International Surgery Journal
Ahluwalia AS et al. Int Surg J. 2021 Jan;8(1):331-338
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: https://dx.doi.org/10.18203/2349-2902.isj20205900

Original Research Article

A comparative study of centchroman versus evening primrose oil in treatment of mastalgia

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Received: 16 December 2020
Revised: 19 December 2020
Accepted: 21 December 2020

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ABSTRACT

Background: Breast pain or mastalgia is one of the most common symptoms presenting to general surgeons. Approximately 60-70% of the women experience some type of breast pain at some point of their lives. Mastalgia may be classified as cyclical and non-cyclical. In cyclical mastalgia the pain intensity is changing during the menstrual cycle. In non-cyclical mastalgia there is no other obvious cause present, the pain is considered to be originating from the breast and the pain remains unchanged during the menstrual cycle. If the pain persists there are a variety of pharmacological agents for treatment of mastalgia. These include 3-6 months course of low dose tamoxifen (10 mg) or evening primrose oil. Other agents include bromocriptine and danazol but are obsolete now days. Newer treatments include centchroman and topical non-steroidal anti-inflammatory preparations. In pursuit of finding an effective safe and economical agent to treat it, plan to compare centchroman to evening primrose oil as treatment of mastalgia.
Methods: In this study, two groups with 40 patients each will be taken and treatment will be given for 12 weeks and follow up to 24 weeks will be done without medication to assess sustained response or recurrence of mastalgia.
Results: Centchroman is a non-steroidal drug found to be effective in the treatment of mastalgia with early and better relief in a time period of 3 months with minimal side effects as compared to evening primrose oil.
Conclusions: This study has demonstrated that Centchroman therapy offers safe, effective and economical alternative to Evening Primrose oil for treatment of mastalgia.

Keywords: Leutinizing hormone releasing hormone, Visual analogue scale, NSAIDS, Sevening primrose oil

INTRODUCTION

Breast pain (also known as breast tenderness, mastodynia, mammalgia, and mastalgia) is defined as pain that is of sufficient intensity to interfere with normal life or lasts for longer than two weeks of menstrual cycle. Breast pain during lactation or after weaning is not included into this definition. Mastalgia has two distinct clinical patterns- cyclical when the pain intensity is changing during the menstrual cycle and non-cyclical when the pain remains essentially unchanged during the menstrual cycle. This type is less frequent.

Mastalgia affects up 2/3rd of women at some point during their reproductive lives. Rarely extra mammary conditions like Tietze syndrome present as mastalgia and a thorough clinical investigation is required to assess the cause.

Causes

Cyclical mastalgia: Cyclical breast pain occurs 1-2 weeks prior to menses. The pain is commonly felt diffusely and bilaterally, with some radiation to upper arm and axilla. It can be more severe in one breast than the other breast and is relieved by onset of menstrual

flow. These patients are usually aged between 30-40 years. Cyclical mastalgia is very often associated with fibrocystic breast changes or duct ectasia and is believed to be caused by aberrations in dynamic hormonal changes like prolactin excess, progesterone deficiency, enhanced dynamic prolactin release.[1-3] Some degree of cyclical breast tenderness is normal in the menstrual cycle, and is usually associated with menstruationand/or premenstrual syndrome (PMS).

***Non-cyclical mastalgia*:** Some degree of noncyclical breast tenderness can be present normally due to hormonal changes in puberty (both in girls and boys), in menopause and during pregnancy. Pain in noncyclical mastalgia arises from causes that are usually anatomical rather than for hormonal in nature. Pain may arise from myofascial pain syndromes, bonylesions.[4] Other cause of non-cyclical breast pain include alcoholism with liver damage (likely due to abnormal steroid metabolism), mastitis and drugs such as estrogen, progesterone, oral contraceptive, digitalis, methyldopa (an antihypertensive), spironolactone, diuretics, oxymetholone (an anabolic steroid), ketoconazole, metronidazole, cimetidine, cyclosporine and chlorpromazine (a typical antipsychotic). Also, shingles can cause painful blistering rash on the skin of the breasts.

At present drugs being used for treatment of mastalgia are evening primrose oil, bromocriptine, gamolenic acid, danazol, tamoxifen, luteinizing hormone releasing hormone (LHRH) analogue gosereline, oral contraceptive pills (centchroman), diuretics and topical non-steroidal anti-inflammatory drug (NSAID) gels[5] with varying efficacy and side effects. In pursuit of finding an economical, safe and effective agent for mastalgia, in this study we plan to study efficacy of centchroman as compared to evening primrose oil for the treatment of mastalgia.

