



The Effect of Centchroman on Mastalgia

Dr.Gogineni Jahnavi¹, Dr.Ganesh Guru²

¹Department of General Surgery, Sree Balaji Medical College and Hospital, Chennai

^{2,1}Department of General Surgery, Sree Balaji Medical College and Hospital, Chennai

(Received: 14 April 2024

Revised: 1 May 2024

Accepted: 18 June 2024)

KEYWORDS

Centchroman,
Mastalgia,
Ormeloxifene,
Visual Analogue
Scale, vitamin E.

ABSTRACT:

Mastalgia, a prevalent issue among women aged 20-40, affects quality of life. Although 2% to 7% of those with mastalgia are diagnosed with breast cancer, most cases involve benign conditions. Effective management typically begins with nonmedical interventions such as reassurance and supportive bras, which alleviate concerns for 75%-80% of patients. For those needing medical treatment, various drugs are used, including Centchroman (Ormeloxifene), a selective estrogen receptor modulator (SERM) with minimal side effects. This study assesses the efficacy of Ormeloxifene in managing mastalgia using the Visual Analogue Scale (VAS) to measure pain regression and predict healing time. The study's objectives include analyzing the demographic profile of mastalgia patients, applying 'triple assessment' (Clinical Breast Examination, Breast Imaging, and Fine Needle Aspiration Cytology) for diagnosis, and comparing the effectiveness of vitamin E and Centchroman in improving quality of life. Conducted over nine months at MR Bangur Hospital, Kolkata, the study involved 104 women aged 18-50 years. Participants were randomly assigned to receive either Centchroman or vitamin E and recorded demographic data, breast pain characteristics, and treatment outcomes using the VAS score. Results indicated a higher prevalence of mastalgia among women aged 20 to 39, with significant demographic and socioeconomic factors influencing its occurrence. Both Centchroman and vitamin E significantly reduced pain scores, with Centchroman showing greater efficacy and cost-effectiveness. The study underscores the need for further research to validate these findings and optimize mastalgia management protocols, highlighting Centchroman as a valuable treatment option with minimal side effects.

Background

Breast pain, or mastalgia, is a prevalent complaint among women aged 20 to 40 who visit surgical outpatient departments (OPD), as first described by Cooper et al [1]. This condition affects a substantial portion of the female population, with approximately 70% of women experiencing breast pain at some point in their lives, many of whom endure moderate to severe pain that significantly impacts their quality of life [2]. A considerable number of these women report breast pain out of concern that it may indicate breast cancer. The high level of awareness about breast cancer, coupled with the fear that mastalgia could be a symptom of this disease, drives many women to seek medical attention [3]. Statistics show that 2% to 7% of women presenting with mastalgia will indeed be diagnosed with breast cancer [4]. Beyond the fear of cancer, mastalgia can

severely disrupt daily activities, leading to significant physical and psychosocial distress for those affected.

Mastalgia is categorized under the Aberrations of Normal Development and Involution (ANDI) classification of benign breast diseases. According to this classification, mastalgia is considered physiological but is classified as a disease when it necessitates more than mere reassurance for management [5,6]. Effective management of mastalgia requires a thorough assessment to exclude other potential pathologies. Nonmedical interventions are often the first line of management and include reassurance and the use of well-fitted external breast supports, such as sports bras. These measures are effective in alleviating the concerns of 75% to 80% of patients. For those requiring medical treatment, several drugs have been utilized, including danazol, bromocriptine, tamoxifen, evening primrose oil,



topical nonsteroidal anti-inflammatory drugs, and more recently, centchroman (Ormeloxifene) [7]. Centchroman, known chemically as C30H55NO3 and sold under brand names such as Sevista and Saheli, is a non-steroidal selective estrogen receptor modulator (SERM). It exhibits antagonistic effects on estrogen receptors in breast tissue while having agonistic effects on cardiac and skeletal tissues. Developed by the Central Drug Research Institute in Lucknow, India, centchroman was introduced into the National Family Welfare Programme in 1995. It is an oral contraceptive that offers the benefit of less frequent administration. In lactating women, centchroman is excreted in breast milk in quantities that are considered unlikely to harm nursing infants. Unlike steroidal oral contraceptives, centchroman is free from common side effects such as nausea, vomiting, weight gain, and dizziness. It does not delay the return of fertility and maintains normal ovulatory cycles, thanks to its low dose and administration schedule of two to three times a week, which minimizes any impact on the hypothalamic–pituitary–ovarian axis. However, it can prolong menstrual period duration in about 10% of cycles and may cause complications in a few cases of polycystic ovarian disease [8]. The development of centchroman represents a significant advancement in the management of mastalgia. Its dual role as an effective contraceptive and a treatment for mastalgia, with minimal side effects, makes it a valuable option for many women. The integration of centchroman into the National Family Welfare Programme underscores its importance and utility in public health. As with any medication, it is crucial for healthcare providers to weigh the benefits against potential side effects and to consider each patient's unique medical history and needs when recommending treatment.

