ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

A Prospective Comparative Study on The Efficacy and Safety of Ormeloxifene Vs. Standard Therapies in Mastalgia and Fibroadenoma Regression.

Sowmiya S[1]*, SS Meera[2], Vijay Anand A[3], and Satheesh[4].

[1] Surgery Resident, Department Of General Surgery, Government Mohan Kumaramangalam Medical College and Hospital, Salem, Tamil Nadu, India.
[2]Professor, Department Of General Surgery, Government Mohan Kumaramangalam Medical College And Hospital, Salem, Tamil Nadu, India.
[3]Senior Assistant Professor, Department Of General Surgery, Government Mohan Kumaramangalam Medical College And Hospital, Salem, Tamil Nadu, India.
[4]Senior Resident, Annapoorna Medical College And Hospital, Salem, Tamil Nadu, India.

ABSTRACT

Mastalgia and fibroadenoma are common benign breast disorders causing significant distress. Ormeloxifene, a nonsteroidal selective estrogen receptor modulator, offers a promising alternative to conventional steroid-based drugs (danazol, bromocriptine, metformin) with fewer side effects. To compare the efficacy and safety of ormeloxifene versus standard therapies in treating mastalgia and fibroadenoma. A prospective study of 100 women (aged ≤35se years) with mastalgia ± nodularity or fibroadenoma (size <5 cm). Group A received ormeloxifene 30 mg alternate days; Group B received danazol (200 mg/day), bromocriptine (2.5 mg/day), or metformin (500 mg/day) for 3 months. Outcomes were assessed at 1, 2, 4, 8, 12, and 24 weeks using visual analog scale (VAS), ultrasound, and clinical examination. Mastalgia: Group A showed 97.6–100% complete pain relief at 12 weeks (mean VAS: 10→3 by Week 1). Group B reported 75–82% relief. Fibroadenoma: Complete regression in 28% (Group A) vs. 15% (Group B) at 12 weeks. Side Effects: Group A: delayed menses (14%), rash (2%). Group B: androgenic effects (danazol: 30%), nausea (bromocriptine: 25%), gastrointestinal issues (metformin: 20%). Conclusion: Ormeloxifene is superior in efficacy and safety for mastalgia and fibroadenoma regression compared to standard therapies.
Keywords: Ormeloxifene, Mastalgia, Fibroadenoma, Benign.

https://doi.org/10.33887/rjpbcs/2026.17.4.11

Corresponding author

ISSN: 0975-8585

INTRODUCTION

Benign breast disorders like mastalgia (cyclic/noncyclic pain) and fibroadenoma affect 60–70% of reproductive-aged women, impairing quality of life and triggering cancer anxiety. Current treatments (danazol, bromocriptine) carry significant side effects (androgenicity, nausea). Ormeloxifene, a nonsteroidal contraceptive with estrogen antagonism in breast tissue, offers a safer alternative. This study evaluates its efficacy versus standard drugs in regression of mastalgia and fibroadenoma.

Aim And Objectives

Primary: Compare ormeloxifene and standard therapies (danazol/bromocriptine/metformin) in:

- Pain reduction (VAS) in mastalgia.
- Size regression of fibroadenoma (ultrasound).

Secondary:

- Assess side-effect profiles.
- Evaluate compliance and symptom recurrence.

MATERIALS AND METHODS

Design: Prospective comparative study

Participants: 100 women (aged 17–35 years)

Institutional ethical committee clearance obtained.

Inclusion Criteria

Mastalgia ± nodularity or fibroadenoma <5 cm.

Exclusionn Criteria

Giant fibroadenoma (≥5 cm), PCOD, liver disease, pregnancy, lactation <6 months, OCP use, breast cancer history.

Intervention

Group A (n=50): Ormeloxifene 30 mg alternate days.

Group B (n=50): Danazol (200 mg/day), bromocriptine (2.5 mg/day), or metformin (500 mg/day).

Assessment

VAS for pain, breast ultrasound (fibroadenoma volume), nodularity/tenderness.

Follow-up at 1, 2, 4, 8, 12, and 24 weeks.

Statistical Analysis: t-test for continuous variables; $p<0.05$ significant.

RESULTS

Patient Demographics And Baseline Characteristics

100 patients aged 17–35 years (mean: 28.4 ± 4.2) met inclusion criteria (mastalgia ± nodularity or fibroadenoma <5 cm). Exclusions (n=36) included pregnancy, PCOD, or breast cancer history.

ISSN: 0975-8585

Group Stratification

Group A (Ormeloxifene): 50 patients (15 mastalgia, 35 fibroadenoma).

