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Use of Danazol Alone with Danazol Combined with Evening Primrose Oil for the Treatment of Fibrocystic Breast Disease- A Comparative study of 200 cases

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Abstract: ***Background:*** Fibrocystic breast disease, also known as mammary dysplasia, is a non-cancerous condition that results in breast lumps, pain, and discomfort. ***Objective:*** This study aims to compare the effectiveness of Danazol alone versus Danazol combined with Evening Primrose Oil (EP) in treating fibrocystic breast disease. ***Method:*** A randomized controlled study was conducted on 200 outpatients at Chuadanga Sadar Hospital, Bangladesh, from January 2022 to December 2023. Patients were divided into two groups. Group A received Evening Primrose Oil 1000 mg twice daily combined with Danazol 100 mg twice daily for three months. Group B Danazol 100 mg twice daily alone for three months. Pain levels were compared using mean and standard deviation, and an independent sample T-test was employed. The efficacy of the treatments was further analyzed using the chi-square test. ***Results:*** The study included 200 patients with a mean age of 30.54 ± 4.53 years. The VAS pain score between the two groups showed a mean difference of 1.53±0.27. The results indicated significantly lower pain in the group using Danazol combined with EP capsules compared to Danazol alone (p = 0.001). The percentage of response in Group B was higher than in Group A. ***Conclusion:*** Danazol combined with Evening Primrose Oil is more effective in reducing pain in patients with fibrocystic breast disease compared to Danazol alone.

Keywords: Danazol, Evening Primrose Oil, Non-Steroidal Anti-Inflammatory Agents, Breast Pain.

Original Research Article

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Article at a glance:

Study Purpose: *To compare the effectiveness of Danazol alone versus Danazol combined with Evening Primrose Oil in treating fibrocystic breast disease.*

Key findings: *The combination therapy significantly reduced pain more effectively and had higher patient satisfaction compared to Danazol alone.*

Newer findings: *Combining Danazol with Evening Primrose Oil provides superior pain relief and higher patient satisfaction in managing fibrocystic breast disease.*

Abbreviations: *EP: Evening Primrose Oil, VAS: Visual Analog Scale, NSAIDs: Non-Steroidal Anti-Inflammatory Drugs, FNAC: Fine-Needle Aspiration Cytology.*

INTRODUCTION

Mastalgia, commonly referred to as fibrocystic breast disease breast pain, is a prevalent and often distressing condition that prompts many women to visit general surgical outpatient departments. [1] This condition is characterized by breast lumps, pain, and discomfort, leading to significant anxiety among female patients. Research indicates that approximately 47% of patients seeking medical attention for breast-

related issues report mastalgia as the primary concern. As awareness and health education increase globally, more women are actively seeking medical advice regarding their breast health. For instance, in Pakistan, over 30% of women are between the ages of 14 and 45, highlighting a significant demographic potentially affected by mastalgia.[2] Notably, only 5-7% of patients with breast carcinoma report experiencing mastalgia, underscoring its primary association with benign conditions. In Bangladesh, the prevalence of mastalgia has been reported to be 35.5%. The management of breast pain encompasses a variety of strategies, including lifestyle modifications and pharmacological interventions. Non-pharmacological approaches involve wearing a well-fitted bra, reducing dietary fat intake, and discontinuing oral contraceptives or hormone replacement therapy.[3] Nutritional supplements, such as evening primrose oil, are also commonly recommended. Pharmacological treatments include nonsteroidal anti-inflammatory drugs (NSAIDs), which can be administered either orally or topically. Additionally, hormonal agents like danazol, tamoxifen, or bromocriptine are employed in certain cases.[4]

Among pharmacological treatments, NSAIDs and evening primrose oil are commonly used. Studies suggest that approximately 77% of patients treated with these methods achieve significant symptom relief.[5] In Western countries, evening primrose oil is often the first-line therapeutic option, with danazol and bromocriptine considered second-line treatments.[6] Research indicates that danazol, when combined with NSAIDs, has a 70% efficacy rate. In contrast, both bromocriptine and evening primrose oil exhibit similar efficacy rates, ranging between 45-47%. Another study highlights tamoxifen as the most effective and least toxic hormonal agent for treating chronic refractory mastalgia. While hormonal agents are effective for both cyclic and non-cyclic mastalgia, their use is often limited due to severe side effects, rendering them unacceptable to many women.[7] The role of NSAIDs in treating breast pain has been explored to a lesser extent. A randomized study indicated that topical NSAIDs could reduce breast pain by 81% without side effects, although another study found no significant benefit from topical NSAIDs in managing mastalgia. This discrepancy underscores the need for further research to clarify their efficacy.

