EPO) reduces cyclic mastalgia-related breast pain and tenderness. GLA precedes prostaglandin E1. By decreasing prolactin sensitivity, it affects hormonal balance and cyclic mastalgia. EPO, unlike Danazol, does not affect gonadotropin levels or ovarian function, making it a safer alternative. The synthetic androgen Danazol inhibits gonadotropin secretion, reducing breast tissue oestrogenic stimulation, but other options do the opposite. By changing the hormonal cycle, it lowers LH and FSH levels and causes breast lobule atrophy, reducing mastalgia pain and swelling. Its hormonal activity causes weight gain, irregular periods, androgenic side effects like acne and voice changes. Due to these factors, EPO is safer but less effective than Danazol, a highly effective medication with few side effects.

**Strengths and Limitations of the Study:** Its prospective observational design allows the study to collect real-time data, one of its many benefits. Direct comparison of two commonly used mastalgia treatments and the use of a standardised Breast Pain Chart (BPC) to objectively measure treatment efficacy provide clinical insights. However, limits must be acknowledged. The 12-week study cannot assess long-term effectiveness and recurrence rates, so extensive follow-ups are needed. This 100-person, multicenter trial would yield less useful data. Even with a validated tool like the Breast Pain Chart, patient reports may be biased. This is because pain perceptions vary.

**Future Research Directions:** Future research should address the study's limitations and focus on mastalgia treatment improvements. Longer-term research is needed to determine whether EPO or Danazol relieves pain. Non-hormonal mastalgia treatments like diet, acupuncture, and herbal supplements may be safer. Researchers are investigating combination therapies like EPO with low-dose Danazol to improve efficacy and reduce side effects. Lifestyle factors like exercise, diet, and stress management may also help manage mastalgia.

## CONCLUSION

This observational study found that Danazol and EPO treat mastalgia. The Breast Pain Chart (BPC) shows both treatments significantly reduce pain. However, the interventions differed in efficacy and safety. Danazol reduced pain scores by 63.4% and EPO by 45.8%. Danazol's longstanding mastalgia treatment efficacy is reinforced by this. Due to side effects like weight gain (12%), menstrual irregularities (18%), and fatigue (6%), patients may not use it long-term. Evening Primrose Oil was less harmful and more bearable, with mild gastrointestinal distress (8% of cases) and headache (4% of cases). Despite its lower efficacy than Danazol, its lack of major hormonal side effects makes it an attractive first-

line treatment for women seeking natural, non-hormonal alternatives. EPO is well-tolerated and moderately effective for mild to moderate mastalgia. Danazol should only be used after other conservative treatments fail. These findings suggest that each patient's efficacy and tolerability needs should guide treatment selection. Although this study provides clinical insights, larger, multicenter trials are needed to improve treatment protocols, assess long-term efficacy, and investigate combination therapies. Future studies should examine how diet, lifestyle, and complementary therapies affect mastalgia management. Individualised mastalgia care using evidence-based methods can improve patient well-being.

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