Pharmacology of centchroman

Centchroman is a novel non-steroidal, selective anti-estrogen receptor modulator. Because of its selective anti-estrogenic action centchroman has been very beneficial in treatment of mastalgia.

Advantages

It is an oral contraceptive and has as advantage of less frequent administration. In lactating women, it is excreted in milk in quantities considered unlikely to have any deleterious effect on suckling babies. It is free from side effects commonly associated with steroidal oral contraceptives like nausea, vomiting, weight gain, dizziness. It does not delay return of fertility. It maintains normal ovulatory cycles because its low dose and 2 to 3 times a week administration minimizes any effect on hypothalamus pituitary ovarian axis. It is used as a non-steroidal, anti-estrogenic oral contraceptive pill and was developed by central drug and research institute (CDRI), Lucknow, Uttar Pradesh, India in 1980s.It was introduced in July 1991 and was marketed in India in 1992 as Saheli.[6] Response rates of about 44% in cyclical pain and 27% in non-cyclical pain have been noted.[7]

METHODS

The study was conducted in the department of general surgery of Shri Guru Ram Das institute of medical sciences and research, Vallah, Sri Amritsar. Eighty cases of breast pain with or without lumpiness were included in this study and divided into two group:

***Group (A)*-**Centchroman group (n=40), in which centchroman 30 mg was given orally every other day for 3 months.

***Group (B)*-**Evening primrose oil group (n=40), in which evening primrose oil orally 3 gm daily was given for 3 months.

The drug treatment was given for a total of 12 weeks and then follow up at 12, 16, 20, 24 weeks was done without medication to assess sustained response or recurrence of mastalgia. The severity of mastalgia was assessed by visual analogue scale (VAS) score ranging from 0-10, zero (0), indicating no pain and ten (10) indicating severe pain. The pain score using VAS will be measured in each group and compared.

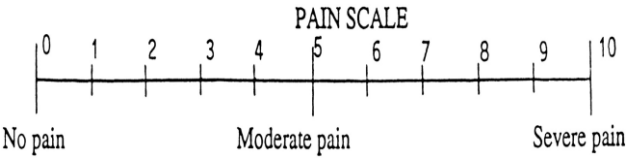

Figure 1: Pain scale.

Sampling technique

A comparative study was done by giving centchroman to first five patients and next five patients were given evening primrose oil. Thus, batches of five were given drugs alternatively till target count of 40 patients each is met in both groups.

Bias was removed by double blinding of the study. Patients were made aware about both the treatment protocols and consent was taken for participation in the study

Study design

Interventional randomized control trial study design used.

Study time

The duration of study was from December 2018 to august 2020.

Inclusion criteria

Both drugs will be given in all women in age group of 20-50 years with mastalgia with or without lumpiness.

Exclusion criteria of centchroman

Exclusion criteria for centchroman excluded past history of breast carcinoma or family history of breast carcinoma, patient with polycystic ovarian diseases and uterine cervical hyperplasia, first six months of lactation, pregnancy or patients who plans pregnancy, patient with discrete and dominant lump which was suspicious of cancer, patient with recent history of jaundice or hepatic impairment, severe allergic states, tuberculosis, renal impairment and patients with extramammary condition causing mastalgia.

Exclusion criteria of evening primrose oil

Exclusion criteria for evening primrose oil excluded History of temporal lobe epilepsy, mania.

Statistical analysis

All analysis was done using SPSS version 21.0. Student 't' test (unpaired), Mann-Whitney test was used for comparing the mean values. To compare prevalence Chi-square test was used.

RESULTS

Out of 80 patients, 28 (35%) patients had cyclical mastalgia and 52 (65%) patients had non-cyclical mastalgia. In group A, 26 (65%) patients had non-cyclical and 14 (35%) patients had cyclical mastalgia. In group B, 26 (65%) patients had non-cyclical and 14 (35%) had cyclical mastalgia as depicted in Table 1 and Figure 2. The mean age in group A was 35 years and in group B was 32.63 years.

In group A, among cyclical mastalgia patients (14) mean pain score initially was 7.71 which gradually decreased to 2.50 at 12 weeks and 0.50 at 24 weeks. In non- cyclical mastalgia patients (26) mean pain initially was 7.92 which gradually decreased to 2.69 at 12 weeks. At 24 weeks mean pain was 0.38, lower than cyclical mastalgia patients. Comparing mean pain score is not statistically significant among cyclical and non-cyclical patients at any visit as depicted in Table 3.

