

Original Article**Outcome of Combined Pharmacological and Surgical Management of Fibrocystic Breast Disease**

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*** For Correspondence****Abstract**

Background: Several treatment options are available for benign breast disease like fibrocystic breast disease (FBD).

Objective: The current study was aimed to evaluate the outcome of combined pharmacological and surgical management of fibrocystic breast disease (FBD) patients.

Methodology: The study was a case-control study and was conducted at the department of surgery in Jahurul Islam Medical College & Hospital, Kishoregonj, Bangladesh for a period of six months. Women diagnosed as fibrocystic breast disease and who were received combined both pharmacological and surgical management were selected as study population. The method involves two groups, the cases group where patients with fibrocystic breast disease having with both pharmacological and surgical therapy were included, and the control group where patients with fibrocystic breast disease only pharmacological therapy were given. Data were collected from the patients by the researcher focused on disease duration, severity, drug management and relevant demographic profile and pre and post-operative assessment of symptoms,

Results: Total 40 patients were considered as case and 40 patients were considered as control. Out of 80 patients, Mean age was 38.6 ± 8.69 (SD) years. Of all, 60% patients come from urban areas with predominantly solvent socioeconomic class (47.5%). Socio-demographic profile and body mass index was similar between both groups ($p > 0.05$). Similarly, across the groups base line VAS score was also had non-significant changes [Surgery & Pharmacotherapy group (G-SP) 5.02 ± 1.36 vs Pharmacotherapy group (G-P) 5.03 ± 1.31 , $p > 0.05$]. During follow up, significant improvement was noticed in both group and mean VAS score was 1.90 ± 1.43 and 2.00 ± 1.32 , respectively ($p < 0.001$ in both groups). Mean VAS score change was found higher in case group who were given both medication and surgery than mean VAS change in control group who were given only medication but the change is not statistically significant ($p > 0.05$). Moreover, significant improvement was noticed in resolution of lump in case group than control ($p < 0.0001$).

Conclusion: Combined surgery and pharmacotherapy is beneficial than alone pharmacotherapy in FBD. Nevertheless, to finalize the comments it needs further larger randomized controlled trial.

Key Words: Fibrocystic Breast Disease, Breast surgery, Pharmacological therapy.

Introduction

Fibrocystic breast disease (FBD), also termed as Fibrocystic change (FC) of the breast is one of the commonest disease affecting women at some time during their life most commonly in age group of 30 – 50 years. It is reported that about 60% of women suffer from this fibrocystic change in their breast during their life period¹⁻³. It is a clinical condition characterized by lumpiness due to formation of cysts in glandular breast tissue⁴. This disease has been recognized also as fibrocystic mastopathy, mammary dysplasia, chronic cystic mastitis⁵ and typical histological appearances are cystic hyperplasia, cystic mastitis, adenosis, and ductal papillomatosis⁴. Traditionally the disease has always been described as benign in nature with very low or almost no potential to develop into a malignant lesion⁶. Literatures demonstrated that FC with proliferative epithelial cell elements have been associated with increased risk of subsequent breast cancer, especially if accompanied by atypical cellular changes⁷. So, management of fibrocystic breast disease is primarily focused on reducing these symptoms (i.e. breast pain or a mass)⁸ which is treated by a vast array of remedies arranging from simple re-assurance and a change in lifestyle, to non-pharmacological and pharmacological agents⁹ and also surgical intervention in limited extent. A wide variety of pharmacological measures are used in case of failure of non-pharmacological approach¹⁰ which include non-steroidal anti-inflammatory drugs (NSAIDs), oral contraceptives, tamoxifen, danazol and bromocriptine⁹. On the other hand, surgical management of fibrocystic changes usually is the result of the recognition of a specific finding (i.e., a dominant mass). Most have insisted on the biopsy because of a “lump” and pain, and the surgeon has complied⁸. However, few recommendations for referral to a surgeon is documented which include, women of 35 years or younger with all dominant, discrete, palpable lesions and women older than 35 years of age with a dominant mass after undergoing mammography¹¹⁻¹².

Although Fibrocystic changes of the breast is not considered a disease¹⁷ but symptoms of it and fear of

subsequent development of malignancy often disrupt the quality of life⁵ of the affected people. So appropriate treatment approach should be applied to reduce their sufferings and very limited data regarding the surgical or combined medical and surgical treatment of FC is available in our country even in the worldwide. For that reason this study will be undertaken with the purpose to evaluate the outcome of combined medical and surgical treatment of FBD.

