



TO STUDY THE EFFICACY OF ORMELOXIFENE IN REGRESSION OF FIBROADENOMA AND MASTALGIA

General Surgery

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ABSTRACT

Ormeloxifene, a novel non-steroidal, selective estrogen receptor modulator birth control pill. Recently has also been used for treatment of fibroadenoma and mastalgia. Since simple fibroadenomas are benign and asymptomatic with no chance of developing into cancer in the future, they are typically treated by natural surveillance. Complex fibroadenomas have a moderate chance of developing cancer, and those that are atypic (with a relative risk of >2) or have a family history of breast cancer should be surgically removed. Some patients, for psychological, physical, or cancer-related reasons, want to have the lump removed. Mastalgia whether cyclic or noncyclic may be severely incapacitating for women. The aim of study to analyse the effect of ormeloxifene on the regression of fibroadenoma and mastalgia. **Materials and Methods:** This study was prospective was conducted at dept of surgery Silchar medical college and hospital, ASSAM (INDIA) for period of 3 years from June 2019 to June 2022. The study population consists of women of reproductive age group (age ≤ 35 years) with mastalgia and fibroadenoma based on Triple Assessment (clinical evaluation, USG and FNAC). After taking written consent from participants in the study, detailed history, demographic details, clinical examination and investigation (USG and FNAC). Patients were prescribed ormeloxifene 30mg on alternate day for 3 months. Patients were followed up at 1 week (to check for tolerance to drug), 3 months and 6 months to assess response to therapy. During follow up, clinical examination, size of breast lump by USG and change in VAS score and breast tenderness was noted. **Results:** From June 2019 to June 2022, 80 patients were studied for effect of ormeloxifene. Age at presentation in our study varied between 15 to 35 years. Maximum number of cases were found in age group of 21-25 years with BMI range of 19-22kg/m² with average BMI of 20.5kg/m². In 22.5% cases there was positive family history. During our study we found right side breast was more commonly involved than left side breast. Number of fibroadenoma ranged from 3-8 in each breast and size of ranged from 0.5 to 3 cm. In our study Majority of patients 58 (72.5%) presented to hospital between 0-90 days. There are significant number of patients 17 (21.25%) presented between 90 days to 1 year. Out of 80 patient's, 28 (35%) were married out of which 18 patients were parous. 62 out of 80 were nulliparous. Overall, final response was noted in terms of complete dissolution or change in size is 44 (55%) patients. Partial response was seen in 36 (45%) patients and no response in 10 (12.75%) patients. increase in size of fibroadenoma was seen in 3 (3.75%) patients. In our study we got very good response in the mastalgia, the VAS scores in these patients dropped from 10 to 2 in 72 patients (90%) in 1st week of taking drug and at end of 1 month almost all the patients were painless. **Conclusion:** A new nonsteroidal medication called ormeloxifene has shown regression in size of fibroadenoma with alleviating mastalgia in most of the cases in three months only. Other alternatives like evening primrose oil, vitamin E, anti-estrogenic receptor blockers like Tamoxifen and androgens like danazol have low patient compliance and numerous side effects. So, Ormeloxifene is more cost-effective and safer it can be used as the first line of treatment for fibroadenoma and mastalgia.

KEYWORDS

INTRODUCTION

In younger age groups, benign breast diseases (BBDs) are frequently diagnosed, with second- and third-decade incidence peaks. A lump is felt by the majority of women, either painfully or not, which causes anxiety of cancer and sends the patient to the breast clinic, where 2/3 of the lumps are benign. Every year, 200,000 people with palpable breast lumps visits a surgeon, the majority of them are benign lesions [1]. The most frequent concern with benign breast conditions is that they will develop into malignancies [2]. Thus, the phrase "benign breast diseases" refers to a diverse range of lesions including developmental abnormalities, epithelial proliferation, and stromal proliferation that can be seen by microscopic examination. The incidence of BBD's is less common after menopause. [3,4].

