

Response of Anti Prolactin (Bromocriptine) Treatment in ANDI (Aberration of Normal Development and Involution) Patients of Breast

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Abstract: ANDI accounts for major workload in breast clinics. There is no single ideal treatment available to treat benign breast diseases. Aim of this study was to find out the response of antiprolactin treatment in ANDI patient. Total 200 patient of ANDI during April 2005-March 2006 who visited Surgical outpatient department of Liaquat University of Medical and Health sciences Jamshoro Pakistan were treated with Bromocriptine. Study was *observational*, non analytic, non comparative. Patient with solitary fibroadenomas, mild to moderate mastalgia or nodularity, solitary cysts, recent history of pregnancy, lactation, hormonal intake, inflammatory or even doubtful malignant lesions were not included in study. Out of total 200 patients received antiprolactin treatment, 148 (74%) responded well and got relieved from symptoms. 52 patients dropped out of treatment out of them 30 (15%) did not respond to treatment and 22 (11%) developed serious side effects. Patients with galactorrhea responded 100% and with adolescent hypertrophy only responded 16.6%. Only 15% were having raised S.Prolactin and all of them responded well without developing serious side effects. Antiprolactin treatment is effective in most of the conditions of ANDI and can be prescribed even in patients with normal serum prolactin levels. Most of the patients do not develop serious side effects.

Key words: ANDI (Aberrations of normal development and involution) • benign breast diseases • bromocriptine

INTRODUCTION

Benign breast disorders classified by the ANDI system constitute the major workload in breast clinics [1]. There are 6 conditions which come under the heading of ANDI [2]. Two are developmental i.e. Adolescent hypertrophy and Fibroadenoma. Two are cyclical i.e. cyclical nodularity and Mastalgia. Two are involutionary i.e. cyst formation or fibrocystic disease and sclerosing adenosis [3]. Benign breast disorders results from an imbalance or inappropriate target gland response to changing tide of circulating hormones [4]. Several studies have shown that Serum Prolactin levels may be increased in Benign breast disease [5-7]. Prolactin plays a very important role in proliferation and differentiation of normal breast epithelium [8]. The pathophysiology, malignant potential and hormonal therapy for benign breast diseases remain controversial [9]. Many of the endocrine agents currently used to treat symptomatic benign breast disorders modify the action or secretion of Prolactin [10]. Over the last few years

Bromocriptine (dopamine agonist and prolactin antagonist) has been used for treatment of benign breast disease but with contradictory results [11]. The aim of our study was to find out the response of antiprolactin treatment in ANDI patients with or without raised serum prolactin levels. Our study was prospective, observational, non comparative.

MATERIALS AND METHODS

This study was conducted in surgical out patient department of Liaquat University of medical and Health Sciences from April 2005 to March 2006. Patients of all age groups suffering from any of the conditions coming under the heading of ANDI were included in study except those who were having solitary Fibroadenoma, mild to moderate cyclical nodularity or mastalgia and solitary cysts, they were treated by other means like simple reassurance, analgesics, excision or aspiration. Total 200 patients were included in this study. All were sent for Serum Prolactin levels. A detailed profarma pertinent to our study was

filled for every patient which included history, examination and investigation findings along with serum prolactin levels. Patients less than 35 years of age were sent for Ultrasound and more than 35 years of age were sent for Mammography when required. Patient with lump sent for FNAC or trucut biopsy and in doubtful cases excisional or incision biopsy was done to rule out malignancy. All patients with inflammatory lesion or clinical, radiological, histopathological or cytological indication of malignancy were not included in study. Patients with recent history of pregnancy, lactation or hormonal intake were also excluded. After taking informed consent all patients were kept on gradual incremental doses of Bromocriptine (for 3-6 months) starting from 1.25 mg at night to 2.5mg BD to avoid side effects. All patients were asked to come for follow up every fortnightly to see the response of treatment and clinical and radiological improvement in ANDI. S.prolactin levels were repeated after three months in those patients who were having raised level before starting treatment. Those patients who did not respond to Bromocriptine for one and half months or those who did not tolerate side effects were switched to other therapeutic options.

