CLINICO-PATHOLOGICAL PROFILE OF MASTALGIA IN AND AROUND KANPUR

S. K. Katiyar, Sanjay Kumar Nigam, P. K. Omar

1. Associate Professor, Department of General Surgery, Rama Medical College Hospital & Research Centre, Kanpur.
2. Associate Professor, Department of Pathology, Rama Medical College Hospital & Research Centre, Kanpur.
3. Assistant Professor, Department of Anaesthesia, Rama Medical College Hospital & Research Centre, Kanpur.

CORRESPONDING AUTHOR
Dr. S. K. Katiyar,
FIAGES, 675,
Singhpur, Kanpur-208017,
E-mail: drskkatiyar59@rediffmail.com,
Ph: 0091 9415044878.

ABSTRACT: Mastalgia is a general term used to describe number of conditions, in which pain is present in one or both breast (s). It is the commonest breast symptom presenting in surgical clinics. Most patients come to the Doctor, because of the fear of malignancy. However the ratio of benign to malignant cases in clinics is 10:1. Simply 3 major type of breast pain may be recognized Cyclical, Non-cyclical pain; extra mammary pain Aim of This study was focused to study the cause of mastalgia i.e. to correlate the clinical diagnosis to the histological examination and conservative management. Female patients between 15 years – 55 years of age with complain of pain in breast were accepted for study. A thorough general as well as local examination was done. Mammography was done in patient above 35 years of age.

The treatment protocol is decided, all patient coming to OPD in first 15 Days of month were given Evening primrose oil in dose of 500 mg 2 cap thrice a day for a period of two months. All those coming in next half were treated with danazol 200mg /day for two months. Patients were called to OPD on every 15th day to assess the response and also to check that the patient was appropriately following the given treatment. The exact cause of mastalgia is still unknown. Severe mastalgia can however disrupt normal life by interfering with sleep, relationship with husband and children and may also affect occupation of working women. In our study we have tried to treat patient with cyclical mastalgia and true mammary non cyclical mastalgia patients using, Evening primrose oil (EPO) and danazol as line drugs. Those not responding were treated with Tamoxifen or Bromocriptine randomly (IInd) line therapy. Danazol and EPO were used again by crossover as IIIrd line therapy.

Mastalgia is a common symptom reported in surgical OPD. The highest incidence of mastalgia was found in patients of 36-45 age groups. Cyclical mastalgia was the commonest type constituting 63.75%. Mastalgia is more commonly seen in left than right breast (40% vs 28.75%). Mastalgia was more commonly observed in multiparous we conclude that Danazol seems to be best available drug for both cyclical and non cyclical mastalgia. However, Tamoxifen approaches the same efficacy in both groups; in fact it has a better response in non cyclical mastalgia group. EPO is better drug for young and for women who do not want their period to be disturbed.

KEY WORDS: Mastalgia, Tamoxifen, Danazol.

INTRODUCTION: Mastalgia is a general term used to describe number of conditions, in which pain is present in one or both breast (s). It is also called Muzodynia. It is one of the most common presenting symptoms of benign breast diseases, which may be cyclical or continuous. **Morrow M** [1] in a study experienced the prevailing apathy towards females with mastalgia. It is the commonest breast symptom presenting in surgical clinics. Most patients come to the Doctor, because of the fear of malignancy. However the ratio of benign to malignant cases in clinics is 10:1. **Adner DN et al** [2] reported that patients with severe mastalgia interfered with sexual activity, physical activity and with social activity. The clinical picture can be divided into cyclical and non- cyclical patterns of pain by studying the simple clinical history. Despite the lack of concrete evidence, it seems likely that breast pain with cyclical pattern is of hormonal origin. Breast pain especially cyclical mastodynia is rarely associated with malignant neoplasm of breast. Patients with mastalgia require treatment but because of spontaneous resolution of pain due to hormonal events like pregnancy and menopause the results of therapeutic response is difficult to assess.

Various therapies ranging from local support vitamin B_2, B_6 E and C, diuretics, NSAIDs, progestational agents thyroxine, plant extracts like vitex agnus castus, evening primrose oil (EPO), Danazol, Bromocriptine, Tamoxifen and lately LHRH analogues have been used to treat mastalgia. There still exists a small but significant group which does not respond to any form of medical treatment this may be due to resistant from or poor diagnostic classification. **Aim** of This study was focused to study the cause of mastalgia i.e. to correlate the clinical diagnosis to the histological examination and conservative management. In order to randomize treatment it was suggested that clinical entities can be distinguished as: **Preece et al** [3]

1. Cyclical pronounced
2. Duct ectasia/ periductal mastitis
3. Tietze's syndrome
4. Trauma
5. sclerosing adenosis
6. Cancer
7. Idiopathic
8. Miscellaneous.