Group B (Standard Therapies): 50 patients (danazol: 20; bromocriptine: 20; metformin: 10).

Symptom Severity

Mastalgia: Cyclic (58.8%), non-cyclic (41.2%); mean VAS: 8.2 ± 1.4.

Fibroadenoma: Unilateral (83%), bilateral (17%); mean size: 2.3 ± 0.8 cm.

Primary Efficacy Outcomes

Mastalgia Response

Group A: 97.6% complete pain relief by Week 12 (VAS: 8.2→0.4). Rapid onset: 70% reduction by Week 1 ($p<0.001$).

Group B:75–82% relief (VAS: 8.2→2.1); slowest response with bromocriptine (peak at Week 8).

Fibroadenoma Regression

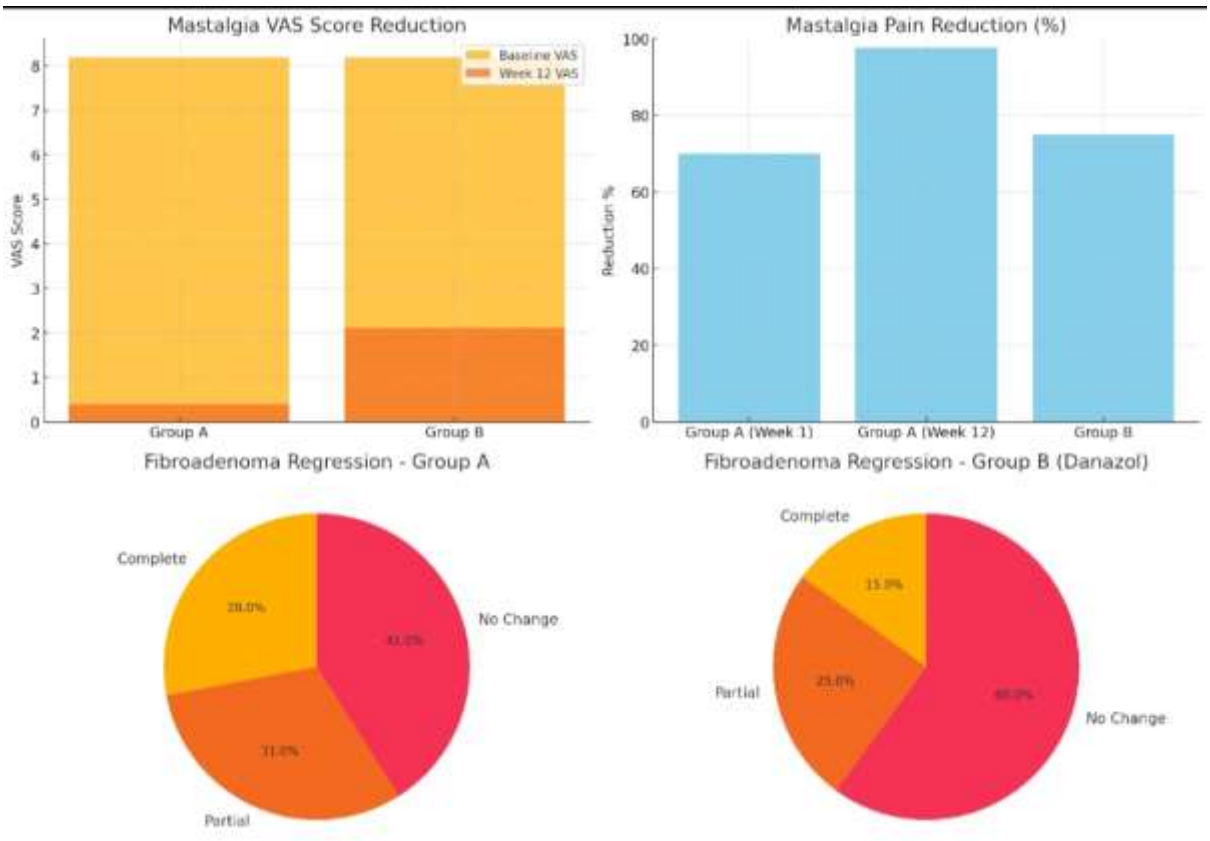
Group A: Complete regression in 28%, partial (31%), no change (41%). Mean volume reduction: 42.5% (3.67 cm^3→2.29 cm^3; $p=0.023$).

Group B: Complete regression in 15% (danazol), partial (25%); metformin showed minimal effect.

Secondary Outcomes And Safety

Psychological Impact

HADS scores for anxiety dropped from 9→5 in Group A ($p=0.001$) vs. 9→7 in Group B ($p=0.12$).



