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" REGRESSION OF FIBROADENOMA IN RESPONSE TO CENTCHROMAN THERAPY" - A RANDOMIZED CONTROL TRIAL

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ABSTRACT

Background:
Fibroadenoma is a common cause of breast lump in young girls. Nearly 10–15 % of lesions regress spontaneously over the period of 6 to 60 months

Aims:
The aim of study was to investigate the role of Centchroman in regression of fibroadenoma in comparison to natural observation in persons who is willing for observation instead of excisional biopsy (enucleation) between 18 -30 yrs old.

Settings and Design:
The study was carried out at the outpatient clinic of Department of General Surgery, Govt. Dharmapuri medical College from November 2015 to October 2016
Study design: Randomized control trial

Material: 80 Patients

Methods and Material:
Patients aged ≤30 years with fibroadenoma were included. Patients with fibroadenoma equal to or larger than 3 cm and with polycystic ovarian disease were excluded. Patients were randomized in two groups. Patients in active therapy arm were prescribed Centchroman 30 mg on alternative days for 12 weeks, and another group was observed without any intervention (control group). Patients were followed at weeks 4, 8, 12, and 24 . USG Breast done at 0 days, 12 and 24 weeks for both groups to assess volume regression

Statistical analysis used:
The collected data was analysed with SPSS 16.0 version.To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference between the bivariate samples in Independent groups (Study group & Control group) Unpaired sample t-test was used. For the repeated measures (Volume zero day, 12th week & 24th week) the Repeated measures of ANOVA with adjustment for multiple comparisons to control the type I error, the Bonferroni test was used.To find the significance in categorical data Chi-Square test was used.

Results:
At the end of 12 weeks follow- up, 38 (95%) patients showed decrease in size in study as compared to 11(27%) in control group. At the end of 24 weeks follow-up, 15 (37.5%) patients showed complete disappearance compared to 5 (12.5%) patients in control group. 22 (55%) patients showed decrease in size as compared to 6 (15%) patients in control group.

Conclusions:
Centchroman therapy in Fibroadenoma treatment showed satistifically significant regression of volume in Patients more than 30 yrs old and young patients (<30 yrs) with suspicious histology, recurrence, family h/o carcinoma breast, anxiousness and no response to conservative management.

KEYWORDS : Dexmedetomidine , Intranasal, Midazolam , premedication

INTRODUCTION:
Fibroadenoma (FA) is the most common tumour of breast in young females (<30 yrs). It is a benign condition. FA is responsible for 15% palpable breast lump. It clinically presents as painless breast lump in reproductive age groups. FA is very rare as new lump over the age of 40 -45 yrs. Most of the FA cases are self diagnosed and consults surgeon in fear of breast cancer. For the patients with small FA (<3cm) below 30 yrs of age without suspicious cytology, simple observation with reassurance is enough because 15 to 30 % FA regress completely by simple observation over 1 to 6 yrs follow-up.

SUBJECTS AND METHODS:
The purpose of this study is to find the REGRESSION OF FIBROADENOMA IN RESPONSE TO CENTCHROMAN THERAPY (ORMELOXIFENE) in persons who is willing for observation instead of excisional biopsy (enucleation) between 18 -30 yrs old.

Study design: Randomized control trial
Material: 80 Patients
Study and follow-up period :6 months

INCLUSION CRITERIA:
1. Diagnosed as FA under triple assessment
2.Age 18 to 30 year
3.Fibroadenoma of sonographic size 3 cm or <3 cm
4.Patient not willing for excision (fear of scar)
5.Willing for observation with signed informed Consent

EXCLUSION CRITERIA:
1. Past history or family history of ca breast
2. Polycystic ovarian disease (PCOD)
3. Liver disease, renal failure
4. Lactation
5. Pregnant and who desire to be pregnant

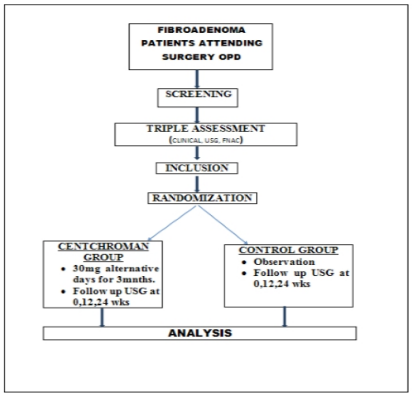
6. Complex fibroadenoma

Patients attending general surgery OPD with complaints of breast lump between 18 to 30 yrs of age subjected for detailed clinical history, clinical examination, ultrasonagram (USG) of both breasts and fine needle aspiration (FNAC)/ core needle biopsy

Patients who diagnosed as fibroadenoma (FA) and willing for simple observation with reassurance at least for 6 months were included in this study after getting informed consent. Willing patients after randomization included in study group and control group. Patients in study group given Centchroman 30mg orally on alternative days and in control group patients were only observed with simple assurance. Study group patients reviewed after 1 week to check tolerance and later follow-up done at 4, 8, 12, and 24 weeks. USG both breasts done at 0 days, 12 and 24 weeks for both groups to assess regression.

