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RESEARCH ARTICLE

A REVIEW OF MASTALGIA IN PATIENTS WITH FIBROCYSTIC BREAST CHANGES COMPAIRINGEFFECTIVENESS OF CENTCHROMAN

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Abstract

Background: Mastalgia and fibrocystic disease of breast (fibroadenosis and fibroadenomaare common among the women in reproductive age group.Mostof the drugs used for these conditions are expensive and have side effects.Centchroman is a novel ono-steroidal antiestrogen,becouse of its selective antiestrogenic action cantchroman used for the treatment of mastagia and fibroadenoma.Centchroman therapy in FA treatment showed statistically significant regression of volume.and regression of pain.

AimsandObjectives:-The purpose of this study is to study the effectiveness of centchroman on mastalgias and fibroadenomasStudy design:Randomized control trial Material: 60 Patients Study and follow-up period 1 Year

Materials and mathods: Patients attending general surgery op with complaints of breast lump less than35 yrs of age will be taken detailed clinical history, clinical examination, ultrasonagram (USG) of both breast and fine needle aspiration (FNAC)/ core needle biopsy Patients who are all diagnosed as fibroadenoma (FA) and willing for simple observation with reassurance at least for 6 months will be included in this study after getting informed consent randomization included in study group and control group. Patients in study group will get Centchroman 30mg orally on alternative days and for control group patients only observation with simple assurance. Study group patients will be reviewed after 1week to check tolerance and later follow-up at 4, 12, and 24 weeks. USG will be done at 0 days, 4, 12 and 24 weeks for both groups to assess regression

Results: The study showed statistical difference in fibroadenoma patients with significant reduction in their sizes in patients treated with centchroman even at 4th week. Further the difference between study and control group became statistically highly significant at 12th and 24thweek.The study did not show any statistical difference in mastalgia patients treated with centchroman at 4th and 8th week. But the difference between study and control group became statistically significant at 12th and 24th week with greater reduction in pain.

Conclusions: Centchroman therapy in FA treatment showed statistically significant regression of volume.Centchroman therapy

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inmastalgias treatment showed statistically significant regression of pain,Long term results beyond 6 months needs further study.It is useful in patient who is willing for observation instead of enucleation of FA .Patients more than 35 yrs old and young patients (<35 yrs) with suspicious histology, recurrence, family h/o carcinoma breast, anxiousness and no response to conservative management are the ideal candidate for active management as excisional biopsy (enucleation of FA).

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Introduction:-

Fibroadenoma (FA) is the most common tumour of breast in young females (<35 yrs) and second most common breast tumour in females. It is a benign condition. FA is responsible for 15% palpable breast lump.It is clinically presents as painless breast lump in reproductive age groups. FA is very rare as new lump over the age of 40 - 45yrs.Most of the FA cases are self diagnosed and consult surgeon in fear of breast cancer. For the patients with small FA (<3cm),below the 35 yrsofage without suspicious cytology, FA is very slow growing hence simple observation with reassurance is enough because 15 to 30 % FA regress completely by simple observation over 1 to 6 yrs follow-up.Breast pain among women, with or without lump is common complaint and a cause of significant anxiety and fear of breast cancer . Annually 200,000 breast disorders are identified and it is noted that most of the palpable lesions are benign . Approximately half of the women in reproductive age group suffer from Benign Breast Diseases (BBD). Among the BBD, mastalgia, fibrocystic disease and fibroadenoma are the most common. Mastalgia (Greek masto-breast and algia-pain) signifies breast pain. It can be classified into twotypes;-Cyclic mastalgia: Characterized by more pain during the menstrual cycle and it is frequently related with fibrocystic breast changes or duct ectasia. Minimal tenderness during menstrual cycle is thought to be typical, and is normally associated with menstrual cycle and/or premenstrual syndrome(PMS)Non-cyclic mastalgia: Characterized by the pain, which is unaltered during the menstrual cycle. This type is not common. It has different causes and difficult to diagnose. Non- cyclical pain is not usually related with the menstrual cycle. Some level of non-cyclic breast tenderness is present because of hormonal changes in adolescence, pregnancy andmenopause.Breastfeeding is additionally one of the reasons for non-cyclic pain. Fibrocystic breast disease is otherwise called Fibroadenosis. Fibrocystic changes can happen in one or both breasts. A post mortem study conducted in 2005 by **Courtillot C et al**., concluded that 50% women had some form of fibrocystic disease and 20% had fibroadenoma.Most of the drugs used for fibroadenosis and mastalgia are expensive and have side effects.This study was conducted to find out the efficacy of centchroman, a Selective Estrogens Receptor Modulator (SERM) onregression of fibroadenosisandmastalgia

