

Original Research Article

Role of danazol in management of mastalgia: a tertiary care experience from North India

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ABSTRACT

Background: Mastalgia is one of the most common complains, for which women consult their general practitioner. Majority of the patients presented with fear of cancer so patient education and availability of quality radiological and pathological services are crucial in the management of patients with mastalgia. This study is aimed to assess the efficacy of danazol on cyclical and non-cyclical mastalgia.

Methods: The study was conducted at Sher-I-Kashmir institute of medical sciences (SKIMS), Srinagar between January 2018 to July 2019. All the patients with mastalgia between 19 to 45 years presenting to surgical OPD were considered eligible for the study. After standard triple assessment, all our patients received 100 mg of danazol twice a day for a period of 3 months. Data was collected and analyzed.

Results: All the patients with mastalgia between 19 to 45 years presenting to surgical OPD were considered eligible for the study. 72% of our patients presented with cyclic mastalgias while as 28% had non cyclic symptoms. 89.65% of patients in cyclic group had responded to cap. Danazol 100 mg twice daily and 81.81% had shown improvement in non-cyclic group. 19 of our patients had side effects due to medications. 14 of our patients developed recurrence after discontinuation of medication.

Conclusions: Danazol is very effective in the management of both cyclical and non-cyclical mastalgias. However, cost of the drug and side effects limits its use. Further studies are needed to examine the long-term effectiveness and sustainability of the effects after stopping the treatment.

Keywords: Breast pain, Cyclic, Non-cyclic, Danazol, Mastalgia

INTRODUCTION

Mastalgia was described in the medical literature as early as 1829 and is the most common complaint among women of child bearing age.¹ Breast pain among women with or without lump is a common complaint and a cause of significant anxiety and fear of breast cancer.² Mastalgia may be cyclic or non-cyclical and extra mammary cause like Trietz syndrome.³

Cyclic mastalgia is related to menstrual cycle and it starts in leuteal phase. The symptoms of cyclic mastalgia include congestion of breast, soreness and feeling of

fullness, heaviness and tenderness.⁴ It appears 7-10 days before menstruation and lasting 1-4 days and causes slight pain and is seen in 8-10% premenopausal women. Non cyclic mastalgia is another type of mastalgia the pain of which does not correlate with menstruation as in cyclic mastalgia and is felt throughout.⁵

Most non cyclic breast pain arises for unknown reasons, yet is believed more likely to have an anatomical rather than hormonal cause. Approximately 16 and 32% of women report breast pain as an adverse effect of estrogen and combined hormonal therapies respectively.⁶ Various modalities like wearing of proper fitting and supportive

bra, heat cold therapy, non-medical means like dietary measures like fat restrictions, avoidance of methyl xanthine and reassurance. Various drugs have been tried so far for mastalgia. Danazol is anti-gonadotrophic that has unique action on pituitary ovarian axis. It is labeled as impedal androgen and had been most popular drug for the treatment of benign breast disorders.

METHODS

Study design

Prospective observational study used for this study.

Study area

The study was conducted at Sher-I-Kashmir institute of medical sciences (SKIMS), department of general and minimal invasive surgery, breast care clinic, Srinagar after obtaining approval from institutional ethical committee.

Study period

The duration for the study was conducted from January 2018 to July 2019.

All the patients with mastalgia between 19 to 45 years of age who presented with breast pain with and without nodularity having visual analog score (VAS) more than 3 were considered eligible for the study. Pregnant, lactating mothers and patients with carcinoma breast, polycystic ovarian disease and VAS<3 was excluded from the study.

After taking proper history, patients were subjected to clinical examination including bilateral breast palpation according to classic procedure and radiological abnormalities. Additional ultrasonography, cytology, and histologic verifications were done when necessary. Patients were given cap. Danazol 100 mg twice a day for 3 months period. All the patients were informed about possible side effect and written informed consent was taken before starting treatment. Any change or side effects were noted down. Response was noted in terms of VAS of breast pain. Patients were given a pain chart and were asked to fill on daily basis from the day of usage of drug for mastalgia. The data thus obtained in 40 patients as prospective observational study was analyzed for patterns and relations.