DISCUSSION WITH RESULTS:

Fibroadenoma (FA) is the most common tumour of females less than 30 yrs old & 20 % of the patients shows bilateral and 20 % shows multiple FA[1]. After verifying various studies about conservative management of mastalgia and benign breast conditions like fibroadenoma and fibroadenosis ,we inferred that only 15 % of fibroadenoma will regress spontaneously over 1 – 6 yrs observation[3,4,5]. Hence, we decided to do this study by assessing regression of fibroadenoma with centchroman theapy instead of simple observation.



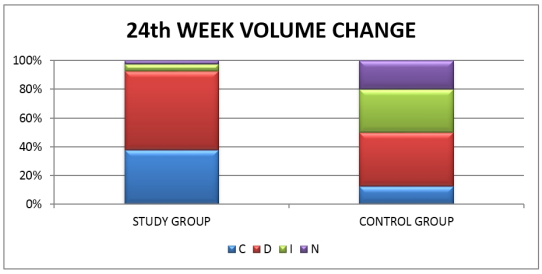
According to the study " Regression of Fibroadenoma with Centchroman: a RCT" done by Praksah laxmichand and Tejwani et al in AIIMS, Department of General Surgery, New delhi between Nov 2004 to Nov 2007 with 6 months follow-up, 31.8 % fibroadenomas in study group who had 30 mg centchroman OD for 90 days daily showed complete disappearance as compared to only 7.69 % in control group. 52.17% fibroadenomas decreased in size in study group as compared to control group.

In our study, patients had centchroman 30 mg OD on alternative days. Among 80 patients, 40 patients were included in study group and 40 patients in control group. Among these, 8 patients(10%) showed bilateral FA presentation. At the end of 12 weeks follow- up, 38 patients (95%) showed decrease in size in study group as compared to 11 patients (27%) in control group.

TABLE-1: 12th WEEK VOLUME CHANGE

SIZE	STUDY GROUP	CONTROL GROUP	TOTAL
Decrease	38	11	44
Increase	2	16	23
No change	0	13	13
TOTAL	40	40	80

At the end of 24 weeks follow-up,15 patients (37.5%) showed complete disappearance as compared to 5 patients (12.5%) in control group. Among these, 22 patients (55%) showed decrease in size as compared to 6 patients (15%) in control group. 21 patients (30%) in control group showed increase in size compared to study group where only 2 patients (5%) showed increase in size.



C-Complete disappearance D-Decrease I-Increase N-No change (In size)

TABLE-2: 24th WEEK VOLUME CHANGE

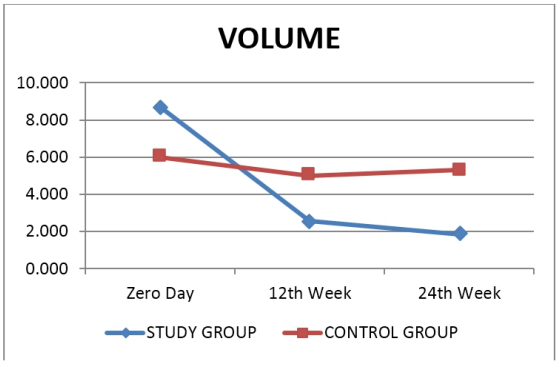
SIZE	STUDY GROUP	CONTROL GROUP	TOTAL
Complete disappearance	15	5	20
Decrease	22	6	37
Increase	2	21	14
No change	1	8	9
TOTAL	40	40	80

VOLUME OF FIBROADENOMA: Size of FA was calculated by doing breast ultrasound using 7.5 – MHZ linear probe on "Siemens versa" ultra sound scanner[2].

Volume in cubic centimetre is calculated by using the following formula

SIZE – a×b×c×0.52

a- largest dimension
b- dimension at right angle to a.
a- a+b/2



In our study, 8 patients (20%) showed menstruation abnormalities as compared to only 3 patients (7.5%) in control group which is satistically insignificant. Only 3 patients (7.5%) showed headache in study group, as compared to patients in control group.

Fibroadenoma is considered as result of increased responsiveness of lobular tissue to estrogen6. Presence of estrogen receptors on tissue obtained from fibroadenoma has been described. Hence, Centchroman (Ormeloxifene) has been used in this study.But decrease in size of the FA even after 12th week (after centchroman regimen getting over) has been observed. Possible explanation may be due to hit and run effect of the drug7, so it needs further study.

STATISTICAL ANALYSIS:

The collected data was analysed with SPSS 16.0 version. To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference

between the bivariate samples in Independent groups (Study group & Control group) Unpaired sample t-test was used. For the repeated measures (Volume zero day,12th week & 24th week) the Repeated measures of ANOVA with adjustment for multiple comparisons to control the type I error, the Bonferroni test was used. To find the significance in categorical data Chi-Square test was used. In all the above statistical tools the probability value .05 is considered as significant level.

LIMITATIONS OF THE STUDY:

This study presents data based on 6 months follow-up only. Long term results of centchroman on recurrent and further decrease in size requires further studies in future.

CONCLUSIONS:

1. Centchroman therapy in FA treatment showed satistifically significant regression of volume.
2. Long term results beyond 6 months needs further study
3. It is useful in patient who is willing for observation instead of Enucleation of FA
4. Patients more than 30 yrs old and young patients (<30 yrs) with suspicious histology, recurrence, family h/o carcinoma breast, anxiousness and those who had no response to conservative management are the ideal candidates for active management of excisional biopsy (enucleation of FA).

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