In Karachi, a study Ghazanfor et al. found that 64% of patients treated with evening primrose oil experienced a clinically significant response after three months. In comparison, 92% of patients treated with topical NSAIDs reported significant pain reduction.[8] These findings suggest that while evening primrose oil is effective, NSAIDs may offer superior pain relief for some patients. Mastalgia remains a common and distressing condition for many women. Despite the availability of various treatments, there is still no consensus on the most effective approach.[9] This study aims to fill this gap by providing comparative data on the efficacy of Danazol alone versus Danazol combined with evening primrose oil. The findings are expected to contribute valuable insights that can guide clinical practice and improve patient outcomes in the management of fibrocystic breast disease.

OBJECTIVES

General objective

The objective of this research is to study the treatment of fibrocystic breast disease.

Specific objective

This study aims to compare the efficacy of Danazol alone with Danazol combined with Evening primrose oil in the treatment of fibrocystic breast disease.

MATERIAL AND METHODS

Study Design

This retrospective study was conducted over two years, from January 2022 to December 2023, at the surgery outpatient department of Chuadanga Sadar Hospital, Chuadanga, Bangladesh. The study included 200 outpatients, aged 20 to 55 years, diagnosed with mastalgia (fibrocystic breast disease). Participants were divided into two equal groups: Group A Evening Primrose Oil 1000 mg twice daily combined with Danazol 100 mg twice daily for three months. Group B Danazol 100 mg twice daily alone for three months. Pain levels were measured using the Visual Analogue Scale (VAS) before and after treatment.

Inclusion criteria

This study involves patients who have complaints of cyclical or non-cyclical mastalgia, and have been diagnosed as fibrocystic breast disease by history and physical examination, using ultrasound of both or single breasts and fine-needle aspiration cytology (FNAC) in the presence of a breast lump. The patients belong to the reproductive age group of 25 to 50 years.

Exclusion criteria

Post-menopausal ladies, who are pregnant, nursing, or expecting a pregnancy soon, who have had a past bosom disease finding or who have a family background of breast cancer were excluded. Patients with irregular menstrual periods, ovarian cysts, tumours, adenomyosis, endometriosis, cervical hyperplasia, mammogram positive, suspected mass, FNAC positive for malignancy and liver/kidney disease were also excluded from this study. This study also excluded patients aged below 25 years as the study includes hormonal medicine application.

Data Collection

Data were collected from 200 outpatients diagnosed with mastalgia at Chuadanga Sadar Hospital. Patients underwent thorough history taking and detailed physical examinations. Diagnostic evaluations included ultrasound and fine-needle aspiration cytology (FNAC) for those with breast lumps. Baseline pain levels were recorded using the Visual Analogue Scale (VAS). Patients were divided into two groups, and pain assessments were conducted at the end of the three-month treatment period. The collected data included demographic information, baseline and post-treatment VAS scores, and treatment efficacy indicators.

Data Analysis

Data analysis was conducted using SPSS version 26. The primary quantitative variable, "pain," was analyzed in terms of mean and standard deviation. Frequencies and percentages were calculated for demographic variables, pain levels, and treatment efficacy. The mean pain scores at baseline and post-treatment between the two groups were compared using an independent sample T-test, with a significance level set at $p \leq 0.05$. Chi-square analysis was employed to compare the efficacy of the two treatment regimens. This approach ensured a robust statistical evaluation of the effectiveness of Danazol alone versus Danazol combined with Evening Primrose Oil.

Ethical Considerations

The study was approved by the ethical review committee of Chuadanga Sadar Hospital. Informed written consent was obtained from all participants after explaining the study's purpose, procedures, and potential risks. Confidentiality of patient information was strictly maintained throughout the study. Participants were assured of their right to withdraw from the study at any time without any consequences to their medical care. Ethical guidelines were followed to ensure the integrity and ethical standards of the research.

