



A COMPARATIVE STUDY OF CENTCHROMAN AND DANAZOL IN MANAGEMENT OF MASTALGIA.

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**ABSTRACT**

Mastalgia is one of the most common presenting symptom in female attending surgical and gynaecological OPD. In majority of patients it can be managed with reassurance and simple medication. But in 10-20 % of patient severe pain affects quality of life and causes severe anxiety. Aim was to compare the effectiveness of Centchroman and Danazol in mastalgia by using visual analogue scale (VAS), Fifty-two patients were taken in study & randomized into two groups with all women presenting with mastalgia with VAS score  $\geq 3$  between ages of 20-40 years. Centchroman (30mg OD for 3 months) in group 1 and Danazol (50 mg bid for 3 months) to group 2 was given and were monitored for VAS for pain and we found that centchroman is more effective than danazol and there was significant difference in parameters in both the groups as Age, VAS score, duration of menstrual cycle, No. of cases with cyclical, non-cyclical mastalgia. Relative risk (RR) of 1.256 at 12<sup>th</sup> week, 2.280 at 24<sup>th</sup> week were noted, P value was found to be significant. It can be concluded that Centchroman therapy is a safe, equally effective, and less costly alternative to Danazol for the treatment of mastalgia.

**KEYWORDS :** mastalgia, danazol, centchroman, visual analogue scale, less costly.

**INTRODUCTION**

Mastalgia is one of the most common breast symptom in patients attending breast clinics<sup>1</sup> all around the world and a cause of significant anxiety and fear of breast cancer. It is measured using visual analogue scale (VAS). It is so common that about 60-70 % women encounter it at least once in their life time<sup>2</sup>. In majority of patients the management is with reassurance and simple medication. But in 10-20 % of cases it is severe pain<sup>3</sup> affecting life quality of the patients. Mastalgia can classified into cyclical or non-cyclical. Till now there is no established cure for this common problem<sup>3</sup>, as etiology is multifactorial. Drug inducing hormonal manipulation such as Danazol, Bromocriptine, Tamoxifen, and luteinizing hormone-releasing hormone (LH-RH) analogue like Goserelin and some effective non-hormonal agents are Non-steroidal anti-inflammatory gels with reassurance and breast support have been used in treatment of mastalgia. Recently, a very commonly used, cheap oral contraceptive pill, Centchroman an Antiestrogen has been used for control of mastalgia and providing relief with minimal side effects in cyclical mastalgia<sup>4</sup>. In this we are evaluating the effectiveness of Centchroman measured by visual analogue scale (VAS), and compare it with Danazol.

**AIM**

The present study was conducted to assess the efficacy of centchroman as compared to danazol in treatment of mastalgia.

**MATERIAL AND METHODS**

A randomized prospective comparative study was conducted on 52 patients with mastalgia admitted in department of surgery of a tertiary care hospital in south west Bihar, India. The inclusion criteria was all women presenting with mastalgia with VAS score  $\geq 3$  between ages of 20-40 years. Duration of study was 6 months. The exclusion criteria included women with past history of breast carcinoma or family history of breast carcinoma, Patients with polycystic ovarian diseases, uterine cervical hyperplasia, First six months of Lactation and Pregnancy. Patients with mastalgia were randomized into 2 groups by sealed envelope random number table technique

handed over by the OPD sister in charge. We used a single blind (investigator assessing the response was blinded) two arm parallel design randomized controlled trial. The study was based on a non-inferiority hypothesis, with the aim of demonstrating an effectiveness of Centchroman either equal to or less than that of Danazol. The patients were given a detailed printed information sheet to explain about nature of breast pain, We additionally educated patients about the chance regarding inadequate or deferred/delayed period/menstruation by Centchroman with signed a consent form. After an initial clinical evaluation and breast imaging with ultrasound (and mammogram for cases over 35 years) to rule out any lumps or mammary ductal disease, Centchroman is considered to exacerbate polycystic ovarian disease and cervical hyperplasia, so an ultrasound scan of the pelvis and a gynecological examination were conducted to rule out patients with these conditions. For three months, patients were given either Centchroman 30 mg OD or Danazol 50 mg BiD. Patients were then monitored for four weeks, eight weeks, twelve weeks, and twenty-four weeks, and their reaction to therapy was measured using the VAS score. The drug therapy was extended for a total of 12 weeks, after which the patient was followed for another 12 weeks without medication to see whether the mastalgia recurred. Patients were asked to keep a pain diary and record episodes of pain daily and start of menstruation. A pain chart with a cyclical pattern of breast pain an premenstrual exacerbation as shown in the diagram below (Fig.A) The magnitude of mastalgia was determined using a visual analogue scale score of 0-10, with 0 indicating no pain and 10 indicating extreme pain.

