Development of breast cancer during postmenopausal hormone therapy in Korea

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Objective: The clinicopathologic characteristics of patients with breast cancer arising during postmenopausal hormone therapy were determined.

Methods: The study included 29 patients diagnosed with breast cancer during postmenopausal hormone therapy (HT group) and 285 patients diagnosed with breast cancer after menopause who did not receive HT (non-HT group). The data were collected at the three affiliated Hospitals of the Catholic University of Korea over a 10 year period. Tumor size, lymph node metastasis, the presence of estrogen receptors, the stage at the time of diagnosis, the method of treatment, the type of operation, the recurrence rate, and the mortality rate were compared between the two groups.

Results: The HT group had smaller tumors than the non-HT group (p=0.0032). In the HT and non-HT groups, 55.2% and 28.6% of the tumors were T1, respectively. In the HT and non-HT groups, 53.9% and 13.4% of the tumors were well differentiated, respectively (p=0.0026). The 5-year survival rate was 100% and 87.6% in the HT and non-HT groups, respectively (p<0.001).

Conclusion: Postmenopausal Korean women who developed breast cancer while taking HT had a higher rate of well differentiated tumors, a higher rate of tumors <2 cm in size, and a higher 5-year survival rate than women who developed breast cancer when not taking HT.

Key words: Menopause; Hormone therapy; Breast cancer

Introduction

Due to the increasing average life expectancy in Korea (> 81.9 years)1, women spend more than one-third of their lives with ovarian hormone deficiency. Postmenopausal hormonal deficiency causes various physical and psychological problems adversely affecting the quality of life and accelerating the aging process. Hormone therapy (HT) is the best treatment choice for alleviating postmenopausal symptoms and protecting patients against fractures arising from osteoporosis.2 Moreover, HT that is started at an early stage of menopause is expected to reduce the risk of cardiovascular diseases.3

The most troublesome side effect of HT, however, is the increased risk of breast cancer.4,5 Breast cancer is the most common invasive cancer in women in the US and the second most common cause of death from cancer following lung cancer. The risk of developing breast cancer throughout life is 12.5%, and increases with age in the US In Korea, the incidence of breast cancer has increased yearly.6 According to the 2005 statistics, breast cancer has become the most common cancer in women (7,317 patients), while it is ranked sixth in mortality among all cancers (1,581 patients).6
Compared to the US, the incidence of invasive breast cancer in Korea peaks at 50 years of age which is pre- or peri-menopausal, and declines thereafter. The incidence of breast cancer in the peri-menopause is 61% and is higher than in the post-menopause.

The risk factors for breast cancer are thought to be pregnancy- and delivery-related reproductive factors, breastfeeding-related factors, dietary factors, a history of benign breast disease and breast cancer, obesity, and a family history of breast cancer. The mechanisms underlying these risk factors are thought to be related to reproductive hormones.

According to multiple observational studies, the risk of breast cancer is increased in women who have used HT for a long period of time, but the excess risk is reduced after use ceases and largely, if not completely, disappears after approximately 5 years. Moreover, the short term use of HT does not affect the risk of breast cancer. Estrogen only therapy does not increase the risk of breast cancer as much as estrogen-progesterone combination therapy. Although there is a report that the prognosis of breast cancer diagnosed during HT is better than breast cancer of a non-user of HT, according to the Women’s Health Initiative (WHI), a large-scale randomized trial conducted by the National Institutes of Health, postmenopausal women who developed breast cancer while taking estrogen as well as progesterin had abnormal mammograms at a higher frequency than women who were not on HT, making the early diagnosis more difficult for those women, and thereby making the cancer in those women diagnosed at a more advanced stage.

There have been few studies of breast cancer diagnosed in women taking HT in Korea. Although the incidence of breast cancer for postmenopausal women is lower than pre- or peri-menopausal women in Korea, the increasing population of post-menopausal women has drawn attention to post-menopausal breast cancer.

In the current study, we conducted a clinical review of hormone regimens, duration of hormone use, and characteristics of breast cancer in post-menopausal women who were diagnosed while taking HT.

We also compared the characteristics of the breast cancer diagnosed in women taking HT with the post-menopausal breast cancer diagnosed in women who were not taking HT during the same period and evaluated the effect of HT on the risk of breast cancer.

Materials and Methods

1. Study subjects

Data were collected from the 29 patients who were diagnosed with breast cancer during post-menopausal HT in the Department of Gynecology and the 285 patients who were diagnosed with breast cancer during menopause who were not taking HT. The data women using HT were matched to women not using HT based on their age at the time of diagnosis. The breast cancers in both groups of women were diagnosed by post-operative pathology.

The data were based on medical records collected at St. Mary’s Hospital of the Catholic University of Korea and Kangnam St. Mary’s Hospital of the Catholic University of Korea during a 10-year period between May 1995 and June 2004. The collected data for the two groups were compared in terms of tumor size, the presence of lymph node metastases, cellular differentiation, the presence of estrogen receptors, the stage at the time of diagnosis, the recurrence rate, and the mortality rate.

Those women in the HT group had received HT for at least 6 months prior to or at the time of a diagnosis of breast cancer. The estrogen only regimen (PREMARIN® [conjugated equine estrogens, USP]; Srogen®[conjugated equine estrogens, 0.625 mg; Sam Il Pharm]) were administered to those women who had undergone a total hysterectomy. An estrogen and progesterone combined regimen (Climen® [estradiol valerate, 2 mg; cyproterone acetate, 1 mg; Bayer Schering Pharma]; TRISEQUENS® [estradiol hemihydrate, 2 mg; norethisterone acetate, 1 mg; estradiol hemihydrate, 1 mg; Novo Nordisk]; *Activelle® [estradiol hemihydrate, 1.03 mg; norethisterone acetate, 0.5 mg; Novo Nordisk]; PREMARIN® [conjugated estrogen tablets, USP] or Srogen® [conjugated equine estrogens, 0.625 mg; Sam Il Pharm] with Provera® [medroxyprogesterone acetate, 2.5 mg; Pfizer Pharmaceuticals Korea]) was administered to those who had an intact uterus. Tibolone (Livial® [tibolone, 2.5 mg; Schering Plough]) was administered to both groups of women.

Those women in the non-HT group had never received HT. The size of the tumor, the presence of metastasis in the lymph nodes, and cellular differentiation were determined based on pathologic results. The stages are based on the TNM stages set by The American Joint Committee and the International Union against Cancer. T1 is a tumor <2 cm in size, T2 is a tumor between 2 and 5 cm in size, and T3 is a tumor ≥5 cm in size. T4 is a tumor with thoracic or skin in-