Fentiman [4] found that simply 3 major type of breast pain may be recognized.

a). Cyclical
b) Non-cyclical pain
c) Extra mammary pain

MATERIAL AND METHODS: Female patients between 15 years – 55 years of age attending the Outpatient Department of surgery, Rama medical college & hospital with complain of pain in breast were accepted for study. A detailed history was taken and noted. It was made sure that the patient had not taken hormonal therapy for the last 6 weeks. Also that the patient's were not pregnant and did not wish to become so within a period of 6 months. Patient who had undergone hysterectomy were excluded from study. For our study the patient had to fulfill all /any of the following criteria.

- The pain had to be of such severity that the physical activity of patient was curtailed.
- The patient had persistent marked pain throughout menstruation cycle.

- The pain was not relieved by mild analgesic (NSAID)
- The pain had to be episodic and exacerbated during the cycle.

A thorough general as well as local examination was done. Mammography was done in patient above 35 years of age. If there was any suspicion a Fine Needle Aspiration Cytology was asked for. If all clinical as well as investigative procedures confirmed that we were dealing with a Benign intramammary disease causing mastalgia the case was deemed fit for our study. We divided the patients into three groups.

Group I cyclical mastalgia
Group II Non-cyclical mastalgia
Group III Post menopausal mastalgia.

The patients were asked to fill up a linear pain scale to the amount of pain they at every 15 days interval for 3 months. The total score was kept 16. The patients were examined each month to study the linear pain scale and to look for any side effect.

TREATMENT: The treatment protocol is decided, all patient coming to OPD in first 15 Days of month were given Evening primrose oil in dose of 500 mg 2 cap thrice a day for a period of two months. All those coming in next half were treated with danazol 200mg /day for two months. Patents with extra mammary pain were offered NSAIDs and local anaesthetic. Patient were asked to make a response chart for their symptoms during the therapy. Keeping CBS scoring system.

CBS I Excellent response no residual symptom
CBS II Substantial response leading some pain considered tolerable.
CBS III Poor response – Substantial pain
CBS IV No response.

Patients were called to OPD on every 15th day to assess the response and also to check that the patient was appropriately following the given treatment. After two months of therapy the score was assessed. If the score were CBS II the same therapy was continued till remission occurs. However if the score was CBS III, IV second line drugs bromocriptine and tamoxifen were used randomly.

Bromocriptine in dose of 1.25-2.5 mg/day
Tamoxifen 20 mg/day

Response was assessed using the same score after 2 month of therapy.

Those cases not responding to the above were again treated with Danazol/ EPO, response assessed after two months using same score.

RESULTS: A total of 104 patients complaining of severe breast pain were examined during the span of 12 months (Nov 2011 – OCT 2012). Out of these 80 cases were deemed fit for the study as they fulfilled the criteria mentioned in material and methods.

TABLE-I AGE

AGE GROUP	NUMBER	PERCENTAGE (%)
15-25	15	18.5%
26-35	30	37.5%
36-45	31	38.75%
46-55	4	5%
TOTAL	80	100%

TABLE –II DISTRIBUTION OF CASES.

TYPE	NUMBER	PERCENTAGE (%)
Cyclical mastalgia	51	63.75%
Non cyclical mastalgia	24	30%
Extramammary pain	5	6.25%
TOTAL	80	100%

TABLE- III RESULT OF Ist LINE THERAPY FOR CYCLICAL MASTALGIA-

DRUG	**NUMBER**	**RESPONSE**	**NO RESPONCE**
EPO	26	9(34.6%)	17(65.38%)
DANAZOL	25	17(68%)	8(32%)
Total	**51**	**26**	**25**

TABLE –IV RESULT OF Ist LINE THERAPY FOR NON CYCLICAL MASTALGIA

DRUG	**NUMBER**	**RESPONSE**	**NO RESPONCE**
EPO	12	2(16.66%)	10(83.33%)
Danazol	12	4(33.33%)	8(66.66%)
	24	6(25%)	18(75%)

TABLE-V RESULT OF IInd LINE THERAPY FOR CYCLICAL MASTALGIA

DRUG	**NUMBER**	**RESPONSE**	**NO RESPONCE**
Tamoxifen	15	10(66.66%)	5(33.33%)
Bromocriptine	10	4(40%)	6(60%)
	25	14	11

TABLE-VI RESULT OF IInd LINE THERAPY FOR NON CYCLICAL MASTALGIA

DRUG	**NUMBER**	**RESPONSE**	**NO RESPONCE**
Tamoxifen	9	4(44.44%)	5(55.53%)
Bromocriptine	9	1(11.11%)	8(88.88%)
Total	**18**	**5**	**13**

TABLE- VII RESULT OF CROSSOVER THIRD LINE THERAPY

DRUG	NUMBER	RESPONSE	NO RESPONCE
Danazole used in patients not responding to EPO	6	4	2
EPO used in patients not responding to Danazole	5	1	4
Non cyclical Danazol	10	4	6
EPO	3	0	3