The aim of the present study is to assess the effect of Ormeloxifene in the regression of mastalgia using the VAS scale and to predict the time for disease healing with its use. The objectives include studying the demographic profile of patients with cyclical and noncyclical mastalgia, establishing the role of ‘triple assessment’ (Clinical Breast Examination, Breast Imaging via ultrasonography, and Breast Pathology via fine needle aspiration cytology) for diagnosis, and understanding the age distribution of patients with mastalgia and pathological diagnoses. Additionally, the

study aims to evaluate the effectiveness of vitamin E and centchroman in managing both cyclical and non-cyclical mastalgia and improving quality of life.

Materials and Methods

Study Design, Area and Period

The research employs a hospital-based prospective randomized study design, ensuring rigorous and systematic data collection and analysis. Conducted in the Department of General Surgery at Sree Balaji Medical College & Hospital, Chennai, Tamil Nadu, the study is situated in a reputable medical institution providing a robust framework for clinical research. The study spans a period of 9 months, allowing sufficient time to observe and assess the effects of the interventions on the participants and to gather comprehensive data for analysis.

Study Population

The target population includes patients attending the Department of General Surgery at Sree Balaji Medical College and Hospital's outpatient department with complaints of breast pain during the study duration.

Sample Size Calculation and Justification

The sample size was calculated using Epi Info (TM) 7.2.2.2, a software developed by the Centers for Disease Control and Prevention (CDC). According to a study by Bansal et al., [9] at the beginning of treatment, Grades 3, 4, and 5 nodularities were seen in 69.5% of cases. Therefore, for this study, $p = 0.695$. The formula used for sample size calculation is:

$$n = 4pq / (L^2)$$

Where,

n = Required sample size

$p = 0.695$ as per the study by Bansal et al. [9]

$q = 1 - p$

L = Loss % (Loss of information) = 13%

Calculation:

Here $p=0.695$, $q=1-p=0.305$, Loss% = 13%

$$4pq = 4 \times 0.695 \times 0.305 = 0.8479$$

$$L^2 = (0.695 \times 0.13)^2 = 0.0082$$



So, $n = 0.8479 / 0.0082 = 103.86 \sim 104$

Thus, 104 patients are required with a power of 87%. Patients were randomly selected from the OPD and assigned into two groups in a 1:1 ratio, resulting in 52 patients per group.

Sampling Techniques and Method of Study

The sampling techniques utilized in this study involved the random selection of patients using random numbers generated from Kevin Conroy's 5120 Random Numbers (RandomNumber.org, 2004). A total of 104 patients attending the Department of General Surgery at MR Bangur Hospital were included, and they were randomly allocated into two groups. One group comprising 52 patients will undergo treatment with Centchroman 30 mg thrice a week for twelve weeks, while the other group of 52 patients will receive vitamin E tablets 400 mg once daily for the same duration. The effectiveness of each treatment was evaluated using the Visual Analogue Scale (VAS), assessing pain severity and changes over the course of the study period.

Inclusion Criteria

The inclusion criteria for the study focus on specific characteristics to ensure a homogeneous patient population. Eligible participants are women aged between 18 and 50 years, presenting with mastalgia that scores 3 or higher on the Visual Analogue Scale (VAS) and persists for more than seven days per cycle. Both patients with mastalgia, whether it is accompanied by nodularity or not, are considered for the study. Additionally, all participants must provide informed consent to partake in the research, ensuring their voluntary and informed involvement.

