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Full Length Research paper

Comparison of tamoxifen with danazol in the management of fibrocystic disease

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Fibrocystic disease, unilateral or bilateral, is a common problem found in women breasts. Successful treatment using tamoxifen (antiestrogen) and danazol (antiandrogen) has been used. We compared the efficacy of tamoxifen and danazol in the treatment of fibrocystic disease. We reviewed the clinical records of patients with fibrocystic disease presenting to the Department of Surgery, University of Shahid Beheshti, between August, 2001 and September, 2005. Medical treatment with either tamoxifen (20 mg/d) or danazol (400 mg/d) was offered and continued until a static response was achieved. The treatment response was compared. Sixty-eight patients with fibrocystic disease were seen in the breast clinic. The median age was 39.5 years (range, 13 - 82), with a median duration of symptoms of 3 months (range, 1 - 90). Twenty-three patients were treated with tamoxifen and 20 with danazol. Complete resolution of the fibrocystic disease was recorded in 18 patients (78.2%) treated with tamoxifen, whereas only 8 patients (40%) in the danazol group had complete resolution. Five patients, all from the danazol group, developed recurrence of disease. Hormonal manipulation is effective in the treatment of patients with fibrocystic disease. Although the effect is more marked for tamoxifen compared with danazol, the relapse rate is higher for danazol.

Key words: Tamoxifen, danazol, fibrocystic disease.

INTRODUCTION

Breast pain in women first described in the early 19th century by Sir Astly Cooper, who suggested that women who sought advice for breast pain were “usually of a nervous and irritable temperament.” This sentiment has persisted despite reports like that of Preece and coworkers, who said that women with breast pain were no more psychoneurotic than those having an operation for varicose veins. Mastalgia remains a poorly characterized, unreason for breast, consultation in general practice (Jay et al., 1996). The term fibrocystic/cystic breast disease is not a distinct disease, but rather a term used to represent a group of breast tissue abnormalities that may occur separately or together. While we associate this "disease" with the menstrual cycle, it is important to remember that women can experience palpable breast irregularities regardless of menstruation. Pathologic descriptions of the disease were recorded as early as the 1880 with the term chronic cystic mastitis identified a decade later.

Tamoxifen (Nolvadex) has been in use for over 20 years and currently is probably the most prescribed anti-cancer medication in the world. It is an orally effective, synthetic, non-steroidal, estrogen antagonist and agonist agent. In studies and trials it has been shown to have only limited side effects. It has produced regressions in women with fibrocystic changes, including precancerous ones, and in those with metastatic breast cancer, where its benefits were first observed. It has increased disease free survival (DFS) and overall survival (OS) rates when given as an adjuvant systemic type of therapy in women with early breast cancers, and it has reduced the incidence of patients, with an adequate specimen for diagnosis of fibrocystic disease in 79%. The age of the patients, the contra lateral breast cancers (Khan and Apkarian, 2002).

Danazol, a synthetic derivative of ethisterone, has

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Table 1. Grading system for fibrocystic disease.

Grade I	No breast mass and mild tenderness and pain
Grade II	A few nudularity and moderate tenderness and pain
Grade III	Nudularity and cyst and tenderness with pain
Grade IV	Sever tenderness and pain

Table 2. Fibrocystic disease comparable in the two groups treated with tamoxifen and danazol.

Tamoxifen	Complete resolution: 18 patients	Decrease in pain: 82%
Danazole	Complete resolution: 8 patients	Decrease in pain: 75%

been successfully used to treat benign breast disease since the first report of its therapeutic effect in 1971. It is thought to act centrally, on the hypothalamus and pituitary, and peripherally on target organs, binding with steroid receptors and affecting steroidogenesis and plasma proteins (San et al., 1985).

METHODS

We reviewed the clinical records of patients with fibrocystic disease presenting to the Department of Surgery, University of Shahid Beheshti, between August, 2001 and September, 2005. Patients with any possible underlying cause for fibrocystic disease, such as endocrine disturbance were excluded. Where bilateral fibrocystic disease was present, the results for the more severely affected breast were included in the analysis. The diagnosis was made by clinical assessment. The degree of fibrocystic disease was measured by protocol on Table 1. Patients were thoroughly examined for signs of breast mass and the presence of pain was also recorded.

