

## Original Research Article

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# Role of centchroman versus danazol in treatment of benign breast disorders

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## ABSTRACT

**Background:** The breast is a dynamic structure that undergoes cyclical changes throughout the menstrual cycle. Any aberration from normal physiological changes in breast produces different problem in breast. Many drugs are used for treatment for these disorders like Danazol, Bromocriptine, Tamoxifen and LH-RH analogue but still no consensus for any drug is present.

**Methods:** The aim of our study was to analyze the effectiveness of drug Centchroman and its comparison with Danazol in treatment of benign breast disorders in respect to symptoms relief, decrease in nodularity and lump size, recurrence, cost and side effects of drug. This prospective study was conducted on 250 patients of benign breast disorders attending surgical OPD between May 2018 to September 2019 in SMS medical college and Hospital, Jaipur.

**Results:** Tolerance and improvements in symptoms in centchroman group was more than danazol (100% vs 92.8%) with less recurrence in former group. While side effects varied between the two groups with menstrual irregularities more common in centchroman group.

**Conclusions:** The study shows that centchroman is safe, more effective and less expensive to Danazol for the treatment of benign breast disorders in long term.

**Keywords:** Benign breast disorder, Breast pain, Breast lump, Centchroman, Danazol

## INTRODUCTION

Benign breast disorders are common in young females, commonly affects population between 20-40 years of age. Pain, lump, nodularity- are common presentations. Different hypothesis for these disorders were given such as increase in estrogen secretion from ovary, deficient progesterone production and increase in prolactin secretion, have led to use of different medical and non-medical therapies.<sup>1</sup>

Danazol is antagonist that acts on pituitary-ovarian axis. Centchroman (ormeloxifene) is a non-steroidal selective estrogen receptor modulator with strong anti-estrogen and weak estrogenic and anti-progestin activity.

## METHODS

This prospective study was conducted on 250 patients of benign breast disorders attending the Surgical Outpatient department between May 2018 to September 2019 in SMS Medical College and Hospital, Jaipur. All women of reproductive age groups (12-44 years) with regular menses, having mastalgia lasting for more than 7 days per cycle, having benign breast lump and nodularity were included in the study and patients having polycystic ovarian disease, cervical hyperplasia and any past history of breast cancer were excluded from the study.

All patients were randomised into two groups after informed consent-Group A of 125 patients and Group B

of 125 patients. Group A were given Danazol 50 mg BD daily for 3 months Group B- were given Centchroman 30mg alternative day for 3 months.

Detailed history was taken and clinically examination was done, then ultrasound of breasts or/ and mammography was done. Fine Needle Aspiration Biopsy (FNAC) was done in all cases of breast lump to confirm the diagnosis and rule out malignancy. FNAC was also done of any dominant nodule in patients presenting with multiple nodules.

Breast pain chart was provided to patients presenting predominantly with mastalgia. Those presenting with nipple discharge underwent cytology of the discharge. All sexually active women were sent for a detailed gynaecological examination and in suspected cases, ultrasound (USG) of the pelvis was done to rule out polycystic ovarian disease and cervical hyperplasia.

The patients were evaluated at one week to assess tolerance to drugs. Subsequently patients were followed at 4 weeks & then at 12 weeks. At each follow up time, response of therapy was assessed in respect to decrease in pain for mastalgia, reduction in lump size and nodularity by clinical and radiological examination (Ultrasonography and Mammography). Then patients were followed for another 12 weeks without medications to assess the sustained response or recurrence of benign breast disorders.

#### Statistical analysis

#### Outcome variables

Symptom relief, decrease in nodularity, and recurrence. Visual analog scale (VAS) (0-10) was used to compare subjective, pain relief (0=no pain, 10=severe pain). Fine needle aspiration cytology was done in all the cases of breast, lump to confirm diagnosis and rule out malignancy and also of any dominant nodule in patients presenting with nodularity in breasts.

#### Outcome analysis

Data was analyzed using relevant statistical methods. Qualitative data was expressed in the form of proportions and percentages. Quantitative data was expressed in mean  $\pm$  SD (Complications). Qualitative data was compared using chi square test. Unpaired t-test was used to infer the difference in means.

## RESULTS

This study was carried on 250 patients of benign breast disorders confirmed by triple assessment in surgical outpatient department between 2018 to September 2019. All patients were randomised into two groups. Group A (125 Patients) were given Danazol and Group B (125 Patients) were given Centchroman.