Due to their high incidence and significant impact on women's lives, it generally attracts more attention among women [5]. BBDs are a group of breast conditions that can range from being normal to being diseased, and 50% of women will experience BBDs at some point during their reproductive lives [6]. Breast lump or nodularity (42%), followed by breast discomfort (66%), is the most common complaint among individuals with BBD. Histologically, it includes conditions such as non-proliferative, proliferative with or without atypia, and atypical hyperplasias, among which atypical lesions are associated with an increased risk of developing cancer [7]. Benign breast disorders, however, vary from person to person. It includes a variety of conditions, such as benign phyllodes tumours, fat necrosis, mastitis, and mastalgia, as well as hyperplasia, cysts, fibroadenomas, intraductal papillomas, sclerosing adenosis, and fibro adenosis. The three BBDs that most women experience are mastalgia, fibroadenoma, and fibro adenosis.

Mastalgia, whether cyclic (linked to menstrual cycles) or noncyclic, can leave a woman seriously disabled. Cyclical mastalgia is a common issue that has been linked to higher rates of mammography use in women. It can be severe enough to interfere with daily activities. Many

mastalgia sufferers are more concerned about the consequences of cancer than they are about the pain itself.

Since simple fibroadenomas are benign and asymptomatic with no chance of developing into cancer in the future, they are typically treated by natural surveillance. Complex fibroadenomas have a moderate chance of developing cancer, and those that are atypic (with a relative risk of >2) or have a family history of breast cancer should be surgically removed. Some patients, for psychological, physical, or cancer-related reasons, want to have the lump removed.

With varying degrees of efficacy, a number of treatment approaches have been investigated in the past, including consoling, supportive therapy, analgesics, evening primrose oil, oral contraceptive pills, tamoxifen, and bromocriptine [8]. Since fibroadenoma is thought to result from lobular tissue that is overly receptive to oestrogen, hormone manipulation has been used to try and slow the formation of fibroadenoma. It has been documented that tissues taken from fibroadenoma have oestrogen receptors [9,10]

As a result, we employed the antiestrogen ormeloxifene to prevent the duct and lobular tissue of the fibroadenoma from proliferating. Originally created in India, ormeloxifene is a brand-new, third-generation nonsteroidal, selective oestrogen receptor modulator birth control pill that has been used as a weekly oral contraceptive for the past 20 years. Recently, it has also been used to treat mastalgia and fibroadenoma because of its strong antagonist (on breast duct and lobular epithelium) and modest agonist (on endometrial and bones) actions.

As an alternative to currently available steroid-based medications with substantial side effects, this study aims to analyse the effect of ormeloxifene on the regression of fibroadenoma and mastalgia.

MATERIAL AND METHODS

This study was prospective was conducted at dept of surgery Silchar medical college and hospital, ASSAM (INDIA) for period of 3 years from June 2019 to June 2022.

The study population consists of women of reproductive age group (age ≤ 35 years) with mastalgia and fibroadenoma based on Triple Assessment (clinical evaluation, USG and FNAC).

Inclusion Criteria

1. History of mastalgia
2. Fibroadenoma < 5 cm Size
3. Age upto 35 years

Exclusion Criteria

1. Giant fibroadenoma (≥ 5 cm)
2. PCOD
3. Cervical hyperplasia
4. Pregnancy
5. Lactation period first 6 months
6. Patient to conceive in near future
7. Patient on other OCP's
8. History of breast ca or family history of breast ca or suspicious of malignancy

Sample Size

Sample size calculated considering the 20% prevalence of fibroadenoma. We found 64 patients are needed. Total 100 patients were screened. 12 patients were excluded and considering the possible loss of patients and data during follow up. 80 patients were analysed.

METHOD

After taking written consent from participants in the study, detailed history, demographic details, clinical examination and investigation (USG and FNAC). Patients were prescribed ormeloxifene 30mg on alternate day for 3 months.

Patients were followed up at 1 week (to check for tolerance to drug), 3 months and 6 months to assess response to therapy. During follow up, clinical examination, size of breast lump by USG and change in VAS score and breast tenderness was noted.

Statistics: - The results were analysed statistically with the help of mean and SD, percentage and paired -t test, where $P < 0.05$ was considered significant.