Aims And Objectives:-

The purpose of this study is to study the effectiveness of centchroman on mastalgiasandfibroadenomasStudy design: Randomized control trial Material: 60 PatientsStudy and follow-up period 1 Year

Inclusion criteria:

Females of age less than 35 who had mastalgia with or without nodularity.Patients with fibroadenomas of size 1.5 to 3cm.Patients consented for inclusion in the study according to designated proforma.Patient not willing for excision (fear ofscar

Exclusion criteria:

Patients more than 35 years ofage,Patients who are pregnant, lactating and planning for pregnancy in near future.Patients with polycystic ovariandisease,Patients who have history of breast carcinoma or family history of breast carcinoma,Patients diagnosed to have associated chest wall disorder and dermatologicallesions,Lactation,Pregnant and who desire to pregnant ,Complex fibroadenoma.

Materials And Methods:-

Patients attending general surgery op with complaints of breast lump less than35 yrs of age will be taken detailed clinical history, clinical examination, ultrasonagram (usg) of both breast and fine needle aspiration (fnac)/ core needle biopsy patients who are all diagnosed as fibroadenoma (fa) and willing for simple observation with

reassurance at least for 6 months will be included in this study after getting informed consent with sign in both hindi and english language .willing patients after randomization included in study group and control group. Patients in study group will get centchroman 30mg orally on alternative days and for control group patients only observation with simple assurance.

Study group patients will be reviewed after 1week to check tolerance and later follow-up at 4, 12, and 24 weeks.usg will be done at 0 days, 4, 12 and 24 weeks for both groups to assess regression.

Observations And Results:-

In fibroadenoma group, at each visit patients were measured the volume of lump using ultrasonography and compared with the volume of lump they had in their previous visit. By this method, patients were categorised into four groups by their response to intervention. At the end of four weeks, in study group, 0/15 patients had complete regression, 4/15 patients had decrease in volume of the breast lump comparing with their first visit, 11/15 patients had same volume of the breast lump as their first visit, 0/15 patients showed increase in volume compared with their first visit. Whereas in control group, 0/15 patients had complete regression, 0/15 patients had decrease in volume of the breast lump comparing with their first visit, all of the control group patients i.e., 15/15 patients had no change in volume of the breast lump when compared with their first visit, 0/15 patients had increase in size of the lump compared with their first visit. when the results were compared, p value(0.0317) was found to be statistically significant.At the end of twelve weeks, in study group, 10/15 patients had complete regression, 5/15 patients had decrease in volume of the breast lump comparing with their third visit, 0/15 patients had same volume of the breast lump as their third visit, 0/15 patients showed increase in volume compared with their third visit. Whereas in control group, 0/15 patients had complete regression, 3/15 patients had decrease in volume of the breast lump comparing with their third visit, 11/15 patients had no change in volume of the breast lump when compared with their third visit, 1/15 patient had increase in size of the lump compared with their third visit. when the results were compared, p value(0.0001) was found to be statistically highly significant.At the end of twenty four weeks, in study group, 12/15 patients had complete regression, 3/15 patients had decrease in volume of the breast lump comparing with their fourth visit, 0/15 patients had same volume of the breast lump as their fourth visit, 0/15 patients showed increase in volume compared with their fourth visit. Whereas in control group, 0/15 patients had complete regression, 3/15patients had decrease in volume of the breast lump comparing with their fourth visit, 11/15 patients had no change in volume of the breast lump when compared with their fourth visit, 1/15 patient had increase in size of the lump compared with their fourth visit. when the results were compared, p value(0.0001) was found to be statistically highly significant.