**Table 1: Tolerance of drug.**

Time	Danazol		Centchroman	
	No. of cases	%	No. of cases	%
At 1st week	116	92.8	125	100

**Table 2: Improvement in mastalgia.**

Time	Danazol (%)	Centchroman (%)
4th week	34 (27.2)	20 (16)
8th week	65 (52)	58 (46.4)
12th week	90 (72)	110 (88)

**Table 3: Improvement in nodularity.**

Time	Danazol (%)	Centchroman (%)
4th week	0	0
8th week	25 (25)	12 (12)
12th week	81 (81)	96 (96)

**Table 3: Recurrence after 24 weeks.**

Time	Drug	Mastalgia (%)	Nodularity (%)
24 weeks	Danazol	58 (52.72)	52 (47.27)
	Centchroman	22 (19.13)	19 (16.52)

**Table 4: Side effect of drugs in treatment in two groups.**

Side effect of drugs	Danazol (%)	Centchroman (%)
Amenorrhoea	8 (6.4)	0
Delayed menses	12 (9.6)	20 (16)
Menorrhagia	6 (4.8)	5 (4)
Scanty menses	4 (3.2)	75 (60)
Allergic reaction	5 (4)	0
Weight gain	8 (6.4)	0
Acne	10 (8)	0
Hirsutism	0	0

## DISCUSSION

Benign breast disorders are one of the most common problems of breast in reproductive age group females. Most of the problems are of mild grade which subsided spontaneously but some are moderate to severe grade which require treatment at some stage of life. Mastalgia is the most common presentation. Many literatures suggest that hormonal alterations mainly with increased estrogen secretion, decrease in progesterone production and increase in Prolactin level are responsible for painful and nodular breast.

Danazol, which was approved by FDA for treatment of mastalgia which suppresses gonadotropin secretion, it

prevents luteinizing hormone surge and inhibits ovarian steroid formation. It is the one of the popular drugs for the treatment of benign breast disorders but its association with certain side effects like amenorrhea, weight gain, acne etc. forces clinician to try other medications.

Centchroman is a novel non-steroidal selective estrogen receptor modulator with strong anti-estrogen and weak anti progestin activity. It also has some weak estrogenic actions on some parts of the body like bones. It was developed at Chandigarh Drug and Research Institute, India and had been used as an alternative to steroid oral contraceptive pills. It was included in National Family Welfare Programme in 1995. Because of its selective anti-estrogen action and advantage of less frequent administration it is commonly used.

Our study showed that Centchroman was tolerated by all the 125 patients (100%) while 9 patients showed some intolerance to Danazol at first week. No group showed regression in nodularity at 4th week but after 8th weeks it was more in group A (25.6%) than group B (19.1%). This dominance of Danazol was not persisted beyond this and after 12 weeks of treatment, regression in nodularity was noticed more in group B (96%) than group A (81.6%). Tejwani et al found similar findings in their study.<sup>1</sup>

In present study initially up to 4 weeks, patients in Danazol group experienced more relief of mastalgia (27.2%) compared to centchroman (16%) but after 12 weeks Centchroman causes more reduction in the mastalgia (88%) compared to danazol (72%) these results comparable to Dhar et al, Srivastav et al and Khanna et al study. Greenblast et al, Pye et al, Watts et al, Gateley et al, Dhar et al, Srivastav et al and Tejwani et al found partial to complete improvement in mastalgia.<sup>2-6</sup>

Nodularity disappears partially or completely with Danazol treatment. Our study shows disappearance of nodularity which was more with Danazol in early period (up to 4 weeks) but with centchroman after 12 weeks. Similar finding also noted by Dhar et al, Srivastav et al, Tejwani et al and Seema Khanna et al.<sup>3</sup>

Recurrence of symptoms is common after treatment. In this study recurrence at 24 weeks is more with Danazol with mastalgia (52.72%), nodularity (47.27%) than centchroman (19.13% and 16.52% respectively). Dhar et al and Tejwani et al found less relapse with Centchroman in their study.

According to Mendoza et al nausea and irregular menses were most frequent side effects of Danazol.<sup>7</sup> In this study side effects were more with Danazol which are mostly menstrual related. All the menstrual irregularity was subsided after stopping medications. Centchroman maintain normal ovulatory cycle and has no apparent adverse effects on endocrine, haematological, liver and lipid function.

## CONCLUSION

We conclude that Danazol is effective drug for benign breast disorders but Centchroman is safe and more effective drug. Although a longer follow up period and further studies is necessary to prove its long-term efficacy.

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