Tamoxifen Therapy for Breast Cancer and Endometrial Pathology

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Abstract

Background: Tamoxifen, used as adjuvant therapy for carcinoma breast in postmenopausal women to prevent relapse has estrogenic effect on the endometrium.

Methods: 104 patients on tamoxifen for more than six months were subjected to a clinical examination and transvaginal sonography. Patients with endometrial thickness > 8 mm were further evaluated by hysteroscopy and endometrial biopsy.

Results: 35(34%) patients were symptomatic. The average endometrial thickness was 11.2 mm which correlated with duration of tamoxifen use. 27(48%) patients had abnormal hysteroscopic findings. 35 (63%) of endometrial biopsies revealed abnormal endometrium. One case of endometrial carcinoma was diagnosed. The results were statistically analysed. There is a significant association between symptomatic status and endometrial thickness and duration of tamoxifen use.

Conclusion: All patients on long term tamoxifen should be annually screened for endometrial pathology.

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Key Words: Tamoxifen; Endometrium; Transvaginal sonography

Introduction

Tamoxifen has been successfully used for more than a decade as adjuvant therapy for breast cancer in postmenopausal women with positive estrogen receptor proteins after conventional primary treatment. An increasing number of reports implicated induction of endometrial change with continued use of tamoxifen. Since tamoxifen confers an increased risk of endometrial cancer, gynaecologic surveillance of asymptomatic women is needed [1]. The present study was conducted to evaluate the effects of tamoxifen on endometrium, when given as an adjuvant therapy for breast cancer. The evaluation was done by transvaginal ultrasonography, hysteroscopy and endometrial biopsy.

Material and Methods

Patients of carcinoma breast on adjuvant tamoxifen therapy at an oncology center of a referral service hospital were included in this prospective study covering the period Oct 1999 to Oct 2001. Patients on tamoxifen for more than six months were subjected to clinical examination and transvaginal ultrasonography (TVS) for endometrial thickness. Endometrial thickness was measured in anteroposterior dimension and was considered normal when less than 8 mm. Patients with endometrial thickness of more than 8 mm were further evaluated by conventional hysteroscopy and endometrial biopsy. Endometrial thickness

was then correlated with hysteroscopic findings, histopathologic findings and duration of tamoxifen treatment.

Results

104 patients of carcinoma breast on tamoxifen treatment were included in the study. 35 (34%) patients were on tamoxifen for a duration of 1 – 2 years whereas only 14 (13%) were on tamoxifen for more than 3 years. 35 patients (34%) were symptomatic, whereas 69 (66%) were asymptomatic (Table 1). 48 patients (46%) showed endometrial thickness of less than 8 mm while 56 (54%) showed endometrial thickness of 8 mm or more. The average endometrial thickness was 11.2 mm which correlated with the duration of tamoxifen use (Table 2). 56 patients with endometrial thickness > 8 mm were subjected to diagnostic hysteroscopy. 29 (52%) had normal hysteroscopic findings, whereas 27 (48%) had abnormal findings like hyperplasia, endometrial polyp or growth. As endometrial thickness increased, the incidence of abnormal finding increased (Table 3). 21 (37%) of the endometrial biopsies revealed normal endometrium whereas 35 (63%) had endometrial pathology. The commonest pathology was endometrial polyp in 12 patients. Endometrial hyperplasia with nuclear atypia in 5 patient had endometrial carcinoma in 1. The endometrial carcinoma occurred in a woman who was treated with tamoxifen for a duration of six years (Table 4). This patient was symptomatic.

Discussion

Ozsner et al have shown that tamoxifen use increases

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Table 1**Duration of Tamoxifen use and symptom status (n-104)**

Duration of use (Tamoxifen)	No of patients	Symptomatic	Asymptomatic
6 months – 1 year	23 (22%)	4	19
1 year – 2 years	35 (34%)	8	27
2 years – 3 years	32 (31%)	15	17
> 3 years	14 (13%)	8	6
Total	104	35(34%)	69(66%)

[P value by chi – square test < 0.01. There is a significant linear trend between the symptomatic status and duration of tamoxifen use]

Table 2**Duration of tamoxifen use and endometrial thickness (n-104)**

Duration of use	< 8 mm thickness	> 8 mm thickness
6 months – 1 year	16	6
1 year – 2 years	14	20
2 years – 3 years	10	21
> 3 years	5	9

[P value by chi – square test < 0.01. There is a significant linear trend between number of patients with > 8 mm endometrial thickness and duration of tamoxifen use]

the risk of endometrial cancer and premalignant change [2]. They also noticed significant relation between endometrial thickness and duration of tamoxifen treatment (P-0.025) as in the present study. Hann et al found abnormal endometrial biopsy in 44% women treated with tamoxifen for less than 5 years whereas 58% of endometrial biopsies revealed abnormal results when duration of tamoxifen treatment was > 5 years [3].

Katase et al concluded that tamoxifen does not appear to increase subsequent endometrial carcinoma in patients with primary breast carcinoma who underwent annual screening for gynaecologic cancer [4]. In contrast, the present study has shown one case of endometrial carcinoma and 5 patients of endometrial hyperplasia with nuclear atypia. This shows significant risk (p-0.026) of premalignant and malignant change in patients on long term tamoxifen.

Peters-Engl et al demonstrated that clinical benefits of tamoxifen greatly outweigh the risk [5]. They recommended annual follow up of patients on tamoxifen. Cohen et al showed that 28.6% of patients on tamoxifen had endometrial pathology [6]. The incidence was significantly more in symptomatic patients. Seoud et al concluded that the value of routine screening for endometrial pathology in patients on tamoxifen is controversial. They found that all patients who developed an abnormal endometrium had abnormal vaginal bleeding [7]. Bernstein et al in a case control study concluded

Table 3**Endometrial thickness and hysteroscopy findings (n-56)**

Endometrial thickness	Normal study	Abnormal study
8 – 9.9 mm	13	5
10 – 11.9 mm	6	6
12 – 13.9 mm	5	7
14 – 15.9 mm	2	3
16 – 17.9 mm	2	3
≥ 18 mm	1	3

Table 4**Histopathological findings (n-56)**

Histopathological finding	No of patients	Percentage
Normal endometrium	21	37%
Endometrial polyps	12	22%
Endocervical polyps	4	7%
Cystic hyperplasia	3	5%
Adenomatous hyperplasia	8	14%
Endometrial hyperplasia with nuclear atypia	5	9%
Endometrial cancer	1	2%
Insufficient sample	2	4%

that endometrial cancer associated with tamoxifen use and the risk increased with the duration of tamoxifen use [8]. Prior use of estrogen replacement therapy (ERT) increased risk associated with tamoxifen use.

In a meta analysis, Macmohan concluded that an association exists between endometrial cancer and tamoxifen use [9].

Conclusion

The present study has shown that long term use of tamoxifen as adjuvant therapy for carcinoma breast is associated with endometrial pathology. Endometrial thickness is increased in such patients and is related to the duration of tamoxifen use (p<.01). There is a significant risk of premalignant and malignant lesions of endometrium in patients on long term tamoxifen. All patients on long term tamoxifen should be annually screened for endometrial pathology.

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