Table 1: Patient distribution in types of mastalgia.

Mastalgia	Group A		Group B		Total	
	No.	%	No.	%	No.	%
Cyclical	14	35	14	35	28	35
Non-cyclical	26	65	26	65	52	65
Total	40	100	40	100	80	100

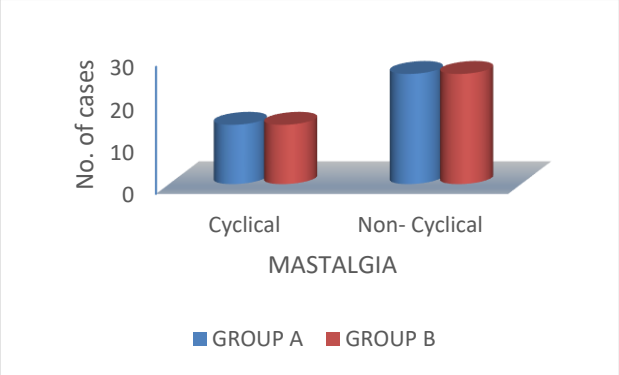

Figure 2: Patient distribution in types of mastalgia.

Table 2: Group a mean pain score in cyclical and non-cyclical mastalgia patients.

Time interval (weeks)	Cyclical mastalgia	Non-cyclical	P value
Initial pain	7.71±0.82	7.92±0.79	0.440
At 12	2.50±1.01	2.69±0.88	0.538
At 16	1.29±1.32	1.85±1.04	0.150
At 20	0.79±0.97	0.96±0.99	0.596
At 24	0.50±1.16	0.38±0.75	0.705

Table 3: Group B mean pain score in cyclical and non-cyclical mastalgia patients.

Time interval (weeks)	Cyclical mastalgia	Non-cyclical	P value
Initial pain	7.21±1.88	7.19±1.29	0.958
At 12	3.57±1.01	3.62±1.09	0.902
At 16	1.79±0.97	2.73±1.11	0.878
At 20	1.93±1.07	1.65±1.16	0.469
At 24	1.50±1.09	1.00±1.13	0.176

In group B, among cyclical mastalgia patients (14) mean pain score initially was 7.21 which gradually decreased to 3.57 at 12 week and 1.50 at 24 weeks. In non-cyclical mastalgia patients (26) mean pain initially was 7.19 which gradually decreased to 3.62 at 12 weeks. At 24 weeks mean pain was 1.00, lower than cyclical mastalgia patients. Mean pain at 20 and 24 weeks was lower in patients with non-cyclical mastalgia as compared to patients with cyclical mastalgia. Comparing mean pain score is not statistically significant among cyclical and non-cyclical patients at any visit as depicted in Table 4.

In cyclical mastalgia patients, initially mean pain score was 7.71 in group A and 7.21 in group B. In group A at 12 weeks mean pain score was 2.50 and gradually decreased to 0.50 at 24 weeks. In group B at 12 weeks, mastalgia was relieved with mean pain 2.57 and 1.50 at 24 weeks. The mean pain score was higher in all visits in group B. So, in group A cyclical mastalgia patients were more relieved. It was statistically significant at 12 weeks (p value 0.001), 16 weeks (p value 0.002), 20 (p value

0.007), 24 (p value 0.023) weeks as depicted in Table 5 and Figure 3.

Table 4: Mean pain of cyclical mastalgia patients in group A and B.

Time interval (weeks)	Group A	Group B	P value
Initial pain	7.71±0.82	7.21±1.18	0.207
At 12	2.50±1.01	3.57±1.01	0.010
At 16	1.29±1.32	2.79±0.95	0.002
At 20	0.79±0.97	1.93±1.07	0.007
At 24	0.50±1.16	1.50±1.01	0.023

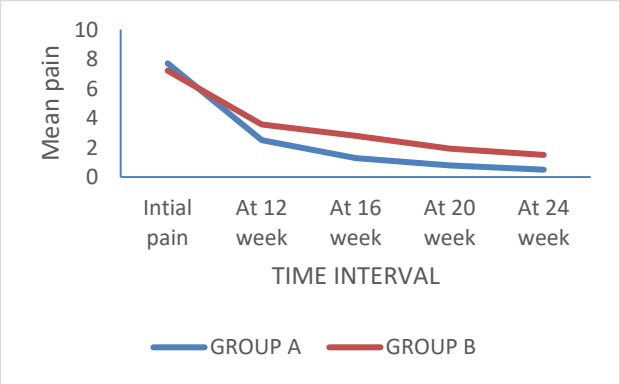

Figure 3: Mean pain of cyclical mastalgia patients in group A and B.