Exclusion Criteria

The exclusion criteria for the study are designed to eliminate confounding factors that could impact the outcomes. Patients with radiological and/or cytological suspicion of breast cancer, those with histologically proven breast carcinoma, or individuals with a past or family history of breast carcinoma are excluded. Additionally, patients diagnosed with polycystic ovarian disease (PCOD), breast abscesses, or galactoceles are not eligible. Lactating mothers and patients currently taking oral contraceptive pills are also excluded, as are pregnant women. Other conditions that preclude participation

include musculoskeletal or chest wall pain, lipoma, and a history of chest trauma, ensuring a focus on primary mastalgia without complications from other potential sources of breast pain.

Method of Measurement of Outcome of Interest

At the initial visit, patients documented pain on a breast pain chart for one month. Patients with persistent breast pain satisfying inclusion criteria were recruited. After clinical assessment and breast imaging via ultrasound, patients were randomized into two groups using a sealed envelope technique. VAS scores were recorded before starting therapy. Centchroman group patients received 30 mg three times a week for 3 months, while the Vitamin E group received 400 mg once daily for 3 months. Patients maintained a "pain diary" to record daily pain and menses. The severity of mastalgia were assessed using the VAS score at the start of treatment, 4 weeks, 8 weeks, and 16 weeks.

Patient safeguards are paramount in this study to ensure ethical standards and patient welfare. Each participant received comprehensive information regarding the study, including its voluntary nature, potential benefits, drawbacks, the necessity of regular follow-up visits, and any financial implications. Written consent was obtained from every participant before they are enrolled in the study, ensuring their informed and voluntary participation. Patient confidentiality is rigorously upheld, with assurances provided that personal information will remain strictly confidential and will not be disclosed or used beyond the confines of the research study. Ethical considerations have been rigorously addressed and approved by the ethical committee, affirming that the study's materials, methods, and protocols adhere to established ethical guidelines and standards, safeguarding the rights and well-being of all participants involved.

Parameters Studied

The study encompasses a comprehensive set of parameters to thoroughly investigate the impact and management of mastalgia. The demographic profile of each patient was recorded, alongside marital status and details regarding age at the birth of the first child and parity. The study documents each patient's history of breastfeeding and menstrual profile, as well as their tobacco and alcohol consumption habits. A thorough



history of any breast disease and prior interventions was noted, along with the patient's drug and medication history. Key focus areas include the profile of mastalgia and other presenting complaints, with VAS scores assessed at the start and at 4, 12, and 24 weeks into the study. Clinical breast examinations were performed, complemented by ultrasound examinations of the breast, and breast FNAC or core needle biopsies was conducted if indicated. The study outlines the management plans provided to patients and monitor any side effects arising from these plans, ensuring a holistic evaluation of mastalgia management.

Study Tools

1. Triple assessment: Clinical breast examination (CBE), breast imaging (ultrasonography and mammography), and breast pathology (FNAC)

2. VAS for pain severity assessment: a 10 cm horizontal line where 0 indicates no pain and 10 indicates severe pain. Pain ≥ 3 on a VAS of 0 to 10 is considered significant and requires therapy.

Statistical Analysis

Statistical analysis was performed using Epi Info (TM) 7.2.2.2. Descriptive statistical analysis was used to calculate means and standard deviations. The Standard Normal Deviate (Z) test was used to compare proportions, and the Chi-square test was used to find associations. One Way Analysis of Variance (ANOVA) followed by post hoc Tukey's Test was used to compare mean values across groups. A p-value <0.05 was considered statistically significant.

Results

The study encompassed a detailed analysis of various demographic and clinical parameters among 104 female patients suffering from mastalgia. The majority of participants (72.2%) fell within the age range of 20 to 39 years, with a mean age of 32.48 years (SD=7.85) and a median of 31.5 years. This age group was notably more affected by mastalgia compared to other age brackets (Z=6.22; $p<0.0001$). Regarding religion, Hindus constituted 78.8% of the sample, significantly higher than Muslims at 21.2% (Z=8.20; $p<0.0001$), reflecting the hospital's location in a predominantly Hindu area. Kolkata residents comprised the largest portion (53.8%) among patients, surpassing other regions significantly

(Z=5.97; $p<0.0001$). Socio-economically, the upper lower class represented 43.3% of patients, higher than lower class (28.8%) and lower middle class (27.9%) groups (Z=7.28; $p<0.0001$). The majority were homemakers (67.3%), significantly more than laborers (32.7%) (Z=7.28; $p<0.0001$). Most patients were married (87.5%), with only 11.5% unmarried and 1.0% widowed (Z=10.89; $p<0.0001$) (Figure. 1f).