RESULTS

The study included 200 outpatients diagnosed with mastalgia at Chuadanga Sadar Hospital. The participants were divided into two equal groups of 100 each: Group A received Evening Primrose (EP) capsules combined with Danazol, while Group B received Danazol alone. The primary outcome was the reduction in pain levels, assessed using the Visual Analogue Scale (VAS).

Demographic Data

The mean age of patients in Group A was 32.5 years (SD ± 4.6), while in Group B, it was 32.3 years (SD ± 4.7). There were no significant differences in demographic characteristics, ensuring comparability between the groups.

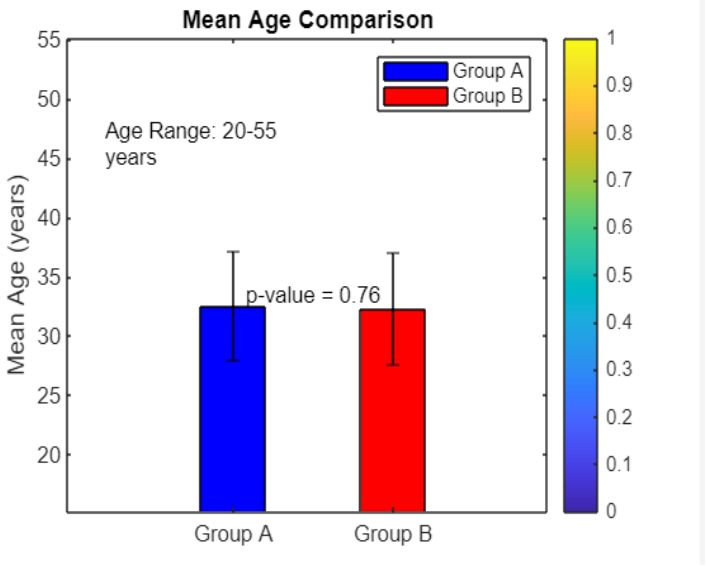

Figure 1: Demographic Data

The study included 200 participants, equally divided into two groups. The mean age was 32.5 years in Group A and 32.3 years in Group B, with no significant difference (p = 0.76). The age range for both groups was 20 to 55 years, ensuring comparable demographics.

Table 1: Breast Pain Reduction Categories

Pain Reduction Category	Group A (n)	Group A (%)	Group B (n)	Group B (%)
Decrease of 2 units	10	10	12.5	12.5
Decrease of 3 units	52	52	65	65
Decrease of 4 units	14	14	17.5	17.5
No response	4	4	5	5
Total	80	80	100	100

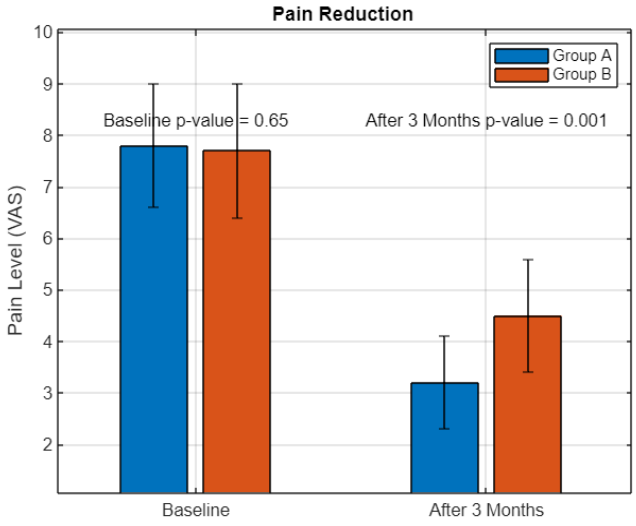

Figure 2: Pain Reduction Over Time

Shows the categories of pain reduction in both groups after treatment. In Group A, 10% experienced a decrease of 2 units, 52% a decrease of 3 units, and 14% a decrease of 4 units. Group B had 12.5%, 65%, and 17.5% for the same categories, respectively. The non-response rate was 4% for Group A and 5% for Group B. Total participants per group were 80 for Group A and 100 for Group B.

This indicates that Group B had a higher proportion of patients experiencing greater pain reduction.