The strict follow up of our patients was advised at 4, 8 and 12 weeks for assessment. Relief of breast pain was considered the main outcome of interest. The severity of mastalgia was noted on a VAS. VAS is usually a horizontal line, 10 cm in length, anchored by word descriptors at each end. The patient marks on the line below, the point that they feel represents their perception of pain. The VAS score is determined by measuring in millimeter from the left-hand end of the line to the point that the patient marks. On this VAS, the 0 indicates no

pain and 10 indicate very severe pain in the breast. This was recorded at baseline and during follow-up.

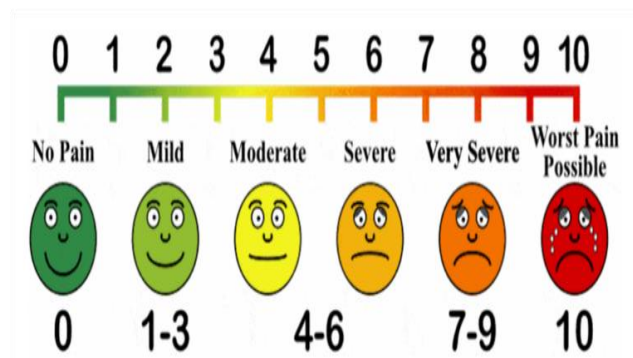


Figure 1: A visual linear analogue scale for measuring pain.

Table 1: Activity tolerance and VAS score relation.

Activity tolerance	Score
No pain	0
Can be ignored	1-3
Interferes with task	3-5
Interferes with concentration	5-7
Interferes with basic needs	7-9
Bed rest required	10

Patients were divided into cyclic and non-cyclic mastalgia group to make it more significant. Type of mastalgia is elicited by maintaining breast pain chart and relation to the menses was noted as cyclical when it occurs 1-2 weeks prior to menses subsiding progressively during menstruation and non-cyclical otherwise.

Statistical methods

The recorded data was compiled and entered in a spreadsheet (Microsoft excel) and then exported to data editor of SPSS version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean ± SD and categorical variables were summarized as frequencies and percentages. Graphically the data was presented by bar diagrams and line diagrams. Student’s independent t-test was employed for comparing continuous variables.

RESULTS

This was a prospective study carried out on 40 patients of benign breast disease confirmed by triple assessment. The age range of the patients was 19-45 years. Most of our patients were above 41 years of age (Table 2). There was no significant difference as far the age of the patients was concerned. 72 percent of our patients presented with cyclic mastalgias while as 28 percent had non cyclic symptoms (Table 3). 30 patients had B/L pain and 10 patients had unilateral pain.

Table 2: Age distribution of patients.

Age (year)	Number	Percentage (%)
≤ 30	9	22.5
31-40	12	30
≥41	19	47.5

Table 3: Type of pain.

Type of pain	No. of patients	Percentage (%)
Cyclic mastalgia	29	72
Non cyclic	11	28

Visual analog score and pain relief

Severity of mastalgia was assessed by VAS pain score change during three months drug therapy ranging from 0 (no pain) to 10 (severe pain). This was recorded at the first visit of patient and follow-up at 1st, 2nd and 3rd months. VAS score of less than or equal to 3 was considered significant in our study. Ladies in both the cyclic and non-cyclic mastalgia experienced significant pain relief at the end of three months therapy. 55% of our patient had significant pain relief at the end of first month danazol therapy. 87.5% patients had significant pain relief at the end of three months treatment (Table 4).

Table 4: Treatment response in mastalgia.

Follow up (month)	VAS score	Cyclic (in no.)	Non-cyclic (in no.)
1 st	≤3	17	5
2 nd	≤3	23	7
3 rd	≤3	26	9

Response to danazol therapy

At end of 1st month, there was significant decrease in mastalgia in both cyclic and non-cyclic group. 58.62% (17 patients) in cyclic mastalgia and 45.45% (5 patients) in non-cyclic showed response to danazol therapy. 18 patients showed no improvement at the end of 4 weeks period.

At the end of 2nd month 79.31% (23 in number) patients responded to treatment in cyclic and 63.63% patient in non-cyclic group. 10 patients continued with pain.

At the end of 3 months 89.65% patients (26 patients) in cyclic and 81.81% patients (9 patients) in non-cyclic had shown improvement. Five of our patients showed no improvement in symptoms.

Patients were followed up for 6 months after discontinuation of drugs. 14 of our patients developed recurrence after discontinuation of medication.

Table 5: Number of patients who achieved pain relief, both cyclic and non-cyclic mastalgia.