In Non-cyclical mastalgia patients, initially mean pain score was 7.92 in group A and 7.19 in group B. In group A at 12 weeks mean pain score was 2.69 and gradually decreased to 0.38 at 24 weeks. In group B at 12 weeks, mastalgia was relieved with mean pain 3.62 and 1.00 at 24 weeks. The mean pain score was higher in all visits in group B. So, in group A non-cyclical mastalgia patients were more relieved. It was statistically significant at 12 weeks, 16 weeks, 20 weeks and 24 weeks as shown in Table 6 and Figure 4.

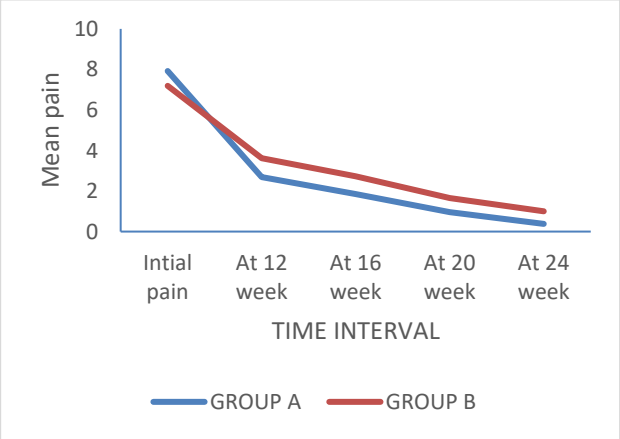

Figure 4: Mean pain of non-cyclical mastalgia patients in group A and B.

Table 5: Mean pain of non-cyclical mastalgia patients in group A and B.

Time interval (weeks)	Group A	Group B	P value
Initial pain	7.92±0.79	7.19±1.29	0.018
At 12	2.69±0.88	3.62±1.09	0.002
At 16	1.85±1.04	2.73±1.11	0.005
At 20	0.96±0.99	1.65±1.16	0.026
At 24	0.38±0.75	1.00±1.13	0.025

There was gradual relief in mastalgia in both study groups. In group A, mean pain score (VAS score) improved from 7.85 at time of inclusion in the study to 2.63 at 12 weeks of therapy and it gradually decreased to 0.43 at 24 weeks. The mean pain score of group B were higher than group A at all visits. The mean pain score was 7.20 at time of inclusion and decreased to 3.63 at 12 weeks and to 1.18 at 24 weeks as shown in Table 6 and Figure 5.

Table 6: Mean pain score (VAS score) in two groups.

Mean pain ± SD (weeks)	Group A	Group B
Initial pain	7.85±0.80	7.20±1.24
At 12	2.63±0.92	3.63±1.05
At 16	1.65±1.16	2.75±1.05
At 20	0.90±0.98	1.75±1.12
At 24	0.43±0.90	1.18±1.07

Using Mann-Whitney test, pain score was compared between both groups. As compared to initial pain, decrease in pain was statistically significant at 12 week (p value 0.001), 16 week (p value 0.001), 20 weeks (p value 0.001), and at 24 weeks (0.001) in both groups.

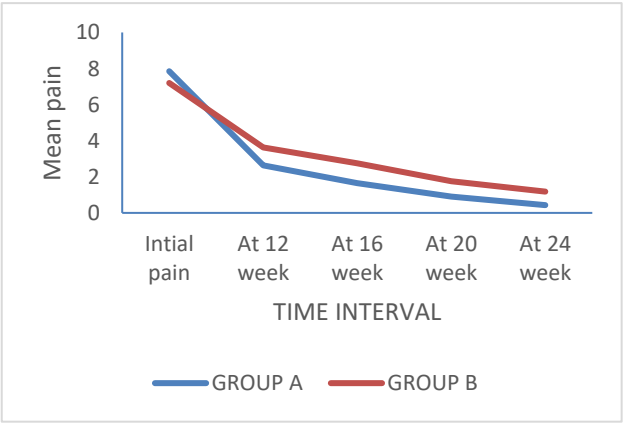

Figure 5: Mean pain score (VAS score) in two groups.