DISCUSSION: The exact cause of mastalgia is still unknown. Severe mastalgia can however disrupt normal life by interfering with sleep, relationship with husband and children and may also affect occupation of working women. In our study we have tried to treat patient with cyclical mastalgia and true mammary non cyclical mastalgia patients using, Evening primrose oil (EPO) and danazol as line drugs. Those not responding were treated with Tamoxifen or Bromocriptine randomly (IInd) line therapy. Danazol and EPO were used again by crossover as IIIrd line therapy. We found that 38.75% of patients complaining of mastalgia were uncommon in age less than 25 years (18.75%) and above 45(5%). Mean age of mastalgia was 33-40 years. In his study of 232 patients at Welsh national school of medicine **Preece et al**[5] found that most frequent age group complaining of mastalgia was 31-45 years (45) closely followed by 41-45 years (40), and 36-40(32). In another study by **Wisbey et al**[6] Welsh national school of medicine at Cardiff (1983) it was seen that in patients of cyclical mastalgia mean age was 35.7(±8.7),where as in patients with non cyclical mastalgia mean age was (42.5±9.8) years. Extra mammary mastalgia was seen in age group (40±10.2) years. In our study we found 88.25% of cases were married out of which 8.30% were nullipara, 29.57% were unipara and 52.11% were multipara, 91% of the parous women breast fed their children. These findings disapprove the earlier belief that the mastalgia was more common in "frustrated unhappy nullipara" as said by **Jeffcoate et al** [7].

Our study recommended the old finding that mastalgia was more common on left side **Preece et al** [5], 40% of cases had pain in left breast, 30% had pain in right side and 30% had pain bilaterally. However, there was no significant difference in side of pain in patients of cyclical mastalgia. Most of the patients in this study were non vegetarians. This complements the earlier belief that mastalgia is seen more commonly in people with deranged lipid profile due to inadequate intake of essential fatty acids. **Gateley et al**[8]**.** In this study we found fibroadenosis (57.5%) as the commonest cause of mastalgia. Fibroadenosis along with fibroadenoma was present in 16.25% cases. Fibroadenosis with hyperplasia and cystic changes were present in 15% cases. This substantiates that mastalgia can be present in normal breast tissue and the whole process is an aberration of normal development and involution (AND) rather than a disease process. **Shukla HS et al** [9] in his study found that patients showing fibrocystic disease and fibrosis showed poor response to therapy.

Pye et al [10] studied effect of EPO, Danazol and Bromocriptine in a randomised trial in patients with mastalgia. They observed grade I or II response in 77% cases with cyclical mastalgia (Danazol 70%, EPO 45% and 47% response to Bromocriptine placebo response was just 19%). In our study a grade I or II response was seen with 50.98% patients using Ist line

therapy, danazol in 17/25(68%) of patients with cyclical mastalgia, however, 32% patients did not respond to treatment using 200mg/day dose. Most of the patients who responded were with two months. Only 34.6% patients responded to EPO using 3gms/day dose for 2 month, 65.38% did not respond. However, 49.02% patients required IInd line drugs. In a study **Mansel et al[11]** found that response rate to danazol is not significantly altered when used in dose of 200mg/day or 400-600mg/day. It has been unanimously agreed that dose of 200mg/day is adequate.

CONCLUSION: Mastalgia is a common symptom reported in surgical OPD. The highest incidence of mastalgia was found in patients of 36-45 age groups. A most 76% patients were in third to fifth decade of their life. Cyclical mastalgia was the commonest type constituting 63.75% followed by non cyclical intramammary pain which was present in 30% cases. Extra mammary pain was seen in 6.25% cases. Mastalgia was more common in married women probably reflecting early age of marriage in our setup. Mastalgia is more commonly seen in left than right breast (40% vs 28.75%).Mastalgia is more commonly seen in premenopausal women than postmenopausal women (95% vs. 5%). Most of the women had normal menstrual history. Mastalgia was more commonly observed in multiparous and uniparous women (52.11% & 29.57%). Mastalgia was more commonly seen in non vegetarians (63.7% vs 36.25%). FNAC reports proved that fibroadenosis was the cause of pain in 88.75% cases and fibroadenoma alone was in 5% cases.

EPO when used as Ist line therapy in cyclical mastalgia, dose of EPO 3gm/day for 2 months is effective in attaining useful response in 4.6%. Danazol when used in dose of 200mg/day for 2 months is effective attaining useful response in 68% cases. However in non cyclical mastalgia the results were 16.66% and 33.33% for EPO and danazol respectively. After use of third drug (crossover of groups) a response of 45.45% was seen in patients with cyclical mastalgia and 30.76% in non cyclical mastalgia. 15/80 patients were resistant to hormonal manipulation.

We conclude that Danazol seems to be best available drug for both cyclical and non cyclical mastalgia. However, Tamoxifen approaches the same efficacy in both groups; in fact it has a better response in non cyclical mastalgia group. EPO is better drug for young and for women who do not want their period to be disturbed.

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