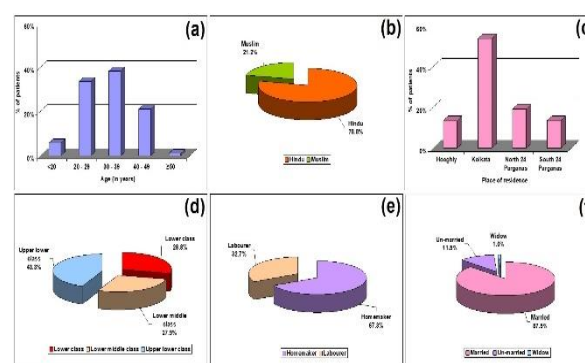


Figure 1. Example of a figure caption.

In terms of parity, 67.3% had 1-2 children, higher than those with 0 (15.4%) or ≥ 3 children (17.3%) (Z=6.22; $p<0.0001$), and the mean age at first childbirth was 22.37 years (SD=2.51), with 67.3% giving birth between ages 20-24 years (Z=6.85; $p<0.0001$). Breastfeeding was prevalent (95.6%) among patients (Z=13.01; $p<0.0001$), while history of oral contraceptive pill use was low (28.3%) (Z=6.22; $p<0.0001$). Most experienced menarche between ages 10-15 years (99.0%) (Z=13.85; $p<0.0001$), and 78.8% reported regular menstrual cycles (Z=8.20; $p<0.0001$) (Figure. 2f).

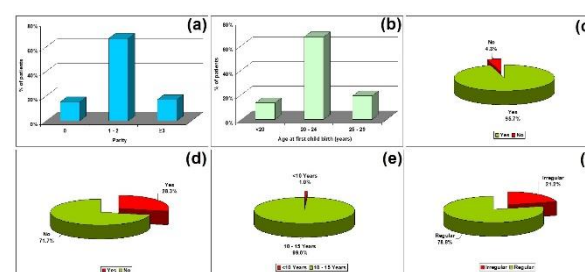


Figure 2. Example of a figure caption.

Daily caffeine intake was common (66.3%) (Z=4.52; $p<0.0001$), whereas family history of breast disease was rare (3.8%) (Z=13.01; $p<0.0001$). The vast majority had no co-morbidities (89.4%) (Z=11.03; $p<0.0001$). Non-



cyclical mastalgia prevailed (72.1%) over cyclical (27.9%) ($Z=6.22$; $p<0.0001$), mostly bilateral (56.7%) rather than unilateral (43.3%) ($Z=1.99$; $p=0.04$). Breast examination revealed mastalgia predominantly in the bilateral breasts (56.7%), with left-sided dominance (24.0%) but no significant difference from right-sided (19.2%) ($Z=0.86$; $p=0.38$).

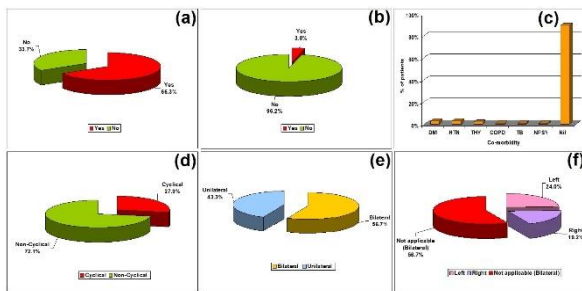


Figure 3. Example of a figure caption.