Methodology

The study was a case-control study and was conducted at the department of surgery in Jahurul Islam Medical College & Hospital, Kishoregonj, Bangladesh for six months period from 12th November, 2017 to 12th May, 2018. Women with FBD and were received combined (both pharmacological and surgical) management. The method involves two groups, the cases (patients with FBD having with both pharmacological and surgical therapy), and the controls (patients with FBD with only pharmacological therapy). Total 40 patients were considered as case and 40 patients were considered as control. Data were collected from the patients by the researcher focused on disease duration, severity, drug management and relevant demographic profile and pre and post-operative assessment of symptoms.

Inclusion criteria:

For case group: Patients aged more than 18 years having discrete dominant, palpable lump in one or both breast with cytological proven negative for malignancy and willing to participate were included.

For control group : Patients aged more than 18 years having discrete dominant, palpable lump in one or both breast with cytological proven negative for malignancy and willing to participate were included.

Exclusion criteria: Patients below 18 years, severely ill, positive for malignancy, pregnant and lactating mothers were excluded.

Study procedure

Before starting of the study, the study protocol was reviewed and got ethical permission from ERC of

JIMC. All FBD patients visited in surgery OPD, were randomly allocated into case-control. The case-control ratio was 1:1. Before enrolment, the study populations were properly described the procedure of the study. During allocation, lottery method was followed to ensure the equal chance to get any of the treatment methods. All of the patients were examined clinically and USG of breast, FNAC & serum prolactin level were measured before selection of study populations.

All the patients were informed clearly about the aims, objectives, benefits and risk of the study. In case of age<18 years, FNAC suggestive of malignancy, pregnancy, lactating mother, others associated breast diseases, diffuse lumpiness& severely ill patients were considered as a criteria of exclusion.

The case group was received surgical excision in the form of lumpectomy followed by pharmacological therapy. The control group was put into cap. Danazol,100mg, twice daily or tab.Bromocriptine, 2.5mg, thrice daily(whose serum prolactin was high) for 3 months. Both case and control group were

re-assessed clinically and by VAS score after 3 months. Written Informed consent were obtained from the patients and/or guardian. Face to face interview was conducted by using a semi-structured questionnaire containing socio-demographic parameters and relevant information. All patients with FBD were followed up for 3 months. And baseline data were compared with post intervention data. After collection of all data, data analysis was done by SPSS 21.

Results

We studied a total of 80 cases of fibrocystic disease of breast visited in the surgery OPD in Jahurul Islam Medical College & Hospital for last six months. 40 of these patients were considered only pharmacological treatment and the rest 40 cases were considered for both surgical and pharmacological management.

Among the 80 evaluable patients, the mean age was 38.6 ± 8.69 years. Most of the patients were in-between 31 and 40 years (42.5%) with a range of 18–60 years. Figure 1 shows a bar chart of age distribution.