Table no.1:- Fibroadenoma Volume Change Study Group.

Volume change	4^{th} week	12^{th} week	24^{th} week
Complete regression C	0	10	12
Decrease in size D	4	5	3
No change N	11	0	0
Increase in size I	0	0	0

Table no.2:- Fibroadenoma Volume Change Control Group.

Volume change	4^{th} week	12^{th} week	24^{th} week
Complete regression C	0	0	0
Decrease in size D	0	3	3
No change N	15	11	11
Increase in size I	0	1	1

Table no.3:- FIBROADENOMA 4^{TH} WEEK.

Volume change	Study	Control	TOTAL
C	0	0	0
D	4	0	4
N	11	15	26
I	0	0	0
TOTAL	15	15	30

Chi- Square test: 4.615 P value:0.0317

Tableno.4:- FIBROADENOMA 12^{T} wk

Volume change	Study	Control	TOTAL
C	10	0	10
D	5	3	8
N	0	11	11
I	0	1	1
TOTAL	15	15	30

Chi- Square test: 22.500 P value:0.0001

Table no.5:- FIBROADENOMA 24^{TH}WK.

Volume change	Study	Control	TOTAL
C	12	0	12
D	3	3	6
N	0	11	11
I	0	1	1
TOTAL	15	15	30

Chi- Square test:16.000 P value:0.0001

In mastalgia group, patients were randomly categorised into study and control groups each containing 15 patients. Patients were followed up in each visit with visual analog score for mastalgia ranging from 0 to 10.At first visit on Day 0, both groups had two patients with VAS 2, both groups had eight patients with VAS 4, and both groups had five patients with VAS 6. Hence both groups were found to be comparable initially before any intervention to beprovided.At second visit on 4^{th} week, 0/15 patients in study group had VAS 0, 3/15 patients in study group had VAS 2, 9/15 patients in study group had VAS 4, 3/15 patients in study group had VAS 6, 0/15 patients in study group had VAS 8 and 0/15 patients in study group had VAS 10. Whereas 0/15 patients in control group had VAS 0, 2/15 patients in control group had VAS 2, 8/15 patients in control group had VAS 4, 5/15 patients in control group had VAS 6, 0/15 patients in control group had VAS 8 and 0/15 patients in control group hadVAS10. When the results were compared, p value (0.6843) was not found to be statistically significant.At fourth visit on 12^{th} week, 8/15 patients in study group had VAS 0, 4/15 patients in study group had VAS 2, 1/15 patients in study group had VAS 4, 2/15 patients in study group had VAS 6, 0/15 patients in study group had VAS 8 and 0/15 patients in study group had VAS 10. Whereas 1/15 patients in control group had VAS 0, 2/15 patients in control group had VAS 2, 8/15 patients in control group had VAS 4, 4/15 patients in control group had VAS 6, 0/15 patients in control group had VAS 8 and 0/15 patients in control group hadVAS10. When the results were compared, p value (0.0067) was found to be statistically highly significant.At fifth visit on 24^{th} week, 12/15 patients in study group had VAS 0, 1/15 patients in study group had VAS 2, 0/15 patients in study group had VAS 4,2/15 patients in study group had VAS 6, 0/15 patients in study group had VAS 8 and 0/15 patients in study group had VAS 10. Whereas 2/15 patients in control group had VAS 0, 1/15 patients in control group had VAS 2, 9/15 patients in control group had VAS 4, 3/15 patients in control group had VAS 6, 0/15 patients in control group had VAS 8 and 0/15 patients in control group had VASWhen the results were compared, p value (0.0010) was found to be statistically highlysignificant.Centchroman drugs were found to have safety profile with minimal side effects. In this study conducted, delayed menstruation and gastritis were the two side effects to get manifested. In study group, 25/30 patients had no side effects whereas 4/30 patients had menstrual delay and 1/30 patient had gastritis. In control group, 28/30 patients had no side effects, 0/30 patients had menstrual delay and 2/30 patients had gastritis. When these results were statistically analysed, they were found to be insignificant. Hence two groups are comparable in view of side effects.The study showed statistical difference in fibroadenoma patients with significant reduction in their sizes in patients treated with centchroman even at 4^{th} week. Further the difference between study and control group became statistically highly significant at 12^{th} and 24^{th}week.The study did not show any statistical difference in mastalgia patients treated with centchroman at 4^{th} and 8^{th} week. But the difference between study acontrol group became statistically significant at 12th and 24th week with greater reduction in pain.