Most patients (63.5%) reported mastalgia persisting beyond 2 years ($Z=3.95$; $p<0.0001$), with few additional complaints like discharge (1.9%) or lump (9.6%) ($Z=11.17$; $p<0.0001$). Treatment with Centchroman (50.0%) and Vitamin E (50.0%) yielded comparable outcomes ($Z=0.01$; $p=0.99$), and most had no breast lumps (90.4%) ($Z=11.31$; $p<0.0001$), nodularity (51.0%) ($Z=4.58$; $p<0.0001$), nipple discharge (98.1%) ($Z=13.57$; $p<0.0001$), or axillary abnormalities (97.1%) ($Z=13.29$; $p<0.0001$). The majority had benign BIRAD scores (BIRAD-1: 51.9%; BIRAD-2: 42.3%) ($Z=5.96$; $p<0.0001$), predominantly fibroadenosis on ultrasound (41.3%) ($Z=6.97$; $p<0.0001$), and normal terminal duct lobular units (93.3%) ($Z=12.16$; $p<0.0001$).

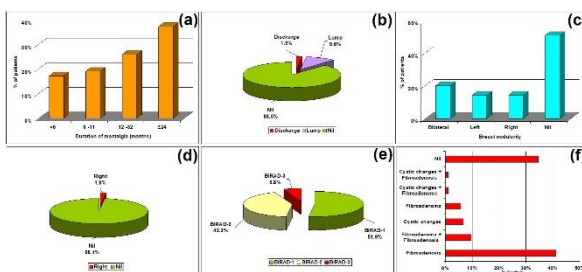


Figure 4. Example of a figure caption.

Pain scores (VAS) significantly decreased over time ($p<0.001$) and differed between Centchroman and Vitamin E treatments ($p=0.002$).

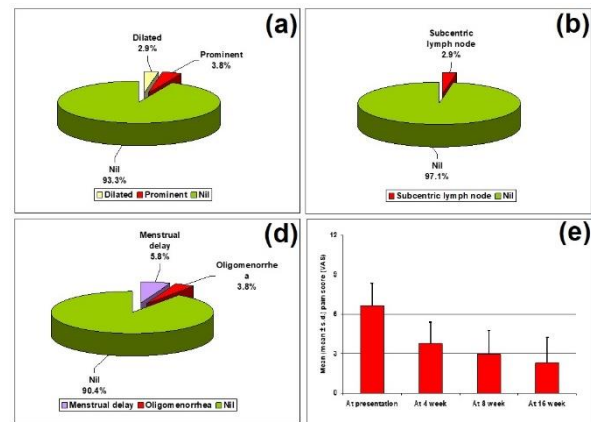


Figure 5. Example of a figure caption.

Thus, this comprehensive study provides detailed insights into the demographic and clinical profiles of patients with mastalgia, highlighting key characteristics and treatment outcomes.

Discussion

Mastalgia, commonly known as breast pain, is a prevalent condition among women, particularly those of reproductive age. This pain can range from mild discomfort to severe pain, significantly affecting quality of life. Understanding the demographic patterns, socioeconomic influences, clinical manifestations, diagnostic approaches, treatment modalities, and limitations associated with mastalgia is crucial for effective management and patient care. Mastalgia primarily affects women between the ages of 16 and 50, with a peak prevalence observed in the reproductive age group. Studies indicate that the average age of presentation for mastalgia is around 32.48 years, with a median age slightly lower at approximately 31.5 years. This demographic distribution underscores the hormonal influence on breast pain, as it coincides with the reproductive years characterized by significant hormonal fluctuations.

Research has consistently shown that mastalgia is more prevalent in younger women, aligning with the hormonal changes typical of this age group. For instance, the onset of cyclical mastalgia, which occurs 1-2 weeks before menstruation, is attributed to the hormonal shifts involving increased estrogen and decreased progesterone levels. These hormonal changes lead to breast tissue engorgement, causing pain that can radiate to the upper arm and axilla. In contrast, non-cyclical mastalgia lacks



a specific relationship with the menstrual cycle, suggesting other underlying mechanisms or triggers. Several studies have highlighted the age distribution of women experiencing mastalgia. For instance, Rathi reported a median age of 34.79 years among their study population, which included women aged 18-50 years. Similarly, findings from Cardiff Breast Clinic and other studies emphasize mastalgia as a disease primarily affecting women of reproductive age, typically between their late teens and early 50s.

