



**OBSERVATION ON ROLE OF CENTCHROMAN VERSUS DANAZOL IN TREATMENT OF BENIGN BREAST DISORDER**

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**ABSTRACT**

Benign breast disorders includes spectrum of conditions which are related to the normal process of reproductive life and to involution. The common problem in benign breast disorders are breast pain, lump and nodularity. Many drugs have been tried for treatment of benign breast disorders like Danazol, Bromocriptine, Tamoxifen & LH-RH analogue but still a suitable drug is debatable. The aim of our study to analyse the effectiveness of drug Centchroman & its compare with Danazol in 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 64 patients of benign breast disorders attending surgical opd. The study shows that centchroman offers a 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**

Mammals are distinguished and named so because they have mammary glands or breasts. From puberty to death, the breast is subjected to constant physical and physiological alteration that are related to menses, pregnancy, lactation and menopause. 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. Benign breast disorders are most common problems and among it pain, lump and nodularity are common presentations. It most commonly affect the population between 20 to 40 years of age (R). Most women visit the clinicians for the fear of cancer so correct diagnosis and simple reassurance for benign, helps a lot. Different hypothesis for benign breast disorder such as increase in estrogen secretion from ovary, deficient progesterone production and increase prolactin secretion, have led to use of different medical and non-medical therapies. Among medical therapies, commonly used drugs are Danazol, Bromocriptine, Tamoxifen citrate, LH-RH analogue like Goserlin, OCP, Evening primrose oil and topical Non-steroidal anti-inflammatory gels. Reassurance, dietary measures like fat restriction and avoidance of methyl xanthines and breast support with sports brassier are nonmedical measures for the treatment of mild pain in breasts. Danazol is anti-gonadotropin that has its unique action on pituitary –ovarian axis. It is labeled as impeded androgen and currently most popular drug for the treatment of benign breast disorders. Centchroman is a non-steroidal Selective Estrogen Receptor Modulator with strong anti-estrogen and weak estrogenic and anti-progestin activity. It was developed in India and used as an alternative to steroidal oral contraceptive pill. Recently, role of Centchroman has been studied in treatment of benign breast disorders with encouraging results.

**MATERIAL AND METHODS**

This prospective study was conducted on 64 patients of benign breast disorders attending the Surgical Outpatient Department. All women of reproductive age groups (12-44years) with regular menses, having mastalgia lasting for more than 7 days per cycle, having benign breast lump and nodularity and not having polycystic ovarian disease, cervical hyperplasia and

any past history of breast cancer were included in this study. All patients were randomised into two groups after informed consent-Group A of 30 patients & Group B of 34 patients. Group A -These were given Danazol 100 mg daily for 3 months, Group B-These were given Centchroman 30mg daily for 3 months Detailed history and clinically examination were done, then ultrasound of breasts or/ and mammography was done. Fine Needle Aspiration Biopsy (FNAC) was done in all cases of breast lump confirm the diagnosis and rule out malignancy. FNAC was also done of any dominant nodule in patients presenting with nodularity in breasts. 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 were assessed by-decrease in pain for mastalgia, decrease 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.

**RESULTS**

This was a prospective study carried on 64 patients of benign breast disorders confirmed by triple assessment in surgical outpatients department. All patients were randomised into two groups. Group A (30 Patients) were given Danazol and Group B(34 Patients)were Centchroman. Centchroman was tolerated by all the 34 patients (100%) while 2 patients in Group A showed some intolerance to Danazol at first week.(Table1)

**Table 1: Tolerance Of Drugs**

Time	Danazol		Centchroman	
	No. of Cases	%	No. of Cases	%
At 1 <sup>st</sup> Week	28	93.33	34	100

At first week and 4<sup>th</sup> weeks, Danazol was more effective (28.57% & 52.38% respectively) in regression of mastalgia than Centchroman (13.04% & 43.47% respectively) but at 12 weeks ,Centchroman won the race of effectiveness in regressing mastalgia (86.95%) to Danazol (71.12%).[TABLE2]. No group showed regression in nodularity in first week but after 4 weeks it was more in group A (23.8%) than group B .This dominance of Danazol not persisted beyond this and after 12 weeks of treatment, regression in nodularity was noticed more in group B (95.62%) than group A(85.71%).[TABLE2]

**Table 2: Improvement In Symptoms**

		Mastalgia	Nodularity	Lump
1week	Danazol	6(28.57%)	00	00
	Centchroman	3(13.04%)	00	00
4 Week	Danazol	11(52.38%)	5(23.8%)	1(1.11%)
	Centchroman	10(43.47%)	2(8.69%)	1(9.09%)
12 Week	Danazol	15(71.72%)	18(85.71%)	2(22.22%)
	Centchroman	20(86.95%)	22(95.62%)	6(54.54%)

There was no response of any drug on size of lump at 1 week of treatment and at 4 weeks regression in lump size was more in group A (11.11%) than group B (9.09%) but after 12 weeks Centchroman was more effective (54.54%) than Danazol (22.22%).[TABLE2]

