A Nationwide Study on Breast Cancer Risk in Postmenopausal Women Using Hormone Therapy in Finland

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ABSTRACT

Since national differences exist in genes, environment, diet and life habits and also in the use of postmenopausal hormone therapy (HT), the associations between different hormone therapies and the risk for breast cancer were studied among Finnish postmenopausal women.

All Finnish women over 50 years of age who used HT were identified from the national medical reimbursement register, established in 1994, and followed up for breast cancer incidence (n= 8,382 cases) until 2005 with the aid of the Finnish Cancer Registry. The risk for breast cancer in HT users was compared to that in the general female population of the same age.

Among women using oral or transdermal estradiol alone (ET) (n = 110,984) during the study period 1994-2002 the standardized incidence ratio (SIR) for breast cancer in users for < 5 years was 0.93 (95% confidence interval (CI) 0.80–1.04), and in users for ≥ 5 years 1.44 (1.29–1.59). This therapy was associated with similar rises in ductal and lobular types of breast cancer. Both localized stage (1.45; 1.26–1.66) and cancers spread to regional nodes (1.35; 1.09–1.65) were associated with the use of systemic ET. Oral estriol or vaginal estrogens were not accompanied with a risk for breast cancer.

The use of estrogen-progestagen therapy (EPT) in the study period 1994-2005 (n= 221,551) was accompanied with an increased incidence of breast cancer (1.31;1.20-1.42) among women using oral or transdermal EPT for 3-5 years, and the incidence increased along with the increasing duration of exposure (≥10 years, 2.07;1.84-2.30). Continuous EPT entailed a significantly higher (2.44; 2.17-2.72) breast cancer incidence compared to sequential EPT (1.78; 1.64-1.90) after 5 years of use. The use of norethisterone acetate (NETA) as a supplement to estradiol was accompanied with a higher incidence of breast cancer after 5 years of use (2.03; 1.88-2.18) than that of medroxyprogesterone acetate (MPA) (1.64; 1.49-1.79). The SIR for the lobular type of breast cancer was increased within 3 years of EPT exposure (1.35; 1.18-1.53), and the incidence of the lobular type of breast cancer (2.93; 2.33-3.64) was significantly higher than that of the ductal type (1.92; 1.67-2.18) after 10 years of exposure.

To control for some confounding factors, two case control studies were performed. All Finnish women between the ages of 50-62 in 1995-2007 and diagnosed with a first invasive breast cancer (n= 9,956) were identified from the Finnish Cancer Registry, and 3 controls of similar age

(n=29,868) without breast cancer were retrieved from the Finnish national population registry. Subjects were linked to the medical reimbursement register for defining the HT use.

The use of ET was not associated with an increased risk for breast cancer (1.00; 0.92-1.08). Neither was progestagen-only therapy used less than 3 years. However, the use of tibolone was associated with an elevated risk for breast cancer (1.39; 1.07-1.81). The case-control study confirmed the results of EPT regarding sequential vs. continuous use of progestagen, including progestagen released continuously by an intrauterine device; the increased risk was seen already within 3 years of use (1.65;1.32-2.07). The dose of NETA was not a determinant as regards the breast cancer risk.

Both systemic ET, and EPT are associated with an elevation in the risk for breast cancer. These risks resemble to a large extent those seen in several other countries. The use of an intrauterine system alone or as a complement to systemic estradiol is also associated with a breast cancer risk. These data emphasize the need for detailed information to women who are considering starting the use of HT.