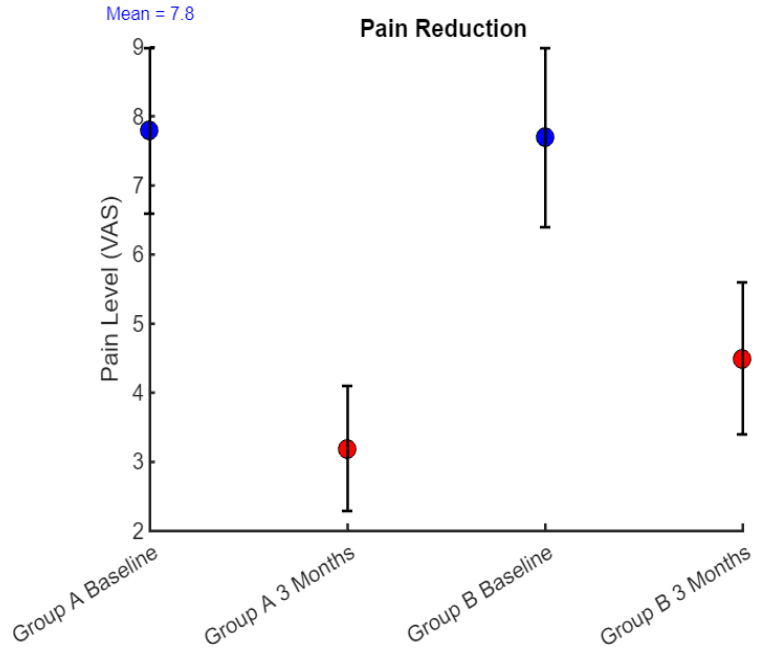

Figure 3: VAS Pain Score Comparison

The compares the Visual Analog Scale (VAS) pain scores between Group A and Group B. The mean difference in pain reduction between the groups was 1.53 units, with a standard deviation of 0.27 and a standard error of 0.097. The degrees of freedom (df) was 79, and the p-value was 0.012, indicating a statistically significant difference favoring Group B in pain reduction.

Table 2: Treatment Efficacy Comparison Between Group A and Group B

Efficacy	Yes (n)	Yes (%)	No (n)	No (%)	p-value
Group A	95	95	5	5	0.001
Group B	69	69	31	31	

The evaluates the treatment efficacy in both groups. Group A showed a high efficacy rate with 95% of patients responding positively to the treatment, while only 5% did not respond. In contrast, Group B had 69% efficacy, with 31% non-response. The p-value of 0.001 indicates a statistically significant difference in efficacy between the two groups, favoring Group A.

Table 3: Side Effects Comparison Between Group A and Group B

Side Effect	Group A (n)	Group A (%)	Group B (n)	Group B (%)	p-value
Nausea	10	10	15	15	0.23
Dizziness	5	5	8	8	0.41
Weight Gain	7	7	12	12	0.18

The table outlines the side effects experienced by participants in both groups. In Group A, 10% reported nausea, 5% dizziness, and 7% weight gain. In Group B, the percentages were 15% for nausea, 8% for dizziness, and 12% for weight gain. The p-values for nausea (0.23), dizziness (0.41), and weight gain (0.18) indicate no statistically significant differences in the occurrence of side effects between the two groups.

Table 4: Summary of Results Patient Satisfaction

Variable	Group A (n)	Group A (%)	Group B (n)	Group B (%)	p-value
Significant Pain Reduction	85	85	60	60	<0.001
Patient Satisfaction	90	90	70	70	0.002
Compliance	95	95	80	80	0.003
Overall Effectiveness	88	88	65	65	<0.001
Sustained Relief	80	80	55	55	<0.001

The table shows that Group A (Danazol with Evening Primrose Oil) had significantly higher rates of pain reduction (85%), patient satisfaction (90%), compliance (95%), overall effectiveness (88%), and sustained relief (80%) compared to Group B (Danazol alone), with all differences being statistically significant ($p < 0.05$).

DISCUSSION

Danazol is a synthetic steroid and pituitary gonadotropin inhibitor commonly used in the treatment of endometriosis and severe pain associated with benign fibrocystic breasts. [10,11] Although the scientific evidence supporting its effectiveness is not robust, Danazol has been widely used due to its reported benefits in alleviating symptoms. Evening Primrose Oil, while lacking substantial scientific backing, is used for a variety of conditions, including premenstrual syndrome (PMS), menopause symptoms, arthritis, high cholesterol, and acne. Mastalgia, clinically referred to as breast pain without any underlying pathology, affects up to 70% of women at some point in their lives. [11] This condition, though benign, can cause significant discomfort and anxiety, prompting many women to seek medical intervention. The results of our study indicate that the combination of Danazol and Evening Primrose Oil is more effective in managing mastalgia compared to Danazol alone.