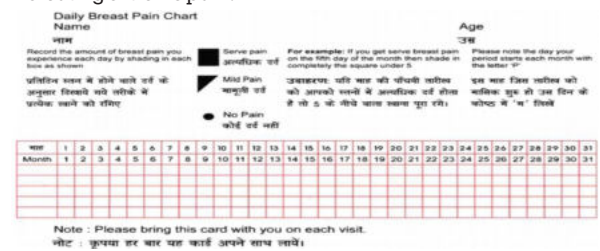


Figure. A

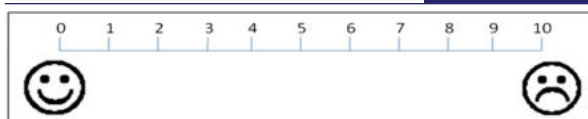


Figure. B “Visual Linear Analogue Scale for measuring pain”

**RESULTS**

Out of 52 patients, 20 were assigned to the Danazol group and 24 to the Centchroman group, 5 patients from Danazol group and 3 from centchroman group were excluded from study as they lost to follow up. In both arms, patient characteristics such as age, pre-treatment VAS score, and cycle length were identical. In both groups, the form of mastalgia (cyclical or non-cyclical) was similarly distributed. The baseline features are presented in Table 1.

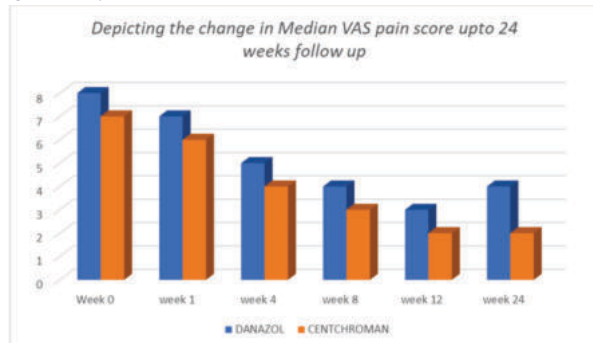
Both groups experienced substantial relief from mastalgia. Patients in the Centchroman group experienced faster relief from mastalgia than those in the Danazol group.

At 12 weeks In danazol 12 out of 20 (60%) and 17 out of 24 (70.8%) in centchroman were relieved of mastalgia.

At the 24-week In danazol 7 out of 29 (35%) and 18 out 24 (75%) in centchroman were relieved of mastalgia.

Relative risk of 2.280 means that the chance of achieving significant pain relief, was 2.280 times greater with centchroman as compared to danazol (Table 3).

**CHART 1.**



Since the VAS pain score was not usually distributed, Pain score was treated as continuous data the data was analysed using the Nonparametric Mann Whitney U test, and the median pain score was plotted against time to see if it changed over time.

Table 1. Comparison of baseline characteristics

	Danazol (mean) n=20	Centchroman (mean) n=24	P-value
Age	31.25	29.96	0.166*
Visual analogue scale score at base line scale 0-10	8.05	7.04	0.037*
Duration of menstrual cycle in days	27.40	28.13	0.415*
Number of cases with cyclical mastalgia	9	9	0.614**
Number of cases with Non-cyclical mastalgia	11	15	0.614**
P values with* by t test, P values with** by chi-square test			

The age, initial VAS score and duration of first menstrual cycle at start of study were normally distributed. Hence these were

analyzed by Student's t- test. Pattern of mastalgia either cyclical or non-cyclical were analyzed by Chi-square test.