In group A, decrease in pain as compared to initial pain was highly statistically significant (p value 0.00) at all visits. Similarly, in group B, decrease in pain was highly statistically significant (p value 0.00) at all visits. Patients in group A experienced early relief of mastalgia as compared to group B. The mean change in pain at 12

weeks was better in group A than group B in all visits. At 24 weeks, mean change in pain was higher in group A than group B as shown in Table 9.

Table 7: Mean pain among two groups.

Time interval (weeks)	Group A	Group B	P value
Initial pain	46.53	34.48	0.015
At 12	30.5	50.49	0.001
At 16	30.63	50.38	0.001
At 20	30.18	48.83	0.001
At 24	32.14	48.86	0.001

Table 8: Mean change in pain.

Mean pain ± SD (weeks)	Group A	Group B	P value
At 12	5.22±1.18	3.60±1.15	0.001
At 16	6.20±1.28	4.45±1.37	0.001
At 20	6.95±1.10	5.45±1.48	0.001
At 24	7.42±1.10	6.02±1.52	0.001

In group A, delayed menstruation was reported by 4 (10%) patients and 36 (90%) patients had no complain regards of menstruation. All patients with delayed menses were counselled, reassured and followed up but drug was continued. No side effects were noted in patients in group B. Although the side effects were seen only in group A, side effects in group A attained statistically significant level (p value 0.040) as depicted in Table 9 and Figure 6.

Table 9: Distribution of side effects.

Side effects	Group A (%)	Group B (%)
Delayed menstruation	4 (10)	0
No side effect	36 (90)	40 (100)

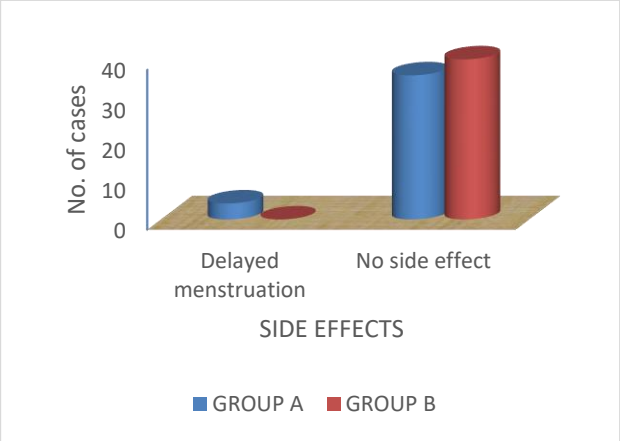

Figure 6: Distribution of side effects.

There were 2 (5%) patients in group A whose mastalgia was not completely relieved after three months of treatment, so they were shifted to another drug (danazol). Danazol 100 mg twice daily was given for 3 months. In group B, a greater number of patients 8 (20%) were not completely relieved and were shifted to Danazol. Shifting to another drug was significant in group B (p value 0.043) in Table 6. So, it shows centchroman is effective and better in mastalgia (Table 10).

Table 10: Shifted another drug (danazol).

Shifted to another drug	Group A (%)	Group B (%)
Shifted to Danazol	2 (5)	8 (20)
Not shifted	38 (95)	32 (80)

P=0.043

DISCUSSION

In this study we have done a comparative study of centchroman versus evening primrose oil in treatment of mastalgia. In present study patients in centchroman group as well as in evening primrose oil group show gradual improvement in symptoms, in terms of decrease in mean pain (VAS) score at 3 months period of treatment. The mean pain score was lower in centchroman group patients at all visits.

In our study of 80 patients, 65% patients had non-cyclical mastalgia and 35% had cyclical mastalgia. Similarly, in a study by Dhar et al of 60 patients in which 90% patients had non- cyclical mastalgia and 10% had cyclical mastalgia.[8] So non-cyclical mastalgia is more common as compared to cyclical mastalgia.