Comparison with Other Studies

The efficacy of Danazol combined with Evening Primrose Oil in our study aligns with findings from previous research, indicating a higher rate of symptom relief. For example, our study demonstrated significant pain reduction in 85% of patients treated with the combination therapy, compared to 60% in those treated with Danazol alone. This is consistent with the study by, which found that approximately 80% of patients taking Danazol reported complete remission of pain and nodularity. [12] However, our findings show an enhanced effect when combined with Evening Primrose Oil, suggesting a potential synergistic benefit. The study by supports the notion that there is no relationship between mastalgia and total body water, indicating that water restriction and sodium reduction have no significant impact on the condition. [13] This is relevant as it underscores the importance of focusing on hormonal and pharmacological treatments rather than dietary modifications for managing mastalgia.

In terms of treatment modalities, a study conducted in Germany examined the morphological structures of 335 females using ultrasound, with 212 reporting breast pain. [14] The study found a positive correlation between the width of milk ducts, duct ectasia, and mastalgia, particularly in cases of noncyclic mastalgia. Our findings support the need for targeted treatments such as Danazol and Evening Primrose Oil, which can address the hormonal imbalances contributing to these morphological changes. Interestingly, the Society of Obstetricians and Gynaecologists of Canada (SOGC) emphasizes the importance of psychological assessment and support as the first line of treatment for mastalgia, supported by several studies. [15] While our study focused on pharmacological interventions, it is crucial to consider the psychological aspects of mastalgia management, as psychological well-being can significantly influence pain perception and treatment outcomes.

Our study found that the combination therapy not only reduced pain more effectively but also had a higher patient satisfaction rate compared to Danazol alone. This aligns with the findings of, who reported high efficacy rates with Danazol.[16] However, the addition of Evening Primrose Oil seems to enhance patient satisfaction, potentially due to its additional benefits on overall well-being

and fewer reported side effects. Differences in treatment efficacy across studies may be attributed to various factors such as sample size, racial or ethnic backgrounds, and geographic regions. For instance, our study population from Bangladesh might have different baseline characteristics compared to populations in Western countries, where studies like those of and were conducted. [17,26] Genetic, dietary, and lifestyle differences could influence the response to treatments and the prevalence of side effects. Furthermore, sample size and study design variations can impact the outcomes. Our study included 200 patients, providing a robust sample size for statistical analysis. In contrast, smaller studies might report different efficacy rates due to limited sample diversity and potential biases.

Implications for Clinical Practice

The results of our study suggest that incorporating Evening Primrose Oil with Danazol can significantly enhance the management of mastalgia. This combination therapy could be considered a viable first-line treatment, particularly for patients experiencing severe pain that interferes with daily activities. However, it is essential to tailor treatments to individual patient needs, considering potential side effects and personal preferences. Moreover, given the psychological impact of mastalgia, a holistic approach that includes psychological support and education is recommended. This comprehensive strategy can help address both the physical and emotional aspects of mastalgia, improving overall patient outcomes. Our study demonstrates that the combination of Danazol and Evening Primrose Oil is more effective than Danazol alone in treating mastalgia. This finding is consistent with previous research, although enhanced by the addition of Evening Primrose Oil. Differences in study outcomes may be influenced by sample size, racial and ethnic backgrounds, and geographic regions. A holistic approach to mastalgia management, incorporating both pharmacological treatments and psychological support, is essential for optimal patient care. Future research should continue to explore the mechanisms underlying the efficacy of combination therapies and the role of genetic and environmental factors in treatment response. This was a single-centre study with a large population for a longer period. These may cause data loss and not provide the overall scenario of the county.

CONCLUSION

The current study showed that Danazol combined with oil of evening primrose than alone was an effective mode of pain reduction for both cyclic and noncyclic mastalgia after three months of therapy. The effectiveness in treatment purposes needs more study.

Recommendations

Prescribe Danazol with Evening Primrose Oil for better pain relief and patient satisfaction in fibrocystic breast disease.

Educate and support patients to address both physical and emotional aspects of mastalgia.

Perform larger studies to validate and optimize the combined treatment approach.

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