Follow up (month)	Cyclic mastalgia	Non-cyclic mastalgia	%	No response
1 st	17	5	55	18
2 nd	23	7	75	10
3 rd	26	9	87.5	5

Adverse drug effects

At the end of the study 13 patients had side effects due to medications which include amenorrhea, delayed menses, mammographic changes, Allergic reaction, weight gain and aches. Delayed menses was the most common side effect seen (Figure 2). These side effects resolved on their own after discontinuation of drug. After 6 months of follow up 26 patients had no pain but 14 patients reported with pain.

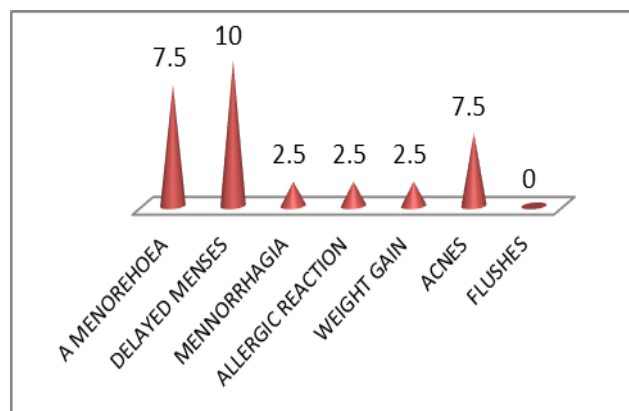


Figure 2: Danazol therapy and side effects.

DISCUSSION

Breast pain is the most common presentation of female in reproductive age group. Mastalgia is a common complaint with 66% of normal women experiencing pain at some points in their lives.⁷ There is considerable discussion about selecting the best method for the primary management of breast pain. Danazol is a synthetic testosterone which binds to the progesterone and androgen receptors, though the precise mechanism of action in the treatment of mastalgia is unknown.⁸

Danazol was first marketed for treatment of endometriosis, but in 1971 Greenblatt and his colleagues reported improvement of breast symptoms in women with endometriosis while taking the drug.⁹ Further reports from the same group described the use of danazol in dosages from 100 to 400 mg daily for three to six months in over 300 women with varying types of benign breast disease and reported total resolution of pain and nodularity in about 80% of patients.^{10,11}

Danazol is the only medication approved by the food and drug administration for the treatment of mastalgia.¹²

In our study patients had significant improvement of mastalgia after a course of three months. 89.65% of patients in cyclic group had responded to danazol 100 mg twice daily and 81.81% had shown improvement in non-cyclic group. 13 of our patients (32.5%) developed side effects including amenorrhea, delayed menses, menorrhagia, allergic reactions and weight gain. Parveen et al in their study showed 76% improvement in mastalgia using danazol 200 mg orally per day and 32% of side effects.¹³

Doberl et al in their study of danazol for six months in their assessment danazol caused marked decrease in mastalgia on VAS.¹⁴ The response to danazol was fairly uniform and statistically significant ($p < 0.005$). During their treatment there was moderate weight gain and menstrual regularities. Danazol appears to be the best agent for the treatment of severe mastalgia and nodularity with a success rate of approximately 75% but its limitations are the side effects.^{15,16}

Dhar et al in their study found danazol 100-200 mg results in weight gain acne, greasy hair and skin, headache, nausea, hirsutism, decreasing size of breast, voice changes (due to androgenic affect) and irregularity of menstruation on higher doses of danazol.¹⁷ In our study we had 32.5% of patients having weight gain, irregular periods, acne, delayed periods.

In our study 14 patients reported back on stopping the medication for 3 months. Which was also noticed by Das et al.¹⁸

Limitations

This study included a smaller number of patients and had a shorter follow-up, although the recurrence rate and morbidities were low. However, for proper validation of these conclusions a long-term prospective clinical study with large sample is required.

CONCLUSION

Patient education, reassurance and appropriate medical and surgical treatment according to the cause of breast pain can reduce the morbidity and improve the outcome of the disease. Non-cyclical mastalgia is more prevalent than cyclical mastalgia among women in our study but it may need confirmation by further large population-based studies. Danazol is effective in moderate to severe mastalgia but due to its side effects and cost effect, it cannot be a drug of choice for the patients with mastalgia. Further studies are needed to examine the long-term effectiveness and sustainability of the effects after stopping the treatment. Much better drug with fewer side effects is need of the hour.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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