RESULTS

Total 200 patients of ANDI were included in our study. Only 30(15%) were having raised S.prolactin levels. Table 1 showing pattern of ANDI along with S. Prolactin levels. Out of 6 patients with Adolescent hypertrophy only in 1 (16.6%) further growth of breast stopped although breast did not regress to normal size. Remaining 5 left treatment either due to severe side effects or due to no response of treatment. Out of 18 patients with multiple fibroadenomas 13 (72%) responded quite remarkably to the treatment in a way that most of the small

fibroadenomas disappeared and only 1-2 of large fibroadenomas remained there which were excised with better cosmetic results. 5 patients dropped out of treatment either due to non responsiveness or side effects. Out of 8 patients with Recurrent fibroadenomas only 2 (25%) patients responded to treatment in the form of complete regression of fibroadenomas remaining either did not respond or developed side effects and were treated by other means. Out of 30 patients with cyclical nodularity 22 (73%) responded well to treatment within a month nodularity reduced remarkably but treatment continued for 3-6 months as residual nodularity was still there. 8 patients dropped out due to non responsiveness or side effects. Out of 48 patients with Mastalgia 38 (79%) responded quite well to treatment and most of the patients got relief from pain within 15 days but still treatment continued for 3 months. Some of the patients developed relapse after stopping treatment in 3 months and were kept on treatment up to 6 months. 10 patients either did not respond or developed side effects. Out of 41 patients with fibrocystic disease 32 (78%) responded well to treatment with clinical improvement of symptoms but ultrasound showed slow regression of cysts size and all of the patients took treatment for up to 6 months for complete regression. 9 patients developed side effects or ultrasound kept on showing no regression in cysts size, so switched to other therapeutic options. Out of 42 patients with fibroadenosis 33 (78%) responded well to treatment in a way that clinically adenosis was disappeared but ultrasound was showing evidence of adenosis even after 3 months of therapy so treatment continued for 6 months. 9 patients did not respond to treatment or developed side effects. 7 patients with galactorrhea and fibrocystic disease all (100%) responded to treatment. Galactorrhea stopped within 3 months of therapy in most of the cases but ultrasound was showing evidence of fibrocystic

Table 1: Conditions of ANDI with raised *S. prolactin* level

S.No	Condition of ANDI	No. of patients	Patients (%)	Number of patients with raised prolactin	Condition with raised prolactin (%)
1	Adolescent hypertrophy	6	3	0	0.0
2	Multiple fibroadenomas	18	9	5	27.0
3	Recurrent fibroadenoma	8	4	1	12.5
4	Cyclical nodularity	30	15	4	13.3
6	Mastalgia	48	24	3	6.25
7	Fibrocystic disease	41	20.5	2	4.8
8	Fibroadenosis	42	21	10	23.0
9	Galactorrhea (with fibrocystic disease)	7	3.5	5	71.0
Total		200	100	30	

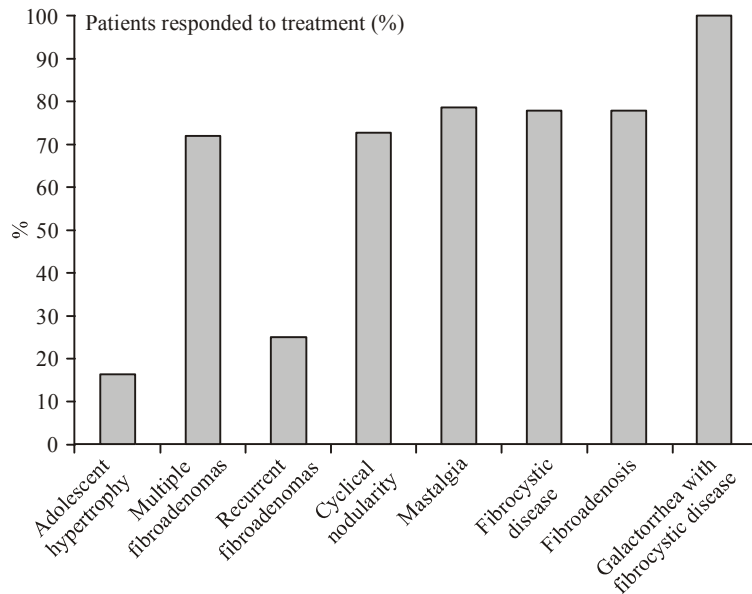


Fig. 1: Graphical presentation of response of antiprolactin treatment

Table 2: Conditions of ANDI and response of antiprolactin treatment

Condition of ANDI	Num of patients	Num of patients responded to treatment	Patients responded to treatment (%)
Adolescent hypertrophy	6	1	16.6
Multiple fibroadenomas	18	13	72.0
Recurrent fibroadenomas	8	2	25.0
Cyclical nodularity	30	22	73.0
Mastalgia	48	38	79.0
Fibrocystic disease	41	32	78.0
Fibroadenosis	42	33	78.0
Galactorrhea with fibrocystic disease	7	7	100.0

Table 3: Overall response of bromocriptine treatment

Response to treatment	Number of patients	Patients (%)
Good response	148	74
No response	30	15
Sever side effects	22	11
Total	200	100

disease so treatment continued up to 6 moths. Table 2 showing condition of ANDI and response of antiprolactin treatment. Fig. 1 showing graphical presentation of response of anti prolactin therapy. Overall 30 (15%) patients who were having raised S.Prolactin levels responded to treatment well and none of them developed sever side effects so all of them continued treatment. Table 3 showing overall response of therapy. None of the patients with raised prolactin level was dropped out of treatment.