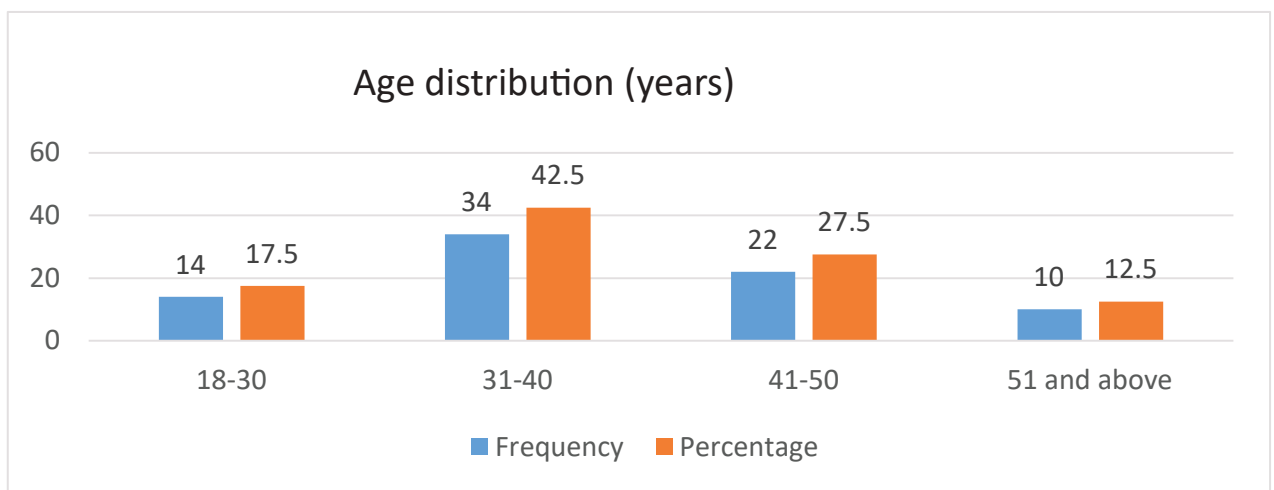


Figure 1: Age distribution of the patients (n=80).

Fibrocystic disease of breast most frequently involved the upper outer quadrant (54%) in this study (n=80). Nine cases had bilateral breast involvement and 14 cases had multifocal involvement of breast. Drug history of the patients (n=80) showed that 36% of the cases had history of OCP intake and 9% had history of Hormone replacement therapy. Fifty five percent of the cases had no history of hormonal drug intake.

Socio-demographic profile and body mass index was similar between both groups ($p>0.05$) (Table 1).

Table I: Comparison of socio-demographic and anthropometric characteristics between case and control group (n=80)

Variable	Surgery & Pharmacotherapy group n(%)	Pharmacotherapy group n(%)	P value
Age (years)	37.77±10.62	39.40±8.73	0.457
Residence (Urban)	26 (65%)	22 (55%)	0.361
Socioeconomic status			
Upper class	18 (45)	20 (50)	0.288
Middle class	16 (40)	10 (25)	
Lower class	6 (15)	10 (25)	
Academic qualification			
Illiterate	4 (10)	4 (10)	0.720
Up to primary	6 (15)	10 (25)	
SSC	12 (30)	10 (25)	
HSC and above	18 (45)	16 (40)	
BMI			
Normal	22 (55)	20 (50)	0.883
Overweight	12 (30)	14 (35)	
Obese	6 (15)	6 (15)	

Assessment of pain in the patients was rated by Visual analog scale (VAS). The score ranged from 0 (no pain) to 10 (extremely severe pain). Pain was tested two times, first before starting the treatment and then after three months of the treatment in both case (n= 40) and control (n= 40) groups. Comparison of baseline VAS score between groups shows that both group had a very similar VAS score before initiation of treatment (p>0.05).

Table II: Comparison of baseline VAS score between case and control group (n=80)

Variable	Surgery & Pharmacotherapy group n(%)	Pharmacotherapy group n(%)	P value
VAS score	5.02±1.36	5.03±1.31	1.00

Case group were managed surgically with adjunct pharmacological therapy whereas control group were given only pharmacological treatment. Paired T- test was done for the comparison of VAS score for pain before and after treatment and reduction of pain was statistically significant in both groups (p < 0.001).

Table III: Comparison of mean value of VAS score for pain before and after treatment in both case and control group (n=80)

Study group	VAS score before treatment Mean±SD	VAS score after treatment Mean±SD	P value
Pharmacotherapy only group (n=40)	5.15 ± 1.33	2.00 ± 1.32	<0.001
Surgery and pharmacotherapy group (n= 40)	5.35 ± 1.42	1.90 ± 1.43	<0.001

Significant improvement (p<0.0001) in lump were noticed in case group than control. Here, in case group, 37 patients (92.5%) out of 40, has got complete regression of lump whereas, 23 patients (57.5%), out of 40 has got complete regression of lump in control group in follow up. Patients who received danazol and who received bromocriptin as pharmacological treatment, didn't differ in their outcome significantly.

Table IV: Comparison of regression of lump in between case and control group (n=80)

Variable	Surgery & Pharmacotherapy group n(%)	Pharmacotherapy group n(%)	P value
Complete regression of lump	37(92.5%)	23(57.5%)	<0.0001

Mean VAS score change was calculated by subtracting post-treatment VAS score from baseline VAS score and then a comparison of mean change was made between case and control group. Mean VAS score change was found higher in case group who were given both medication and surgery than mean VAS change in control group who were given only medication (p>0.05).