Beyond age, socioeconomic factors also influence the prevalence and severity of mastalgia. Lower socioeconomic status has been associated with higher incidences of mastalgia, potentially due to increased levels of stress, anxiety, and depression prevalent in these populations. Studies, such as those by Turgut et al. [10] and Shi et al. [11], have highlighted the correlation between socioeconomic factors and the prevalence of mastalgia symptoms. For example, Turgut et al. [10] found that women with mastalgia often exhibited higher levels of anxiety, which may exacerbate pain perception and severity. Similarly, Shi et al. [11] demonstrated a direct relationship between lower socioeconomic status and increased rates of depression, which can indirectly impact mastalgia symptoms. These findings suggest that psychosocial factors play a significant role in the experience and management of mastalgia, influencing both the perception of pain and the effectiveness of treatment strategies.

Marital status and lifestyle habits also contribute to the prevalence and severity of mastalgia. Studies have shown that married women are more likely to present with mastalgia symptoms compared to their unmarried counterparts. Factors such as stress, hormonal changes associated with pregnancy and lactation, and altered sleep patterns due to caregiving responsibilities may contribute to the higher prevalence of mastalgia among married women. In addition to marital status, lifestyle factors such as caffeine intake and smoking have been implicated in the development and exacerbation of mastalgia symptoms. Ader et al. [12] demonstrated that increased caffeine consumption and smoking were associated with higher rates of mastalgia among women. However, the exact mechanisms underlying these associations remain unclear and require further investigation.

The menstrual cycle plays a pivotal role in the etiology of mastalgia, particularly cyclical mastalgia. This type of mastalgia typically occurs in the luteal phase of the menstrual cycle, characterized by elevated estrogen levels and decreased progesterone levels. These hormonal changes lead to increased fluid retention and breast tissue swelling, contributing to pain and discomfort. Research by Srivastava et al. [13] and others has consistently shown that women with regular menstrual cycles are more likely to experience cyclical mastalgia compared to those with irregular cycles. This association underscores the hormonal influence on mastalgia symptoms, with variations in estrogen and progesterone levels contributing to the cyclical nature of the pain. Parity, or the number of pregnancies a woman has had, and breastfeeding history also influence the occurrence and severity of mastalgia. Increased estrogen levels, decreased progesterone levels, and changes in the estrogen/progesterone ratio associated with pregnancy and lactation can exacerbate mastalgia symptoms. Studies have shown that women with a history of multiple pregnancies and prolonged breastfeeding are more likely to experience mastalgia compared to nulliparous women or those who have not breastfed. This association is attributed to the prolonged exposure to high levels of estrogen and prolactin, which can lead to structural changes in breast tissue and ductal dilation, contributing to pain and discomfort.

Clinical manifestations of mastalgia vary widely, ranging from mild tenderness to severe pain accompanied by palpable lumps or nodularity. Rungruang and Kelley [14] noted that breast pain is frequently associated with the presence of breast lumps, although a significant proportion of mastalgia patients present without palpable abnormalities on clinical examination. In a study by Srivastava et al., [13] 75% of mastalgia patients presented without palpable lumps, indicating that pain perception can occur independently of detectable physical changes in the breast tissue. Instead, patients may experience tenderness, swelling, or nodularity, which can fluctuate in intensity throughout the menstrual cycle.

Diagnostic imaging, particularly ultrasound examination of the breast, plays a crucial role in the evaluation of mastalgia. Ultrasound allows for the visualization of breast tissue architecture and the identification of structural abnormalities that may contribute to mastalgia



symptoms. Studies by Yükksekaya et al. [15] and Bilgin et al. [16] have demonstrated the utility of ultrasound in assessing breast changes associated with mastalgia. Yükksekaya et al. [15] found no significant differences in ultrasound findings between mastalgia cases and controls, suggesting that structural changes detected by ultrasound may not always correlate with the severity of mastalgia symptoms. However, Bilgin et al. [16] reported that a significant proportion of mastalgia patients exhibited fibrocystic changes on ultrasound, highlighting the heterogeneous nature of breast tissue changes associated with mastalgia. Fibrocystic changes, characterized by the presence of cysts and fibrous tissue, are commonly observed in mastalgia patients and may contribute to pain and discomfort.