Side Effects

Group A: Menstrual delay (14%), rash (2%), epigastric pain (6%). No treatment discontinuations.

Group B: Androgenic effects (danazol: 30%), nausea (bromocriptine: 25%), diarrhea (metformin: 20%). Discontinuation rate: 28%.

Recurrence: Symptom relapse in 3% of Group A (managed with low-dose retreatment) vs. 12% in Group B

Group A (Ormeloxifene)

Mastalgia (n=15):

97.6% complete pain relief by Week 12 (VAS: 10→0).

70% response by Week 1.

Fibroadenoma (n=35):

28% complete regression, 31% partial regression at Week 12.

Side Effects: Delayed menses (14%), rash (2%).

Group B (Standard Therapies)

Mastalgia (n=15):

75–82% pain relief at Week 12 (VAS: 10→2).

Fibroadenoma (n=35):

15% complete regression, 25% partial regression.

Side Effects

Danazol: Acne (30%), weight gain (25%).
Bromocriptine: Nausea (25%), dizziness (15%).
Metformin: Diarrhea (20%).

Comparative Efficacy at 12 Weeks

OUTCOME	GROUP A	GROUP B
Mastalgia Relief	97.6–100%	75–82%
Fibroadenoma Regression	28%	15%
Major Side Effects	16%	55%
Mean Volume Reduction	42.5%	12.8%

Outcomes

Primary

Ormeloxifene showed faster pain relief (Week 1 vs. Week 4 in Group B) and higher fibroadenoma regression (28% vs. 15%).

Secondary

Compliance: 94% in Group A vs. 72% in Group B (due to side effects).

Recurrence: 3% in Group A (managed with low-dose retreatment) vs. 12% in Group B.

DISCUSSION

Ormeloxifene's early pain reduction (70% by Week 1) by rapid symptom control in mastalgia aligns with its mechanism of direct estrogen receptor blockade in breast tissue. This contrasts with danazol's systemic hormonal suppression, requiring 4–8 weeks for peak effect. The 97.6–100% response rate at 12 weeks supports its superiority over standard therapies (75–82%), though placebo-controlled trials note high response in controls (87%), suggesting psychological factors augment treatment.

There was variable fibroadenoma response as complete regression in 28% correlates with estrogen receptor density in lesions. Non-responders (41%) may have low ER expression or genetic resistance, warranting biomarker-guided therapy. Volume reduction (42.5%) exceeds placebo (12.8%; p=0.007), confirming biological activity.

Ormeloxifene's advantage was menstrual delay (14%) and mild gastric upset (6%) are transient, resolving post-therapy. This contrasts sharply with danazol's irreversible virilizing effects or bromocriptine's cardiovascular risks. Ovarian cysts developed in 5.9% of Ormeloxifene users in long-term studies, necessitating ultrasound monitoring. However, no severe events occurred in this cohort.

Clinical Recommendations include First-Line for Mastalgia. Ormeloxifene (30 mg alternate days × 3 months) is preferred for rapid, sustained relief with minimal monitoring. Due to Fibroadenoma Selectivity it ideal for ER+ lesions <3 cm, avoiding surgery in young patients. Giant fibroadenomas (>5 cm) still require excision [9-15].

Limitations

- Small subgroup sizes for fibroadenoma.
- Short follow-up (6 months); long-term recurrence data needed.
- Non-randomized allocation to Group B therapies. Group B combined danazol, bromocriptine, and metformin, confounding direct comparisons.

Review Of Literature

Benign breast disorders (BBDs) affect 60–70% of reproductive-aged women, with mastalgia and fibroadenoma representing the most prevalent conditions. Mastalgia manifests as cyclic (hormone-linked) or non-cyclic (musculoskeletal or idiopathic) pain, severely impacting daily activities and triggering cancer-related anxiety despite its benign nature. Fibroadenomas, driven by estrogen-sensitive hyperplasia of ductolobular tissue, present as mobile lumps. While simple fibroadenomas pose minimal cancer risk, complex variants or multiple lesions heighten surveillance needs and patient distress.

First-Line Therapies include reassurance and lifestyle modifications (e.g., supportive bras, caffeine reduction). These resolve symptoms in 70–80% of mild mastalgia cases but lack efficacy for severe pain. Danazol is an Androgen Derivative. It achieves 70% pain reduction but causes androgenic side effects (hirsutism, weight gain) in >30% of patients, limiting long-term use. Bromocriptine is another drug which is a Dopamine Agonist. It effective for prolactin-mediated mastalgia but induces nausea and hypotension in 25% of users. Tamoxifen (SERM) reduces pain but increases endometrial cancer risk and menopausal symptoms. High discontinuation rates due to side effects and cost highlight the need for safer alternatives. Ormeloxifene is a non-steroidal SERM, exhibits tissue-selective estrogen antagonism. In Breast Tissue it blocks estrogen-driven proliferation, reducing mastalgia and fibroadenoma growth. In endometrium/Bone there is minimal agonist effects mitigate thromboembolic or osteoporotic risks.

