Does raloxifene therapy affect mammographic breast cancer screening in postmenopausal patients?

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Summary

Objective: The aim of the study was to determine mammographic breast density changes during raloxifene therapy in postmenopausal patients

Materials and Methods: Fifty-five cases who were using raloxifen therapy were included in this retrospective analysis. Raloxifene was given for osteopenia and osteoporosis according to low bone mineral density measured by dual-energy X-ray absorptiometry (DEXA). None of the patients were using hormone replacement therapy 12 months before the initiation of raloxifene treatment or during the study. Mammographic breast density was determined by mammography before the initiation of raloxifene treatment (baseline) and after 12 to 16 months of therapy. The Breast Imaging Reporting and Data System (BI-RADS) breast density score was used for the evaluation of mammographic density.

Results: There was no change in mammographic breast density when the baseline and the first mammography taken after the initiation of therapy were compared ($p = 0.32$). There was no significant correlation between the duration of raloxifene treatment and mammographic density measured after raloxifene treatment ($r = -0.158$, $p = 0.25$). Only in one patient did the BI-RADS classification of 2 change to 3 after 12 months of therapy.

Conclusions: In conclusion, raloxifene therapy for 12 to 16 months does not increase mammographic breast density in postmenopausal women with low bone mass.

Key words: Breast cancer; Mammography; Raloxifene.

Introduction

The effect of different hormones on mammographic density was stressed in two retrospective studies performed in our clinic [1, 2]. Tibolon, a similar selective estrogen receptor modulator, does not seem to have any effect on mammographic breast density [2].

Raloxifen is a tamoxifen analog belonging to the benzothiophen group of the selective estrogen receptor modulator family [3]. The alkyl-amino-etoxic side chain is responsible for the antiestrogenic affect of raloxifen and the nitrogen in this side chain specifically reacts with the aspartate in the estrogen receptor to induce the antiestrogenic effect. Under in vivo conditions, raloxifen inhibits the proliferation of breast cancer cells more effectively than tamoxifen [4].

Mammographic screening decreases the incidence and mortality rate of breast cancer [5, 6]. One important factor that may reduce the sensitivity of mammography is mammographic density changes [7, 8]. The aim of the study was to determine mammographic breast density changes during raloxifen therapy in postmenopausal patients.

Material and Methods

Fifty-five cases who were admitted to the Ege University Medical Faculty Gynecology Department's Menopause Clinic between June 2002 and June 2004 and using raloxifen therapy were included in this retrospective analysis. The records of patients using raloxifene therapy were retrieved retrospectively. None of the patients were using hormone replacement treatment 12 months before the initiation of raloxifene treatment or during the study. The mean age of the patients was 50.4 ± 3.6 (43-58). Eighteen (34.7%) of the patients were in surgical menopause and the 37 (67.3%) were in natural menopause. The mean duration of raloxifen treatment was 13.4 ± 12 (12-16) months. The demographic variables are summarized in Table 1.

The presence of osteopenia or osteoporosis was defined as a lumbar spine or femoral neck bone mineral density (BMD) ≥ 1 SD below the normal peak bone mass for healthy premenopausal women (T-score ≤ 1).

Raloxifene hydrochloride 60 mg/day (Evista, Lilly, USA) was given for osteopenia or osteoporosis according to low bone mineral density measured by dual-energy X-ray absorptiometry (DEXA). The mammographic breast density was determined by mammography before the initiation of raloxifene treatment (baseline) and after 12 to 16 months of therapy.

The American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) breast density score was used for the evaluation of mammographic density [9]. Mammographies were obtained by Siemens Mammomat 3000, Germany. For the primary evaluation, mammograms were rated according to the BI-RADS breast categories of (1) almost entirely fatty, (2) fatty with scattered fibroglandular densities, (3) heterogeneously dense breast tissue (which could obscure a small mass), and (4) extremely dense breast tissue (which lowers the sensitivity of mammography). A secondary evaluation of the mammograms was performed to compare the change in breast density, regardless of whether the change was sufficient to alter the BI-RADS breast density category (non-BI-RADS assessment).

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Table 1. —The demographic variables of the study population.

	Minimum	Maximum	Mean ± standard deviation
Age (years)	43	58	50.4 ± 3.6
Menopausal age (years)	41	55	46.9 ± 3.9
Menopause duration time (months)	12	171	37 ± 27.2
Body mass index	24.4	31.7	28.3 ± 1.7

Results

There was no change in mammographic breast density when the baseline and the first mammograph after the initiation of the therapy was compared ($p = 0.32$).

Mammographic densities were reported as classification 1 (n = 8, 14.5%), classification 2 (n = 28, 50.9%), classification 3 (n = 17, 30.9%) and classification 4 (n = 2, 3.6%) at baseline and after 12-16 months of raloxifene treatment. There was no significant correlation between the duration of raloxifene treatment and mammographic density measured after raloxifene treatment ($r = -0.158$, $p = 0.25$). Only in one patient did the BI-RADS classification of 2 change to 3 after 12 months of therapy.

Discussion

The amount of fibroglandular density affects the radiologist's ability to detect breast cancer. Breast cancer is detected most easily in predominantly fatty breasts, with detectability decreasing as radiographic density increases. Approximately 50% of breast cancers are detected by mammography as masses [10]. Such masses may be obscured by dense tissue and be difficult to detect. Mandelson *et al.* [11] reported that mammographic density was a strong risk factor for breast cancer detected in the interval after a negative mammogram.

Jackson *et al.* [12] compared mammographic changes in breast density that are associated with raloxifene or continuous combined hormone therapy in postmenopausal women older than 60 years who had a bone mineral density T-score of ≤ -1. After 12 months of treatment, 0.9% of the women who received raloxifene had increased mammographic breast density compared with 27.4% of the women who received continuous-combined hormone therapy ($p < .001$). In the continuous-combined hormone therapy group, 77% of the women reported breast tenderness at some time during the study, compared to 22% of the women in the raloxifene group.

In conclusion, raloxifene therapy for 12-16 months does not increase mammographic breast density in postmenopausal women with low bone mass.

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