Table no.6:- Mastalgia Study Group.

VAS score	Day 0	4^{th} week	12^{th} week	24^{th} week
0	0	0	8	12
2	2	3	4	1
4	8	9	1	0

6	5	3	2	2
8	0	0	0	0
10	0	0	0	0

Table no.7:- Mastalgia Control Group.

VAS score	Day 0	4^{th} week	12^{th} week	24^{th} week
0	0	0	1	2
2	2	2	2	1
4	8	8	8	9
6	5	5	4	3
8	0	0	0	0
10	0	0	0	0

Chi- Square test: 0.759 P value:0.6843

Table no.8:- Side Effects.

Side effects	Study	Control	TOTAL
None	25	28	53
Menstrual Delay	4	0	4
Gastritis	1	2	3

Chi- Square test: 4.543

Discussion:-

Fibroadenomas and mastalgias are the most common benign breast disorders. Fibroadenomas are the second most common neoplasm of females. After verifying lot of studies regarding conservative management of mastalgias and benign breast conditions, I decided to conduct this study in my hospital for my dissertation comparing with patients kept under simple observation. It is well known fact that 15 % of fibroadenomas will regress spontaneously over one to six years of observation.As per my study patients on centchroman were put on alternative day single dose regimen of dose 30 mg. Both study group patients and control group patients were regularly followed at 4^{th} week, 12^{th} week and finally at 24^{th} week. Totally 60 patients were taken in this study, out of which 30 patients were categorised into fibroadenoma group and the other 30 patients into mastalgia group. Out of 30 patients in fibroadenoma group, 15 patients were randomised into study group and the remaining 15 patients were put into control group. Similarily in mastalgia group of 30 patients, 15 were taken into the study group and the rest 15 patients were randomised into controlgroup.The study showed statistical difference in fibroadenoma patients with significant reduction in their sizes in patients treated with centchroman even at 4th week. Further the difference between study and control group became statistically highly significant at 12th and 24th week. The study did not show any statistical difference in mastalgia patients treated with centchroman at 4th and 8th week. But the difference between study and control group became statistically significant at 12th and 24th week with greater reduction in pain.

Conclusion:-

Centchroman is a safe nonsteroidal drug for the treatment of mastalgia and fibroadenoma. Centchroman therapy in FA treatment showed statistically significant regression of volume.Centchroman therapy in mastalgias treatment showed statistically significant regression of pain.Long term results beyond 6 months needs further study. It is useful in patient who is willing for observation instead of enucleation of FA. Patients more than 35 yrs old and young patients (<35 yrs) with suspicious histology, recurrence, family h/o carcinoma breast, anxiousness and no response to conservative management are the ideal candidate for active management as excisional biopsy (enucleation of FA).In terms of management of fibroadenosis ,centchroman is a safe and cost effective drug with significant efficacy on regression of fibroadenosis with minimal side effect.

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