However, its intensity and duration were noted. Cytological examination was performed with fine-needle aspiration to rule out underlying malignancy. Three options of treatment were offered after discussion with the patients, and they included: (1) tamoxifen (20 mg/d), (2) danazol (400 mg/d). The prescription of tamoxifen or danazol was not randomized but was at the discretion of the clinicians. The medical treatment was continued until a static response was achieved. The patients were followed up regularly at the clinic, and the response was monitored.

RESULTS

Between August, 2001 and September, 2005, 68 patients with idiopathic fibrocystic disease were seen in the breast clinic. The median age was 39.5 years (range, 13 - 82), with a median duration of symptoms of 3 months (range, 1 - 90). Thirty patients had fibrocystic disease on the right side and 31 on the left side, whereas 7 patients had bilateral fibrocystic disease. Twenty-three patients were treated with tamoxifen and 20 with danazol. One patient was treated with both tamoxifen and danazol.- Fine-needle aspiration cytology (FNAC) was performed in 37 disease were comparable in the two groups treated with tamoxifen and danazol, respectively (Table 2). Eleven patients in the tamoxifen group and 8 patients in the danazol group had mass and pain in all of cases. The median duration of treatment was 3 months in both groups, with a range of 1 to 12 months in the tamoxifen group and a range of 1 to 6 months in the danazol group. There were no significant side effects recorded in either group. Complete resolution of the fibrocystic disease was recorded in 18 patients (78.2%) treated with tamoxifen, whereas only 8 patients (40%) in the danazol group had complete response. There was a decrease in pain in 82% of the patients in the tamoxifen group and 75% of the danazol group. The recurrence rate in tamoxifen and danazole mentioned in Table 3 developed in five patients from 6 to 48 months after discontinuation of therapy.

DISCUSSION

Fibrocystic disease is a common finding in women breast. Fibrocystic changes, which occur in approximately 60% of premenopausal women, are a normal finding. The term "fibrocystic disease" originated from the histologic description of cysts or increased stromal tissue in women whose breasts were biopsied for various reasons (Wilson and Sellwood, 1976). The name was changed to "fibrocystic changes" in the 1980s, and is considered a variant of normal. Although, arbitrary, the term "fibrocystic disease" is used now when fibrocystic changes occur in conjunction with severe pain, nipple discharge, or a degree of lumpiness sufficient to cause suspicion of cancer.

The major aim of therapy in women with fibrocystic disease is to relieve breast pain. Studies on the risk of breast cancer in women with mastalgia are conflicting, reporting both increased risk and decreased risk (Khan and Apkarian, 2002; Sarnelli and Squartini, 1991). Simple reassurance that the patient most likely does not have breast cancer provides adequate relief for 85% of women. Symptomatic relief also may be achieved with the use of a soft brassiere with good support.

Some study results show that tamoxifen therapy was

Table 3. Recurrence rate in tamoxifen and danazole.

Treatment	6 Months)	1 Year	2 years
Tamoxifen	2 (8/7%)	3(13%)	5(21/7%)
Danazol	4(20%)	7(35%)	9(45%)

associated with a 28% reduction in the overall annual rate of benign breast disease. The incidence of adenosis, cyst, duct ectasia, fibrocystic disease, hyperplasia, and metaplasia was statistically significantly lower among the tamoxifen-treated women than among the placebo-treated women (San et al., 1985) and also appropriate selection of women at high risk for HR+ disease may improve the risk-benefit ratio of tamoxifen intervention (Veronesi et al., 2007).

When there is a reduction in estrogen-induced stimulition of normal breast tissue, a reduction in breast symptomatology is likely to be associated with fewer complaints of pain and swelling. The fact that tamoxifen duration of symptoms, and the grade of the fibrocystic therapy had an effect on benign breast disease, regardless of clinical history, superior to danazole for tumorigenesis at an even earlier stage than previously thought.

We are most aware that tamoxifen use is associated with adverse events such as deep vein thrombosis, pulmonary embolism, stroke and endometrial cancer (Fisher et al., 1998). Danazol also proved effective in the reduction of cyst diameter in women with cysts fewer than 20 mm in diameter, which had not been punctured. Side effects were cycle irregularities and weight gain and oiliness of skin and hair, and acne (Radivojevic, 1991; Brookshaw, 1979). About tamoxifen there was a tendency for patients with more severe symptoms to respond better to the higher dosages, and for the elimination rate for all grades of severity to improve with time and side effects were not severe. And of the expected type including weight gain, oiliness of skin and hair, and acne. This study confirms that tamoxifen offers very well therapeutic results compare to danazole for the treatment of the frequently persisting benign breast disease.

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