

# Response to different medical treatment options for mastalgia in fibrocystic breast disease

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## ABSTRACT

**Background:** Fibrocystic breast disease is the most common type of benign breast disease and mastalgia is the most common symptom of fibrocystic breast disease. Various types of medical management are given as a gold standard treatment for that. The aim of this study was to compare the effects of different commonly used medical management options of mastalgia of fibrocystic breast disease on the quality of life of patients and their side effects as well.

**Methods:** This quasi-experimental study was carried out in Out-patients Department of General Surgery, BIRDEM General Hospital, Dhaka, from July 2018 to June 2019. Total 45 patients with fibrocystic breast disease were selected according to the eligibility criteria and were allocated to two groups by alternative random selection. In non-pharmacological treatments receiving group, lifestyle modification advices along with evening primrose oil were given. On the other hand, in pharmacological treatment receiving group, bromocriptine and danazole were given according to some selection criteria of the patients. Response of treatments to each group and side effects were determined at one month, three months and six months follow-up respectively. Mastalgia was measured by visual analogue scale (VAS) score and quality of life was calculated by modified WHO-QOL scoring in each follow-up.

**Results:** Patients had an average age of 30.24±6.93 years with a majority in the age group 31-35 years (33.3%). Most patients were married (64.4%), housewives (62.20%), from middle-class groups (62.20%), multiparous (57.78%) and the majority had absence of the family history of breast diseases (84.45%). Majority of them presented with cyclical mastalgia (57.78%), bilateral mastalgia (60%) and mastalgia with lumpiness (44.4%). Among the patients who received non-pharmacological treatment, mastalgia improved in 34.78% cases and patients received pharmacological treatment, mastalgia improved in 72.73% cases. Different domains of quality of life were improved significantly in patients who received pharmacological treatment. Though majority of the patients had side effects due to pharmacological treatment, they were well tolerated.

**Conclusion:** Despite having various side effects, pharmacological management by danazol or bromocriptine was well tolerated to our patients and a dramatic improvement was observed on quality of life than the non-pharmacologically treated patients.

**Keywords:** fibrocystic breast disease, mastalgia, evening prime rose oil, EPO, danazol, bromocriptin, quality of life.

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## INTRODUCTION

Benign breast disease (BBD) is an umbrella term for various non-malignant breast lesions, such as cysts, tumors, trauma, mastalgia, and nipple discharge.<sup>1</sup> Fibrocystic breast disease (FBD) is the most common type of benign breast disease and mastalgia is the most common symptom of FBD.<sup>2</sup> Fibrocystic breast disease represents a spectrum of clinical, radiological and histological findings of the breast in both asymptomatic and symptomatic women. It is a condition of breast where there may be breast pain, breast lumpiness, nodularity and sometimes breast lump; which can sometimes cause discomfort, often periodically related to hormonal influences from the menstrual cycle. Mastalgia causes concern and fear of breast cancer and has negative effects on quality of life.<sup>3</sup> Mastalgia caused by fibrocystic breast disease is treated by breast specialists as well as by those not specialized in breast diseases.<sup>4</sup> Unfortunately, these patients are treated inappropriately for prolonged duration with non-pharmacological management by Evening Primrose Oil<sup>2,5</sup> in a fear of more side effects of pharmacological managements by certain drugs.<sup>6</sup> Inappropriate selection of non-pharmacological treatment as a first line management option, sometimes creates financial burden and unchanged or recurrence of clinical symptoms.<sup>7</sup> Recent population based and breast clinic-based studies suggest that up to 70% of women experience breast pain in their lifetime.<sup>8</sup> Moreover, 10% of symptomatic participants had suffered breast pain for over half their lives. Of the symptomatic participants, 41% and 35% reported breast pain affecting the quality of life.<sup>9</sup> Fifteen percent of women who present to a breast clinic with mastalgia will require treatment.<sup>8,9</sup>