RESULT

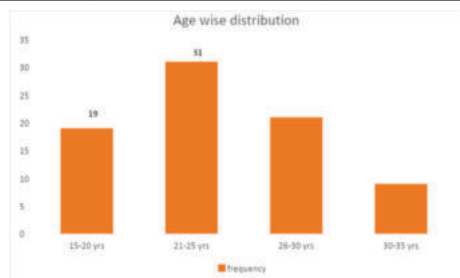
From June 2019 to June 2022, 80 patients were studied for effect of ormeloxifene

1. Age Wise Distribution

Age at presentation in our study varied between 15 to 35 years. Maximum number of cases were found in age group of 21-25 years with BMI range of 19-22kg/m² with average BMI of 20.5kg/m². In 22.5% cases there was positive family history. Table 1

Table 1

Age(years)	n (%)	BMI	Positive family history
$<15-20$	19 (23.75%)	18-20	2
21-25	31 (38.75%)	19-22	6
26-30	21 (26.25%)	20-21	6
30-35	9 (11.25%)	23	4
Total	80		

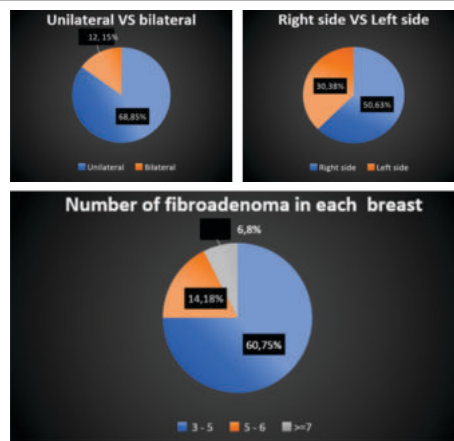


2. Breast Lump Characteristics

During our study we found right side breast was more commonly involved than left side breast. Number of fibroadenoma ranged from 3-8 in each breast and size of ranged from 0.5 to 3 cm. Table 2.

Table 2

	U/L	B/L	Rt side	Lt side	No. of fibroadenoma in each breast		
					3-5	5-6	≥ 7
N	68	12	50	30	60	14	6
%	85%	15%	62.5%	37.5%	75%	17.5%	7.5%

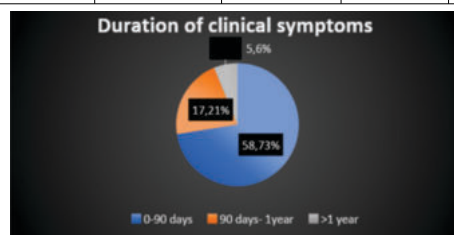


3. Duration Of Clinical Symptoms Of Breast Lump

In our study Majority of patients 58 (72.5%) presented to hospital between 0-90 days. There are significant number of patients 17 (21.25%) presented between 90 days to 1 year (Table 3), reason for this delay presentation could be fear from surgery treatment and unawareness of medical management, Table 3.

Table 3

	0-90 days	90-1 year	> 1 year	
Frequency (n)	58	17	5	80
%	72.5	21.25	0.06	100



4. Obstetrics History

Out of 80 patient's, 28 (35%) were married out of which 18 patients were parous. 62 out of 80 were nulliparous, Table 4.

Table 4

	Frequency (n)	%
Nulliparous	62	77.5
Parous	18	22.5

5. Size Of Breast At Different Time Interval (by USG)

Response of ormeloxifene therapy was evaluated at end of 3rd and 6th month and was recorded in terms of size by ultrasonography, Table 5.

Table 5

Volume	Disappear, n (%)	<1 cm ³ , n (%)	1-2 cm ³ , n (%)	2-3 cm ³ , n (%)
At beginning of treatment	0	15 (18.75)	27 (33.75)	38 (47.5)
At the end of 3rd month	6 (7.5)	10 (12.5)	35 (43.75)	29 (36.25)
At the end of 6th month	32 (40)	18 (22.5)	14 (17.5)	16 (0.25)

6. Response In Size Of Fibroadenoma To Ormeloxifene (Clinically And On USG)

Overall, final response was noted in terms of complete dissolution or change in size is 44 (55%) patients. Partial response was seen in 36 (45%) patients and no response in 10 (12.75%) patients. increase in size of fibroadenoma was seen in 3 (3.75%) patients, Table 6.