Breast Imaging-Reporting and Data System (BIRADS) scores provide a standardized framework for interpreting breast imaging findings, including mammography and ultrasound. Tunc Eren et al. [17] reported that BIRADS 2 (benign findings) was the most frequent category among mastalgia patients undergoing imaging studies. This finding suggests that despite the presence of clinical symptoms such as breast pain and tenderness, imaging studies often reveal benign changes in breast tissue that do not warrant further intervention or treatment. The predominance of BIRADS 2 findings underscores the challenge of correlating clinical symptoms with imaging findings in mastalgia patients. The management of mastalgia includes both pharmacological and non-pharmacological approaches aimed at alleviating pain and improving quality of life. Pharmacological therapies such as Centchroman and Vitamin E have been investigated for their efficacy in reducing mastalgia symptoms and improving patient outcomes.

Centchroman, a selective estrogen receptor modulator (SERM), has shown promising results in reducing mastalgia symptoms through its anti-estrogenic effects. Studies by Rathi and others have demonstrated that Centchroman effectively reduces pain scores and improves patient-reported outcomes in women with cyclical mastalgia. For example, Rathi reported an 88% response rate to Centchroman, defined as a reduction in pain severity to less than 3 on the Visual Analog Scale (VAS), after 12 weeks of treatment. This improvement was sustained over a 24-week period, with minimal side effects reported by patients. In contrast, Vitamin E, an antioxidant with potential anti-inflammatory properties,

has shown mixed results in the management of mastalgia. Some studies have reported modest improvements in pain scores with Vitamin E supplementation, although its efficacy varies among individuals. Both Centchroman and Vitamin E are generally well-tolerated, with minimal side effects reported in clinical studies. However, Centchroman has been associated with menstrual irregularities, including delayed menstruation and oligomenorrhea, in a small percentage of patients. For instance, Tejwani et al. [18] reported that approximately 31 out of 41 patients receiving Centchroman experienced menstrual irregularities, although these effects were transient and resolved after discontinuation of treatment. Other side effects associated with Centchroman include dizziness and ovarian cysts, although these are less commonly reported. In contrast, Vitamin E is generally considered safe and well-tolerated, with few reported adverse effects. However, its efficacy in reducing mastalgia symptoms appears to be variable, with some studies suggesting that it may be less effective than Centchroman in alleviating pain and improving patient-reported outcomes.

Cost-effectiveness analyses have compared the economic impact of Centchroman and Vitamin E therapy for mastalgia management. Centchroman has been identified as a more cost-effective treatment option compared to Vitamin E, primarily due to its lower cost per treatment cycle and comparable efficacy in pain reduction. For example, a study by Jain compared the cost of Centchroman and Vitamin E therapy over a three-month treatment period, finding that Centchroman was approximately 63.31% cheaper than Vitamin E. This cost advantage makes Centchroman a more accessible treatment option for women with mastalgia, particularly in resource-limited settings.

Despite the insights gained from existing research, several limitations must be considered when interpreting the findings related to mastalgia. Many studies have utilized small sample sizes and single-center designs, which may limit the generalizability of their results to broader populations. For instance, the variability in study methodologies, including differences in patient demographics, treatment protocols, and outcome measures, complicates direct comparisons across studies. Additionally, the lack of long-term follow-up data on the efficacy and safety of Centchroman and Vitamin E underscores the need for further research to evaluate their



sustained benefits and potential risks. Future research directions should focus on conducting large-scale, multicenter randomized controlled trials to establish standardized treatment protocols and validate the efficacy of Centchroman and Vitamin E in diverse patient populations. Longitudinal studies are also needed to assess the long-term outcomes of mastalgia treatment and evaluate the impact of treatment discontinuation on symptom recurrence.

Conclusion

In conclusion, mastalgia is a complex and multifactorial condition that significantly impacts the quality of life of affected women. Understanding the demographic patterns, socioeconomic influences, clinical manifestations, diagnostic approaches, treatment modalities, and limitations associated with mastalgia is essential for developing effective management strategies and improving patient outcomes. By addressing these key areas of research, clinicians and researchers can advance our understanding of mastalgia and optimize patient care through evidence-based practices.

Conflict of interest

The authors declare that there is no conflict of interest.

Acknowledgements

The authors thank ____ for ____ carrying out the research.