Non pharmacological options of medical managements includes some life style modifications (LSM) like- an appropriately fitting and supportive bra, avoidance of caffeine drinks, reduction of dietary fat, increase fiber rich diet, physical exercise to reduce weight and relaxation training are said to be helpful for the treatment of mastalgia<sup>10</sup> and some nutritional supplementations like oil of evening primrose (EPO) will help more than half of these women<sup>5,10,11</sup>. For those with intractable symptoms, Pharmacological options of medical management like- an anti-gonadotropin, (Danazol<sup>6</sup>), or a prolactin inhibitor (Bromocriptine<sup>5</sup>), may be tried. Very rarely, it is necessary to prescribe an anti-estrogen, for

example tamoxifen<sup>12,13</sup>, or a luteinizing hormone-releasing hormone (LHRH) agonist to deprive the breast epithelium of estrogenic drive. Surgical interventions have a limited role in the management of mastalgia<sup>5</sup> but last-resort options for unresponsive and severe debilitating breast-pain include mastectomy with reconstruction.<sup>14</sup>

The aim of our study was to assess the responses of various medical treatment options of mastalgia of FBD on women's quality of life as well as side effects of used medications.

## METHODS

It was a quasi-experimental study carried out in Outpatient department (OPD) of General Surgery, BIRDEM General Hospital, Dhaka, from July 2018 to June 2019. Forty five patients with fibrocystic breast disease (FBD) presented in OPD of BIRDEM General Hospital, Dhaka, Bangladesh; based on some selection criteria. The inclusion criteria were: women of reproductive age group and patients diagnosed as fibrocystic breast disease by clinical, radiological or cytological examinations within the study period. Patients with suspected breast lesion or diagnosed breast malignancy, pregnant, lactating women and who are planning to have pregnancy in near future, history of any breast surgery or having congenital disability of breast were excluded from this study.

A thorough history of each patient was obtained and careful physical examination carried out of each patient. Hormonal assay and USG of both breasts were done in every patient but Mammography and FNAC were done only in suspected cases to exclude FBD and occult breast carcinomas, particularly in patient having family history of breast diseases.

Patients were allocated to two groups by alternative random selection (first one to non-pharmacological and second one to pharmacological, third to again non-pharmacological treatment receiving group and so on). Non-pharmacological treatments receiving group were given life style modification (LSM) advices along with Evening Primrose Oil (EPO). The LSM advices were wearing a supportive bra, exercise to reduce weight, reduction of mental stress by relaxation therapy, some dietary advices such as reduction of fat and caffeine intake, increase dietary fiber intake, etc. Evening Primrose Oil (EPO) was given orally in a dose of 1000mg

thrice daily. In pharmacological treatment receiving group Bromocriptine and Danazole were given according to some selection criteria of the patients. Bromocriptine was given orally in a dose of 2.5mg twice daily, in those patient with increased prolactin level, having no known hypersensitivity to it, not taking any anticonvulsant, not having uncontrolled diabetes, severe ischemic heart disease or migraine. On the other hand, Danazole was given orally in a dose of 100mg twice daily in patients with normal prolactin level, hyperestrogenaemia, patients with no undiagnosed genital bleeding, previous thromboembolic disorders or markedly impaired hepatic, renal or cardiac functions. In both groups oral analgesics were given according to the severity of mastalgia. Acetaminophen was given 500mg thrice daily for VAS 2-4 and Ibuprofen was given 200mg twice daily for VAS e" 6 in initial visit for one week to alleviate the severity of pain in both groups. Patients were advised not to take any analgesic after initial one week and report if the pain became intolerable.

Response to each group of treatments, side effects & compliance of the patient were determined at 1 month, 3

months and 6 months follow up respectively. Mastalgia was measured by VAS score and QOL were calculated by modified WHO-QOL scoring (field trial version) in each follow up.

Any side effects, willingness to continue the treatment were also asked to every patient in each follow up. No treatment was changed before 3 months of therapy, no matter what the response was. This study focused simply on the comparison of the two groups of medical treatments of mastalgia and their responses of QOL at beginning and after 6 months of treatment.

## RESULTS

Total number of respondents were 45. Highest respondents of our study were aged between 31 to 35 years (33.3%) and no respondents were aged between 45 to 50 years (0%). Mean age of the respondents were 30.24±6.93 years of SD. Among the attended, maximum patients were married (64.4%), house wife(62.20%), middle class (62.20%), multipara (57.78%), had regular menstruation (77.8%) and absence of family history of breast disease among them was more (84.45%) (Table I).