DISCUSSION

Female patients with breast complaints come to surgical clinics with various symptoms including breast lump, nodularity, pain, nipple discharge etc [12]. Many women have breast symptoms but fortunately very few have breast cancer [13]. Breast tissue in females is under the influence of various hormones and subjected to constant physiological variation through out life. These changes lead to various pathological conditions [14]. Majority of these lumps come under the heading of ANDI (Aberrations of normal development and involution) [15]. In benign breast disease there is a connection between disease and Serum Prolactin level [16]. For the management of benign breast disease no ideal agent exists and the choice of drugs will depend on efficacy, side effects and cost [17]. Most of the study shows that Bromocriptine (an anti prolactin agent) at the dose of 5mg/day for 3 months, effectively control the benign breast disease with minimal side effects [11, 18]. We selected 200 patients who were suffering from one of the conditions coming under the heading of ANDI for treating with Bromocriptine. Only 15% patients were having raised S.Prolactin remaining 85% were having normal Prolactin levels. Out of 6 patients with adolescent hypertrophy only 1(16.6%) patient responded to Bromocriptine by showing arrest of growth but there was no regression of size. This result is in favor of result of Arscott [19] who suggested that etiology of this condition may involve breast tissue hypersensitivity to hormones other than Prolactin. 72% patients with multiple fibroadenomas and 25% patients

with recurrent fibroadenomas responded to Bromocriptine in a way that there was marked reduction in number and size of fibroadenomas. Although we did not find any reference regarding use of Bromocriptine in cases of fibroadenomas except in study by Parlati [11] who got significant reduction in size and clinical improvement in breast lesion with the use of Bromocriptine. With the significant response in our study we recommend use of Bromocriptine in cases of multiple fibroadenomas to prevent further recurrence and for cosmetically better results of surgery due to small size and reduced number of lesions. 73% patients with cyclical nodularity responded to treatment by showing significant and sustained reduction in nodularity and tenderness. This result is comparable to study by Maddox [17] and Nazli [18] who got same results. 79% of patients with Mastalgia responded to Bromocriptine which is equal to results by Nazli [18], Deliiski [20] and Mansel [21]. 78% of patients with Fibrocystic disease and Fibroadenosis responded to Bromocriptine as all of them got marked relief from pain and mammary tension after a few days of treatment, adenomatous and cystic nodules become smaller and softer often with disappearance of the smaller ones. This is less than study by Mussa [22] who got relief in 91% of patients but it is near equal to study by Tserotas [23] who got 77% patients of fibroadenosis and fibrocystic disease getting good result with Bromocriptine. All 7 (100%) patients with Galactorrhea along with fibrocystic disease responded to Bromocriptine which is in favor of study by Sakiyama [24] who showed promising results of Bromocriptine in Galactorrhea. Overall 74% of patients with ANDI responded to treatment although only 15% were having raised Prolactin level. This result shows that antiprolactin can be prescribed even in those patients who have normal prolactin level, as the cause of pathology might not be raised prolactin but it could be hypersensitivity of breast tissue to normal circulating prolactin level. 52 (26%) patients dropped out of treatment either due to intolerability of side effects or due to non responsiveness of therapy. 30 (15%) patients did not respond to treatment. All of these non responsive patients were having normal prolactin level before treatment, so the reason of pathology must be some other hormone or some environmental or nutritional factor. 22 (11%) patients developed major side effects of Bromocriptine like severe nausea, vomiting, headache or anorexia and left the treatment. This result is against study by Gumm [25] and Smith [26] who have said in their study that due to higher side effects profile Bromocriptine is rarely indicated. Our result is in favor of result of Nazli

[18] who said in her study that majority of side effects were mild or moderate.

Conclusion of our study is that Bromocriptine is highly effective drug in most of the conditions of ANDI except Adolescent hypertrophy. It is effective even in those patients who have normal serum Prolactin levels. This indicates that it is not always raised prolactin level which is responsible for ANDI but it could be hypersensitivity of breast tissue for normal circulating levels of prolactin that's why even those patients with normal prolactin get relief from antiprolactin therapy. Side effects are mostly mild to moderate and usually avoided by giving gradual incremental doses. Patients with raised serum prolactin will always get relief from symptoms with antiprolactin therapy and will not develop serious side effects.

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