At 24<sup>th</sup> weeks (i.e. 3 months after stopping drug), 19 patients in Group A and 20 patients in Group B reported for follow up. Recurrence of mastalgia and nodularity were more with Danazol(57.89% & 52.63% respectively)than Centchroman (25% & 20% respectively). [TABLE 3]

**Table 3: Recurrence After 24weeks**

		Mastalgia	Nodularity
24Weeks	DANAZOL	11(57.89%)	10(52.63%)
	CENTCHROMAN	5(25%)	4(20%)

Danazol is very expensive in comparison to Centchroman in treatment of benign breast disorders and about 7.5 times costlier[TABLE 4]

**Table 4: Costs Of Treatment With Two Drug To Each Patient**

costs	Danazol	Centchroman
Per day	Rs 15 PER 100mg tablet	Rs 2 PER 30 mg tablet
Per month	Rs450	Rs 60
In 3 month	Rs 1350	Rs 180

Majority of patients (70.58%) in Group B patients had scanty menses followed by delayed menses (11.76%) while out of 30 patients in Group A patients 6.66% had delayed menses,3.33% patients had amenorrhoea 3.33% had menorrhagia. Group A patients also had acne (6.66%),allergic reactions in the form of urticaria (6.66%) and weight gain (3.33%) which were not seen in Group B patients [TABLE 5].Hirsutism was not noticed in any Group.

**Table 5: Side Effects Of Drugs In Treatment In Two Groups**

Side Effect of Drugs	Danazol	Centchroman
Amenorrhoea	1(3.33%)	00
Delayed Menses	2(6.66%)	4(11.76%)
Menorrhagia	1(3.33%)	1(2.94%)
Scanty Menses	00	24(70.58%)
Allergic Reactions	2(6.66%)	00
Weight Gain	1(3.33%)	00
Acne	2(6.66%)	00
Hirsutism	00	00

## DISCUSSION

Benign breast disorders are one of the 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 in some stage of life. Mastalgia is the most common presentation. Many literatures suggest that hormonal alterations mainly 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, prevent luteinizing hormone surge and inhibits ovarian steroid formation<sup>14</sup>. It is the one of the popular drug 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<sup>14</sup>.

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 body like bones. It was developed at Chandigarh Drug and Research Institute, India and had been used as an alternative to steroidal oral contraceptive pills .It was included in National Family Welfare Programme in 1995<sup>19,14</sup>. Because of its selective anti-estrogen action and advantage of less frequent administration, **Dhar A, Srivastav A** conclude after their clinical trial that it is safe to use in the treatment of mastalgia and fibroadenoma. Some study also found anti neoplastic property of centchroman similar to Tamoxifen.

In this study a comparative observation was noted between Danazol and Centchroman . Centchroman was tolerated by all patients where as Danazol arm showed some intolerance.

This supported the similar findings by **Tejwani et al** (2011) in their study. **Greenblast et al**(1977), **Pye et al** (1985), **Watts et al**(1987),**Gateley et al** (1991),**Kontostolis et al** (1997),**Dhar A ,Srivastav A** (2007) and **Tejwani et al** (2011) found partial to complete improvement in mastalgia. In present study also initially upto 4 weeks Danazol arm experienced more relief of mastalgia but after 12 weeks Centchroman causes more reduction in the symptom which is accordance to **Dhar A , Srivastav A** and **Seema Khanna et al** (2016) study. Nodularity disappears partially or completely with Danazol treatment which was shown by many studies like **Baker et al**(1979),**Humphrey et al**(1979), **Nezhat et al** (1980),**Mansel et al** (1982),**Gorin et al** (1984),**Tobiassen et al** (1984),**Tejwani et al** (2011).Present study also 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 A , Srivastav A** (2007),**Tejwani et al** (2011) and **Seema Khanna et al** (2016).

Recurrence of symptoms is common after treatment. In this study recurrence at 24 weeks is more with Danazol with mastalgia (57.89%), nodularity (52.63%) than centchroman (25% and 20%respectively). **Asch et al** (2007) found 34.6% recurrence in mastalgia of cases treated with Danazol. **Dhar et al** (2007) & **Tejwani et al** (2011) found less relapse with Centchroman in their study. Danazol is 7.5 times more costly than Centchroman. In **Seema khanna et al**(2016) study cost of one month therapy of Danazol is 720 Rs in india which is much more than Centchroman(20 Rs).

According to **Ortiz-Mendoza et al** (2004) nausea and irregular menses were most frequent side effects of Danazol. In this study side effects are more with Danazol which are mostly menstrual related. All the menstrual irregularity are subsided after stopping medications. Centchroman maintain normal ovulatory cycle and has no apparent adverse effects on endocrine, haematological, liver and lipid function. (**Kamboj VP et al** ;1977,**Lal J et al** ;1995,**Gupta RC et al** ;1995).

## CONCLUSION

This study shows that Danazol is effective drug for benign

breast disorders in early period but Centchroman offers a safe, more effective and less expensive in long term. Recurrence of disease are also less with Centchroman. As the numbers of cases under this study are small, so further studies with larger number of patients are needed to determine superiority of Centchroman over Danazol which is suggested in present study.

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