**Table I** Demographic characters of the respondents (N= 45)

Demographic characteristics	Types	Frequency	Percentage
Age (years)	16 to 20 years	4	8.9
	21 to 25 years	10	22.2
	26 to 30 years	11	24.4
	31 to 35 years	15	33.3
	36 to 40 years	3	6.7
	41 to 45 years	2	4.4
	46 to 50 years	0	0
Marital Status	Single	13	35.6
	Married	32	64.4
Occupational status	House wife	24	62.20
	Student	14	24.40
	Service holder	7	13.30
Socio-economic status	Poor class	4	8.9
	Lower middle class	28	4017.80
	Middle class	28	62.20
Menstrual history	Higher class	7	15.60
	Regular	35	77.8
	Irregular	5	11.1
Obstetric history	Oligomenorrhoea	3	6.7
	Menorrhagia	2	4.4
	Nullipara	19	42.22
	Multipara	26	57.78
Family history of breast disease	Present	7	15.56
	Absent	38	84.45

Maximum patients presented with cyclical mastalgia (57.78%) and mastalgia with lumpiness (44.4%) and bilateral breasts involvement (60%) (Table II) in initial visit.

Hormonal assay of the patients showed 60% had high serum Prolactin, 20% had high serum Estrogen and 4.4% had low serum Progesterone (Table III).

Among 45 respondents, all the respondents (100%) had USG of both breasts, 19 (42.20%) did Mammogram and 5 (11.10%) did FNAC to confirm the nature of suspected breast lesion (Figure 1). More than fifty one percent of respondents underwent non-pharmacological and 48.9% underwent pharmacological managements. More

improvements occurred by pharmacological management in VAS pain score after completion of 6 months follow up (Table IV). In pharmacological treatment received group 40.91% respondents treated with Danazole and 59.09% treated with Bromocriptine.

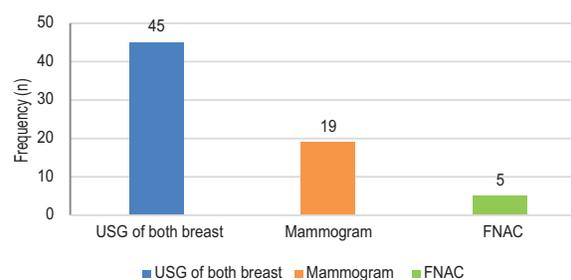
After 6 months follow up, 72.73% had pain improvement in pharmacologically treated group and 34.78% had pain improvement in non-pharmacological group. Significant difference had been found between both groups. Here VAS 0-2 was considered as pain improvement and VAS 4 and above was considered as non-improvement of pain (Table V).

**Table II** Clinical findings of the respondents in initial visit (N=45)

Clinical presentation	Details	Frequency	Percentage
Presentation of patients on initial visit	Mastalgia only	11	24.4
	Mastalgia +Lumpiness	20	44.4
	Mastalgia +Nodularity	9	20
	Mastalgia+ Breast Lump	5	11.1
Side of involvement of Breast	Right breast	6	13.3
	Left breast	12	26.7
	Both breasts	27	60
Types of Mastalgia	Cyclical	26	57.78
	Non-cyclical	19	42.22
Total		45	100

**Table III** Hormonal assay of the study subjects (N=45)

Hormone	Normal	High	Low
Serum Prolactin	18 (40)	27 (60)	-
Serum Estrogen	36 (80)	9 (20)	-
Serum Progesterone	38 (84.4)	-	2 (4.4)



**Figure 1** Types of investigations done (N=45)

**Table IV** Distribution of VAS pain score at initial and subsequent visits in each group separately

Pain Score (VAS)	Non- pharmacological Managements (n=23)				Pharmacological Managements (n=22)			
	Initialvisit	After1 M	After3 M	After6 M	Initialvisit	After1 M	After3 M	After6 M
0	0	0	3	5	0	5	9	11
2	6	10	4	3	5	10	2	5
4	12	10	8	9	11	4	9	4
6	5	3	8	6	5	3	2	2
8	0	0	0	0	1	0	0	0
10	0	0	0	0	0	0	0	0
Total	23			23	22			22

Response of three domains of WHO-QOL in non-pharmacological and pharmacological treatment groups separately after completion of treatment after 6 months shows improvement was significantly higher in pharmacological group in all domains (Table V).