In our study patients in group A (centhchroman) out of the 40 patients 30 (70%) had a pain score of 0, 6 patients had pain score of 1, 2 patients had pain score of 2, after 3 months of discontinuation of drug. A study by Udayakumar et al was conducted to study effect of centchroman (ormeloxifene) in regression of fibroadenosis and mastalgia and to evaluate its adverse effects. In this study centchroman was given for 3 months in group of 51 patients. After 3 months of discontinuation of treatment, at 6 months out of 51, 46 (90%) patients had pain score of 0, one patient with pain score of 2 and four with pain score of 6.[3]

In our study visual analogue scale on presentation is ranging from 4 to 10. After 3 months of treatment significant reduction in VAS was observed in both the groups. But on comparison at the end of 3 months of treatment reduction in VAS Score was much more with centchroman than with evening primrose oil. A study was conducted by Anjana Nigam et al which aims to analyse the impact of ormeloxifene and evening primrose oil in treatment of mastalgia. The study had a total of 90 patients complaining of mastalgia. This study was a prospective comparative study. Patients were divided into 2 groups. Groups were allotted on alternate basis. Group 1 which included patients who were given ormeloxifene for a period of three months at a dose of 30

mg twice a week and group 2 which included patients who were given evening primrose oil 1000 mg once a day for 3 months. The study was conducted in department of surgery, Dr. BRAM hospital Raipur. The results were recorded on a monthly bases for a period of 3 months. VAS (visual analogue scale) of pain was used to record changes in pain on consumption of drug. At the time of enrolment, patients had VAS score ranging from three to seven. Gradual reduction of pain was seen in both the groups. After the first month of treatment 60% of the patients reported VAS score reaching to zero and the percentage increased to 87% after third month of the treatment. After one month of treatment reduction in pain which was recorded on visual analogue scale was similar in both the groups. But patients in group 1 (ormeloxifene) recorded a greater reduction in pain on VAS pain scale at the end of second and third month when compared to patients in group 2 (evening primrose oil). Ormeloxifene is more effective than evening primrose oil in long term in the treatment of mastalgia.[4]

There was significant relief of mastalgia in both groups in our study. Patients in centchroman group experienced early alleviation of mastalgia as compared to patients in evening primrose oil group. In our study after 12 weeks of treatment 80% of the patients in centchroman were relieved of mastalgia and at 24 weeks the effect of the drug still persisted with 95% patients reporting relief from mastalgia. VAS score of ≤3 was considered as relief from mastalgia. In a study by Lakhmichand et al after 12 weeks of therapy 89.7% patients in centchroman group were relieved of mastalgia. At 24 weeks follow up (i.e., 3 months after stopping drug) the percentage of pain free patients in centchroman group slightly reduced to 71.1%.[6]

In our study, after 12 weeks of treatment with centchroman 80% were relieved of mastalgia (mean pain score ≤3). After 24 weeks 95% patient were relieved of mastalgia. (2 patients were shifted to danazol at end of 3 months of treatment). In our study, effect of centchroman persisted even after discontinuation of drug in contrast to some studies in which symptomatic relief was not sustained. Thakur et al revealed that at end of 3 month 87.5% were symptom free. On follow up for 6 months, 83.92% were symptom free.[9] Rathi et al show centchroman significantly alleviated mastalgia with minimal side effects. Overall patients reporting to be pain free at 12 weeks were 88 and 85% at end of 24 weeks. The effect of drug persisted till completion (24 weeks) of study.[10] In a study by Jain et al 63.3% of the patients reported of pain relief at three months. At six months the effect of drug still persisted in term of lower mean VAS score, as compared to pre-treatment mean VAS score. At six months 30.8% of patients reported of pain relief as compared to 63.3% at 3 months.[11]These observations suggest that the achieved level of symptomatic relief was not sustained after discontinuation of treatment with centchroman. In a study by, Dhar et al reported 100% patients were painless at end of one month.[12]

In our study, after 12 weeks of treatment with evening primrose oil 45% were relieved of mastalgia (mean pain score ≤3). After 24 weeks, 80% patient were relieved of mastalgia (8 patients who were shifted to danazol at the end of 3 months of treatment). In our study, effect of evening primrose oil persisted even after discontinuation of drug. A study by Qureshi et al revealed that a total of 25 patients complaining of mastalgia were treated with evening primrose oil. Out of the 25 patients 64% were recorded to be pain free after three months of treatment.[13] Plomres et al study reveals that both fish oil and evening primrose oil effectively decrease the breast pain. The results of a study by Kornek et al also show that after one month of evening primrose oil, just 3 out of 19 patients (15.3%) had still pain and after 3 months treatment, 100% of them were relieved.[14]