Table V: Comparison of mean VAS score change between case and control group (n=80)

Variable	Surgery & Pharmacotherapy group n(%)	Pharmacotherapy group n(%)	P value
Mean change in VAS score from baseline to after intervention	3.20±1.60	2.80±1.38	0.236

Discussion

Fibrocystic changes are sometimes asymptomatic; however, when painful, patients would seek medical advice. Many modalities of treatment including non-pharmacological and pharmacological approach are available for treatment of mastalgia associated with fibrocystic disease of breast^{13,14}. In this study surgical and pharmacological combined therapy was compared with that of pharmacological therapy in the treatment of mastalgia associated with palpable discrete lump.

Total 80 patients were included in the study. 40 patients were randomly allocated as case group receiving surgery in the form of lumpectomy followed by pharmacological treatment and another 40 patients were considered control and were given pharmacological management only. Pharmacological treatment was provided in the form of Danazol or Bromocriptine on the basis of serum prolactin level. In case group, only 1 patient was given bromocriptine and 3 patients from control group. But they didn't differ in their outcome significantly from the patients who received danazol. Mean age of all patients were 38.6 ± 8.69 years and majority patients belonged to 31-40 years. This is concordant with the findings of Hernandez et al¹⁵. In another similar study Pastides and colleagues¹⁶ found majority patients aged between 40 – 49 years which is one decade higher than the present study. The higher prevalence in lower age group in this region can be explained the lesser age of menopause in the region.

Majority patients came from urban area constituting 60% of the population. Most of the patients were comparatively well educated and coming from upper socio-economic class. Sixty six out of 80 patients were married (82%). A similar ratio (126 out of 175 married) was noted in the study by Kumar and colleagues¹⁷. Breast pain and palpable discrete mass are the symptoms most frequently described by women presenting to general practitioners or breast clinics¹⁴. In the present study, 54% patients had disease in the upper outer quadrant of breast (54%), nine cases had bilateral breast involvement and 14 had multifocal involvement of breast. Rimsten¹⁸ found that 7% patients presents with bilateral involvement and majority of the cysts occur in upper outer quadrant of the breast which is similar the findings of present study.

Patients on a regimen of combination oral contraceptives are protected from development of fibrocystic disease and related pathologic conditions such as adenoma, fibro-adenoma, and atypical

hyperplasia¹⁹. But this study found that 36% patients had history of oral contraceptive intake. This implies that these were either taking single hormone contraceptives or were not taking OCP regularly. In this study majority of the patients were overweight (33%) and 15% patients were obese (15%) constituting 48% population having BMI above normal. Chen et al.²⁰ in their study found that those with higher percent body fat or lower total lean mass had increased risk of developing fibrocystic disease of breast. Baseline VAS scores for pain was 5.02 ± 1.36 for patients who received surgery and pharmacotherapy and 5.03 ± 1.31 for patients who received pharmacotherapy only. Both case and control group were assessed after 3 months. Pain reduced statistically significantly in both groups after the end of treatment. Resolution of lump was found in 37 patients out of 40 in case group whereas 23 patients out of 40 in control. Patients who received surgery along with pharmacotherapy improved more than the group with pharmacotherapy only, which is of statistical significance. Shirah et al.²¹ studied the effect of Danazol and found it 100% effective in reduction of pain as well as reduction of cyst. Hernandez et al.¹⁵ compared deep oscillation therapy with NSAID and medroxi-progesterone and found that pain reduced in the three therapies applied. In deep oscillation group this reduction was statistically significant. Deep oscillation therapy produces a tissue-relaxing moderate vasoconstriction effect which favors local edema reabsorption and fibrosis reduction.

Very few studies have evaluated the effectiveness of surgery in the treatment of fibrocystic disease of breast. The present study showed that surgical management in addition to pharmacotherapy has statistically significant improvement in the mean pain reduction as well as regression of lump size. Fibrocystic breast disease showing increased proliferation possesses increased risk of malignant transformation as noted by Santen and Manset in an article published in The New England Journal of Medicine in 2009²². Therefore, patients with fibrocystic disease who are at more risk to have malignant transformation and having painful, palpable, dominant lump could be considered for surgical intervention. Otherwise, surgery for the management of pain cannot be advised based on this single center small scale study.

Conclusion

It was observed that significant improvement was seen in combined surgery and pharmacotherapy group compared to only pharmacotherapy group in terms of

pain control and resolution of lump. Based on the result, combination of surgery and pharmacotherapy can be recommended as a treatment modalities for fibrocystic breast disease especially in-case of palpable, dominant lump and it should be based on expertise of the relevant physicians and patients choice.

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