Side effects of different Pharmacological treatment options shows Danazole had maximum side effects, of

them menstrual irregularity (15.6%) was most common. Patients treated by Bromocriptine, maximum complained of headache (11.1%). Patients treated non-pharmacologically by Evening Primrose oil (EPO) caused bloating in 6.7% and headache in 2.2% patients. (Table VI).

**Table V** Distribution of the respondents by 6 months follow up of non-pharmacological and pharmacological treatment using QOL parameters

Domains of QOL	Facets incorporated within domains	Non pharmacological(n=23)		Pharmacological(n=22)		P value
		Improved (%)	Not Improved (%)	Improved (%)	Not Improved (%)	
<b>Physical domain</b>	Pain	8(34.78)	15(65.22)	16(72.73)	6(27.27)	*0.006
	Physical health	9(39.13)	14(60.87)	16(72.72)	6(27.27)	*0.008
	Energy & Fatigue	8(34.78)	15(65.22)	15(68.18)	7(31.82)	*0.001
	Sleep & Rest	10(43.48)	13(56.52)	17(77.27)	5(22.72)	*0.05
	Self esteem	7(30.43)	16(69.57)	14(63.64)	8(36.36)	*0.031
<b>Psychological domain</b>	Concentration/ Attention	9(39.13)	14(60.87)	13(59.09)	9(40.91)	*0.002
	Negative feeling (Anxiety, Depression)	6(26.09)	17(73.91)	12(54.55)	10(45.46)	*0.003
<b>Social relationship</b>	Personal relationship	8(34.78)	15(65.21)	12(54.55)	10(45.46)	*0.151
	Sexual life	7(30.43)	16(69.57)	13(59.09)	9(40.91)	*0.08

\*P value was determined by Chi-square test.

**Table VI** Distribution of side effects of different Pharmacological and non-pharmacological treatment options

Adverse effect	DANAZOLE Frequency (%)	BROMOCRIPTINE		ENING PRIMROSE OIL(EPO)	
		Adverse effect	Frequency(%)	Adverse effect	Frequency (%)
Weight gain	6(13.3)	Headache	5(11.1)	Bloating	3(6.7)
Menstrual irregularity	7(15.6)	Nausea	2(4.4)	Headache	1(2.2)
Headache	5(11.1)	Dyspepsia	2(4.4)		
Nausea	2(4.4)	Non specific	3(6.7)		
Acne	1(2.2)				
Non specific	4(8.9)				

## DISCUSSION

Mastalgia with or without breast lump in FBD is common complaint among the patients and a cause of significant anxiety and fear of female breast cancer in Bangladesh as well as all over the world.

In this study maximum respondents were age between 31 to 35 years (33.3%). The mean age of the respondents were  $30.24 \pm 6.93$  years of SD. Similar observations were found in some previous studies by Scurr et al.<sup>9</sup> and in a recent study done by Godazandeh et al.<sup>15</sup>

Observing the demographic data of our study respondents, maximum patients were married (64.4%), housewife (62.20%), multiparous (57.78%), had regular menstrual cycle (77.8%) and from middle class group (62.20%). Most of our respondents did not have family history of breast disease (84.45%). Similar observations were found in some previous study by Jahdi et al.<sup>2</sup> and Çomçalý et al.<sup>16</sup> showed majority of their respondents were housewife<sup>2</sup>, unemployed<sup>16</sup>, married<sup>2,15,16</sup> and multiparous<sup>2,15,16</sup>.