In a study by Tejwani et al danazol was given once a day at a dose of 100 mg.[6] At 12 weeks of treatment 69% of the patients were reported to be pain free. By the end of 24 weeks the response rate of drug was reduced and only 42% of the cases were reported to be pain free. In a meta-analysis of 4 randomized trials, it was found that danazol has a highly significant role in treatment of mastalgia, as compared to placebo. Amenorrhea is the main side effect of danazol. If given at a dose of 600-800 mg per day the incidence increases up to 100%. The other side effects are acne, increase in weight and hirsutism. All the adverse effects of danazol are in direct proportion to the amount of dose given. Presently, severe side effects hinder the use of danazol in most breast centers and it is reserved as a second line drug for mastalgia.[6] In a study conducted by Srivastava et al bromocriptine, danazol and tamoxifen were found to be successful in alleviation of mastalgia.

In our study out of the 40 patients in centchroman group, 4 patients had delayed menstruation. No other side effect was noted in centchroman group. So, menstrual irregularity is the only side effect of centchroman that is observed in our study. Similarly, Udayakumar et al reported that out of 51 patients taking centchroman, 10 patients had menstrual delay and 3 patients had epigastric pain during course of treatment.[2] Fifteen out of thirty patients in a study by Jain et al reported side effects.[11] All these patients belong to group centchroman. Eight (26.7%) patients reported of dizziness. Dizziness was mild in intensity and after one month of cessation of treatment it was completely resolved. Dizziness is not a common side effect of centchroman and has not been reported by any of the other studies in its use for mastalgia.[6] 13.3% patients reported of menstrual irregularities. 8.3% patients receiving 30 mg centchroman on alternate days for treatment of mastalgia reported of amenorrhea and delayed menstruation. At six months follow up all the side effects were relieved and the returned to normal menstrual cycle. In a study by Tejwani et al scanty menstruation was reported in 31 of the 41 patients who received centchroman 30 mg per day for three months. In their study, delayed menstruation was seen in six patients and had menorrhagia was reported in

two patients.[6] In patients receiving 30 mg centchroman daily menstrual irregularities are more common when compared to patients receiving centchroman on alternate days. In a study by Kumar et al oligomenorrhea was reported in only 12 out of 75 patients taking centchroman 30 mg orally twice a week for treatment of mastalgia.[15]

Adverse effects like vomiting, nausea, dizziness and weight gain are uncommon. Once the drug is discontinued there is return of fertility as ovulation is not disturbed. Normal ovulatory cycles are maintained. Centchroman has no apparent adverse effects on hematologic, endocrine, liver function and life-threatening complications like thrombosis, heart attack or stroke have never been reported with use of centchroman.[6]

In our study no side effect was seen with use of evening primrose oil. Similarly, in two studies one evening primrose oil in treatment of mastalgia, no side effect was noted.[16,17] In a study by Qureshi et al out of 25 patients only one patient had side effect of nausea and altered taste.

CONCLUSION

In an effort to find a better treatment for mastalgia, we tried centchroman, a novel nonsteroidal chemical that is marketed in India and that could be a choice of the future. In this study, centchroman and evening primrose oil were given orally for 3 months in 40 patients each. Both are effective in relieving mastalgia, both cyclical and non-cyclical mastalgia. However, patients taking centchroman experienced early and better relief of mastalgia. Side effects like vomiting, nausea, dizziness and weight gain are not observed with centchroman. As centchroman does not disturb ovulation it does not delay return of fertility (after discontinuation). It has only one adverse effect, delayed menstruation. It maintains normal ovulatory cycles. However, further evaluation is needed for patient compliance and comfort regarding use of both drugs in future studies.

Keeping in mind the observations made and discussion the following conclusions have been drawn: In both groups mean pain (VAS) score gradually decreased and relief of mastalgia in both cyclical and non-cyclical mastalgia was seen. Mean pain (VAS) score in centchroman group was lower as compared to evening primrose oil group at all visits. There was significant difference in patients having side effects among two groups. In centchroman group delay in menstruation was noted (in 10%) whereas in Evening Primrose oil group was free from any side effect. However, there was significant difference in number of patients shifted to other drug(danazol) in evening primrose oil group as significant resolution of mastalgia did not occur. After 24 weeks of cessation of drug, the effect of drugs still persisted in both the groups but relief from mastalgia was higher with centchroman and it is cost effective and easily available compared to evening primrose oil.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Ahluwalia AS, Bhatia P, Chhabra AS. A comparative study of centchroman versus evening primrose oil in treatment of mastalgia. Int Surg J 2021;8:331-8.