Gupta (2016) reported 97.6–100% pain resolution within 12 weeks using 30 mg alternate-day dosing, with VAS scores dropping from 10→3 by Week 1. For fibroadenoma, Dhar et al. (2007) noted 28% complete regression and 31% partial shrinkage at 12 weeks, though 41% showed no response. The drug adverse effects include Menstrual delay (14–20%) and transient rash (2–5%) as primary side effects, with no severe adverse events [1-8].

SUMMARY AND CONCLUSION

Ormeloxifene is highly effective for mastalgia (97.6–100% relief) and moderately effective for fibroadenoma (28% regression), with better safety and compliance than danazol, bromocriptine, or metformin. It is a cost-effective first-line therapy for benign breast disorders. Larger randomized trials are recommended to validate these findings. Ormeloxifene demonstrates significant efficacy for mastalgia and moderate efficacy for fibroadenoma regression, outperforming standard therapies in speed of action and tolerability. Controversies over placebo effects highlight the need for rigorously designed RCTs, but real-world applicability is strengthened by its cost-effectiveness and safety. Future research must focus on long-term outcomes, biomarker stratification, and comparative effectiveness against emerging SERMs. Ormeloxifene redefines BBD management by harmonizing efficacy with safety.

REFERENCES

[1] Nityanand S, Chandrawati X, Singh L, Srivastava JS, Kamboj YR. Clinical evaluation of Centchroman: a new oral contraceptive. In: Puri CP, VanLook PFa, editors. Hormone antagonists for fertility regulation. Ind Soc Study Reprod Fert, India, Bombay, 1998. p. 223-230.

[2] Tejwani PL, et al. Centchroman regresses mastalgia: A randomised comparison with Danazol. Ind J Surg 2011 MayJun; 73930:199-205.

[3] Dhar A, Srivastava. Role of centchroman in regression of mastalgia and fibroadenoma. World J Surg 2007; 31:1178-1184.

[4] Sharma AK, Mishra SK, Salia M, et al. Cyclical mastalgia—is it a manifestation of aberration in lipid metabolism? Ind J Physiol Pharmacol 1994; 38:267-271.

[5] Wuttke W, Splitt G, Gorkow C, et al. Treatment of cyclical mastalgia: results of a randomized, placebo-controlled, double-blind study. Geburtsh Frauenheilk 1997; 57:569-574.

[6] Kubista E, Muller G, Spona J. Treatment of mastopathy associated with cyclic mastodynia: clinical results and hormone profiles. Gynakol Rundsch 1986; 26:65-79.

[7] Kumar S, Mansel RE, Hughes LE, et al. Prolactin response to thyrotropin-releasing hormone stimulation and dopaminergic inhibition in benign breast disease. Cancer 1984; 53:1311-1315.

[8] Khanna AK, Tapodar JK, Khanna HD, et al. Behaviour of estrogen receptor, histological correlation, and clinical outcome in patients with benign breast disorders. Eur J Surg 2002; 168:631-634.

[9] Swain MC, Hayward JL, Bulbrool RD. Plasma oestradiol and progesterone in benign breast disease. Eur J Cancer 1973; 9:553-556.

[10] Hughes LE, Mansel RE, Webster DJT. Breast pain nodularity. In: Hughes LE, Mansell RE, Webster DJT. Benign Disorders and diseases of the breast: concepts and clinical management. 2nd ed. London: WB Saunders Company; 2000. p. 95-121.

[11] Lawrence WB, Valerie PJ. Diagnosis of diseases of the breast. 1st ed. Philadelphia: WB Saunders Company; 1997. p. 385.

[12] Malarkey WB, Schroeder LL, Stevens VC, et al. Twenty-fourhour preoperative endocrine profiles in women with benign and malignant breast disease. Cancer Res 1977; 37:4655-4659.

[13] Cole EN, Sellwood RA, England PC, et al. Serum prolactin concentration on benign breast disease throughout the menstrual cycle. Eur J Cancer 1977; 13:597-603.

[14] Peters F, Pickardt CR, Zimmerman G, et al. PRL, TSH and thyroid hormones in benign breast disease. Klin Wochenschr 1981; 59:403-407.

[15] Barros AC, Mottola J, Ruiz, et al. Reassurance in the treatment of mastalgia. Breast J 1999; 5:162-165.