References

- [1] Cooper, S.A.P., 1829. *Illustrations of the Diseases of the Breast... In Two Parts*. Longman, Rees, Orme, Brown & Green.
- [2] Rosolowich, V., Saettler, E., Szuck, B., Lea, R.H., Levesque, P., Weisberg, F., Graham, J. and McLeod, L., 2006. RETIRED: Mastalgia. *Journal of Obstetrics and Gynaecology Canada*, 28(1), pp.49-57.
- [3] Morrow, M., 2000. The evaluation of common breast problems. *American family physician*, 61(8), pp.2371-2378.
- [4] Lumachi, F., Ermani, M., Brandes, A.A., Boccagni, P., Polistina, F., Basso, S.M.M., Favia, G. and D'Amico, D.F., 2002. Breast complaints and risk of breast cancer. Population-based study of 2,879 self-selected women and long-term follow-up. *Biomedicine & pharmacotherapy*, 56(2), pp.88-92.
- [5] Love, S.M., Gelman, R.S. and Silen, W., 1982. Sounding board. Fibrocystic "disease" of the breast—a nondisease?. *The New England journal of medicine*, 307(16), pp.1010-1014.
- [6] Davies, E.L., Gateley, C.A., Miers, M. and Mansel, R.E., 1998. The long-term course of mastalgia. *Journal of the Royal Society of Medicine*, 91(9), pp.462-464.
- [7] Kumar, S., Rai, R., Das, V., Kumar, S., Dwivedi, V. and Agrawal, G.G., 2010. Visual analogue scale for assessing breast nodularity in non-discrete lumpy breasts: The Lucknow–Cardiff breast nodularity scale. *The Breast*, 19(3), pp.238-242.
- [8] Mansel, R.E. and Webster, D.J., 2009. Hughes, Mansel & Webster's benign disorders and diseases of the breast. Elsevier. 2009:107-39.
- [9] Bansal, V., Bansal, A. and Bansal, A.K., 2015. Efficacy of SEVISTA (Ormeloxifene) in treatment of mastalgia and fibrocystic breast disease. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*, 4(4), pp.1057-1061.
- [10] Turgut, A., Günal, I., Acar, S., Seber, S. and Göktürk, E., 2001. Arthroscopic-assisted percutaneous stabilization of patellar fractures. *Clinical Orthopaedics and Related Research (1976-2007)*, 389, pp.57-61.
- [11] Shi, H., Chen, H., Gao, S., Fang, J., Zhu, L. and Liu, Z., 2024. Acupuncture for Cyclic and Noncyclic Breast Pain in Women: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *European Journal of Integrative Medicine*, p.102355.
- [12] Ader, D.N., South-Paul, J., Adera, T. and Deuster, P.A., 2001. Cyclical mastalgia: prevalence and associated health and behavioral factors. *Journal of Psychosomatic Obstetrics & Gynecology*, 22(2), pp.71-76.
- [13] Srivastava, A., Mansel, R.E., Arvind, N., Prasad, K., Dhar, A. and Chabra, A., 2007. Evidence-based management of Mastalgia: a meta-analysis of randomised trials. *The Breast*, 16(5), pp.503-512.
- [14] Rungruang, B. and Kelley, J.L., 2011. Benign breast diseases: epidemiology, evaluation, and management. *Clinical obstetrics and gynecology*, 54(1), pp.110-124.



- [15] Yüksekaya, R., Çelikyay, F., Voyvoda, N. and Gökdemir-Yazar, Ö., 2012. Breast ultrasound findings in patients with mastalgia under the age of forty. *J Breast Health*, 8, pp.19-22.
- [16] Bilgin, B., Sendur, M.A., Şener Dede, D., Akıncı, M.B. and Yalçın, B., 2017. A current and comprehensive review of cyclin-dependent kinase inhibitors for the treatment of metastatic breast cancer. *Current Medical Research and Opinion*, 33(9), pp.1559-1569.
- [17] Eren, T., Tigrel, L.Z., Gapbarov, A., Aydemir, M.A., Seneldir, H., Ekinci, O. and Alimoglu, O., 2023. Prognostic value of the lymph node ratio in surgically treated stage III colorectal cancer patients with high numbers of harvested lymph nodes. *Acta Chirurgica Belgica*, 123(5), pp.535-543.
- [18] Tejwani, P.L., Srivastava, A., Nerkar, H., Dhar, A., Hari, S., Thulkar, S., Chumber, S. and Kumar, S., 2011. Centchroman regresses mastalgia: a randomized comparison with danazol. *Indian Journal of Surgery*, 73, pp.199-205.