Clinical presentations in initial visit showed maximum respondent had cyclical mastalgia (57.78%) and 42.22% had non-cyclical mastalgia. Similar observation was noted in a previous study by Rajswaroob et al.<sup>17</sup> and Nirhale et al.<sup>8</sup>

In this study maximum respondents (60%) had both breasts involvement, 26.7% had left breast and 13.3% had right breast involvement. In a previous study by Sangma MB et al.<sup>18</sup> observed maximum respondents had right breast involvement (48%), the left breast was affected in 40% patients while only 12% cases both breasts were affected, that differs from our observation. In this study maximum respondents presented with mastalgia with lumpiness (44.4%), followed by mastalgia only (24.4%), mastalgia with nodularity (20%) and only 11.1% had mastalgia with breast lump. In a previous study of 49 patients by Nirhale et al.<sup>8</sup>, it was observed that 'mastalgia only' was the most common symptom and accounted for 61.25 % patients, beside 35% had 'mastalgia with lump', which is different from our observation. In our study hormonal levels of respondents showed, 60% had high serum Prolactin, 20% had high serum Estrogen and 4.4% had low serum Progesterone level. Smith et al.<sup>19</sup> showed in his previous study, the frequently detected hormonal abnormality related with mastalgia was increased Prolactin level, Progesterone deficiency and Estrogen excess.

USG of both breasts was done for all 45 patients (n=45), Mammogram was done for 19 (42.2%) patients and FNAC was done for 5 (11.10%) patient, who presented with breast lump along with mastalgia to confirm fibroadenosis/ fibroadenoma and to rule out malignancy and suspected breast lesions. In a previous study by Rajswaroob et al.<sup>17</sup> did same type of investigations.

In this study 51.1 % respondents underwent non-pharmacological treatment by LSM and EPO and 48.9% underwent pharmacological treatment, where 40.91% respondents treated with Danazole and 59.09% treated with Bromocriptine depending on the selection criteria.

In this study quality of life (QOL) in non-pharmacological treatment receiving group- in physical domain: pain 34.78%, physical health 39.13%, energy and fatigue 34.78% and sleep and rest 43.48% had improvement. In psychological domain: 30.43% had improvement of self-esteem, 39.13 % had improvement in concentration/attention and 26.09 % had improvement in negative feeling. In social relationship domain: in personal relationship 34.78% and in sexual life 30.63% had improvement. Beside in pharmacological treatment receiving group in physical domain: pain 72.73%, physical health 72.72%, energy and fatigue 68.18% and sleep and rest 77.27% had improvement. In psychological domain: in self-esteem 63.64%, concentration/attention 59.09% and 54.55% negative feeling had improvement. In social domain: 54.55% personal relationship and 59.09% sexual life had improvement. In all domains improvements were significantly higher in pharmacological group.

Similar observation was seen in a previous study by Rajswaroob et al.<sup>17</sup> where he showed drug treatment was significantly effective for mastalgia. P. Ganz et al. observed mood and emotional functioning were same among all patients, with no differences by type of medical treatment received<sup>20</sup> which is abit differ from our observation.

In this study majority of side effects occurred due to Danazole. Chronologically they are menstrual irregularity (15.6%), weight gain (13.3%), headache (11.1%), nausea (4.4%), acne (2.2%) and nonspecific side effects (8.9%). Beside headache (11.1%), nausea (4.4%), dyspepsia (4.4%) and nonspecific side effects (6.7%) due to Bromocriptine. Whereas only 6.7% had bloating and 2.2% had headache due to Evening Primrose oil (EPO).

Here a single patient sometimes complained of multiple side effects.

Almost similar observation was seen in some previous study by Rajswaroob et al.<sup>17</sup> and Neogi P et al.<sup>21</sup> and Nirhale et al.<sup>8</sup>

There are some limitations of our study. This study was performed in a single tertiary care hospital among small available population size.

### Conclusion

Mastalgia, being a common symptom of fibrocystic breast disease, causes anxiety among the women of reproductive age group and burdens the health care facilities of our country. In this study, we found pharmacological managements by Danazole or Bromocriptine in precisely selected group of patients were well tolerated and a dramatic improvement was observed in overall quality of life of our patients. Despite of having various side effects of different pharmacological managements of mastalgia, we recommend timely use of them in the precisely selected patients of fibrocystic breast disease can help in reduction of their sufferings, cost of prolonged treatments by improving the quality of life in a relatively shorter period of time.

Further large study is recommended involving multiple centers and long term follow up.

**Authors' contribution:** Mostary S, Maitra TK were involved in study designing, data collection, compiling, data analysis. Mostary S. wrote the manuscript. Rests were involved in overall supervision.

**Conflict of interest:** Nothing to declare.

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