Table 6

Response	At the end of 3rd month, n (%)	At the end of 6th month, n (%)	Overall result, n (%)
Complete dissolution/ response	9 (11.25%)	35 (43.75%)	44 (55%)
Partial response (50% decrease in size clinically and by USG)	11 (13.75%)	25 (31.25%)	36 (45%)
No response	3 (3.75%)	7 (8.75%)	10 (12.75%)
Increased in size	0	3 (3.75%)	3 (3.75%)

7. VAS score was analysed in 80 patients. 68 patients (85%) complained of severe pain with VAS score of 10 and 12 patients (15%) were having score between 6 to 9 of VAS score. In our study we got very good response in the mastalgia, the VAS scores in these patients dropped from 10 to 2 in 72 patients (90%) in 1st week of taking drug and at end of 1 month almost all the patients were painless.

DISCUSSION

Fibroadenomas are the common disorders found in surgery OPD in young women. Multiple fibroadenoma is a rare benign disease so natural history and etiopathogenesis is poorly understood.

On studying the patient's characteristics, the age at presentation in our study varied between 15 to 35 years. Maximum patients 31 (38.75%) were in age group of 21- 25 years. Similar to Kumar et al who stated that most of the benign breast diseases faced by the respondents who are between the age category of 11-30 years whereas Bagale et al pointed out that most cases lie between the age category of 21-40 years [11,12]

In our study 68 patients (85%) had U/L involvement of which 50 patients (62.5%) were having right side involvement, similar to Shashikala et al indicated that most of the cases seen in right breast [13]. Sagar stated that 40% of seen in right breast. [14]

Usually in multiple fibroadenoma, average number in a single breast is 3-5 but more numbers have been reported previously in various studies including this study.[15] similarly in our study 6 patients (7.5%) had masses more than 7 in each breast.

A strong family history was found to be associated with multiple fibroadenoma in many studies and in our study, it was found 18 patients (22.5%) of cases were having positive family history.[16]

In our study we got very good response in the mastalgia, the VAS scores in these patients dropped from 10 to 2 in 72 patients (90%) in 1st week of taking drug and at end of 1 month almost all the patients were painless. Similar to study conducted by Gupta N. A Prospective Study to Study the Efficacy and Side Effects of Ormeloxifene in Regression of Mastalgia and Fibroadenoma 97.6 to 100% of women in the mastalgia group reported complete relief at 12 weeks of therapy with a decrease in VAS score from 10 to 3 in the first week of therapy itself while 28% of fibroadenoma group reported complete relief at 12 weeks of therapy [16].

In our study we found complete dissolution of fibroadenoma in 55%, partial response in 45% and no response in 12.75%. The results are consistent with that of Brahmachari Evaluating the Effect of Ormeloxifene on Multiple Fibroadenomas and Mastalgia [17] and Dhar et al, Tejwani et al and Gupta et al who studied the effect of Ormeloxifene in the management of mastalgia and fibroadenoma [18,19,20]

CONCLUSION

A new nonsteroidal medication called ormeloxifene has shown regression in size of fibroadenoma with alleviating mastalgia in most of the cases in three months only. Other alternatives like evening primrose oil, vitamin E, anti-estrogenic receptor blockers like Tamoxifen and androgens like danazol have low patient compliance and numerous side effects.

So, Ormeloxifene is more cost-effective and safer it can be used as the first line of treatment for fibroadenoma and mastalgia . since fibroadenoma does not have any proven proof of a propensity to

malignant transformation, a more drastic treatment like surgery can be avoided in favour of using the medicine ormeloxifene, which is affordable, compliant, safe, and has few side effects.

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Conflict of Interest: None declared

Ethical Approval: The study was approved by the Institutional Ethics Committee

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