Table 2. Effect of centchroman and danazol on mastalgia

Weeks	Danazol median VAS (range in parenthesis) n=20	Centchroman median VAS (range in parenthesis) n=24	P value Mann-Whitney U test comparing danazol with centchroman
0	8(5-10)	7(2-10)	.023
1	7(2-9)	6(2-8)	.024
4	5(3-8)	4(0-7)	.004
8	4(2-7)	3(0-8)	.208
12	3(2-5)	2(1-5)	.011
24	4(2-5)	2(1-7)	.002
P value (to assess change in pain score over time with in a group Green House Geisser test)	0.00 repeated ANOVA	0.00 repeated ANOVA	

The pain response over a period of time within same group was analyzed by using Repeated Measure Analysis of Variance (Repeated measure ANOVA). P-value less than 0.05 was considered significant. All values are two sided.

Table 3. Relative risk of significant “pain Relief” Centchroman versus Danazol.

At 12 weeks	1.256	0.675-2.338
At 24 weeks	2.280	1.126-4.617
Here centchroman is considered as “Exposure” and Danazol as the “Reference” category. RR of 2.280 indicates that centchroman is 2.280 times more effective in achieving pain relief when compared to Danazol.		

**DISCUSSION**

Danazol act as anti-gonadotrophin, lowering serum levels of luteinizing hormone (LH) and follicle stimulating hormone (FSH) and preventing ovulation. Its function is unclear since it only interferes with FSH and LH levels at higher doses. It is highly successful drug for extreme breast pain and nodularity, with a 70% success rate<sup>3</sup>. It outperforms bromocriptine in the treatment of cyclical mastalgia. Danazol, at a dosage of 100 mg once daily, was effective in 60% of cases after 12 weeks. The side effects of Danazol mainly amenorrhea, the incidence of which increases up to 100% with dose at 600 mg per day, weight gain, acne, amenorrhea and hirsutism. Danazol's side effects are all dose related. Danazol is currently reserved as a second line drug for mastalgia. Centchroman (Ormeloxifene-C30H35NO3) is a nonsteroidal and selective oestrogen receptor modulator. It does not interfere with ovulation, so does not hinder the restoration to fertility (after stopping). In less than 10% of cycles, it has only one side effect i.e delayed menses. There are no negative side effects such as nausea, vomiting, weight gain, or dizziness or on endocrine, hematologic, liver, or lipid function, or any severe side effects such as heart attack, stroke, or thrombosis. Centchroman is of low-cost and easily accessible for treatment of mastalgia (trade name SAHELI by Hindustan Latex Ltd., normal price Rs 2 per 30 mg tablet per day, compared to Danazol, which costs Rs 15 or more for 100 mg per day) and is more effective than Danazol and evening primrose oil for pain relief.<sup>7</sup> Since there were no significant side effects and some women skipped doses of alternate day treatment, the duration of administration was later increased to once daily. The median age in present study was 30.5 years. This correlates with the median age of 34 years for cyclical mastalgia in the study done by Davies et al.<sup>6</sup> When Centchroman was administered on a regular basis as opposed to an alternate day schedule,

the initial response was more pronounced. Danazol had a response rate of 60% after 12 weeks. A higher proportion of women in the Centchroman group continue to be pain-free even after quitting the treatment, implying a longer carry-over effect. At 24 weeks, the response to pain relief was 75 percent better with Centchroman (75 percent - 35 percent = 25 percent). In the study conducted by Tejawani et al, on 39 patients and after 12 weeks of treatment with Centchroman, 89.7% were relieved of pain similarly<sup>7</sup>. Dhar et al, for Centchroman in mastalgia, they found a 100% relief after 12 weeks of treatment with this drug.<sup>5</sup> Bansal V et al, studied effect of Centchroman on 203 patients and reported that after 12 weeks of treatment the mean VAS was similarly found to be 1.21.<sup>8</sup> In two separate studies Rathi et al, and Srivastava et al, reported more than 85% relief in pain after 12 weeks of treatment with Centchroman which supports present study.<sup>9,10</sup>

### CONCLUSION:

This study found that Centchroman therapy is a safe, at least equally effective, and less costly alternative to Danazol for the treatment of mastalgia

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