Association between hormone replacement therapy and occurrence of breast cancer

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Abstract: Using hormone replacement therapy for relieving menopausal symptoms and also for preventing some diseases such as hip fractures had led to a widespread use of it in postmenopausal women but there is a concern about risks of breast cancer occurrence using HRT. In this study, 1000 women older than 40 years old without any clinical symptoms were selected. They were referred to a radiology center for a screening mammography. By using a questionnaire the information about using HRT was gathered. 16.7% of cases were using HRT and 83.3% had no history of using HRT. Among 1000 cases, 13 mammograms had signs of malignancy. In these cases 7.7% was using HRT and 92.3% didn't have any history of using HRT. It was concluded that there isn't any statistically significant association between the development of breast cancer and using HRT (P=0.604).
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1. Introduction

Breast cancer is the most frequent cancer among women, and it is also the most common cause of cancer death in both developed and developing regions (Ferlay, 2010). Various risk factors have been described for development of breast cancer. One of them is HRT .Using hormone replacement therapy for relieving menopausal symptoms and also for preventing some diseases such as hip fractures had led to a widespread use of it in postmenopausal women. Concern that hormone replacement therapy (HRT) may cause breast cancer has existed since the time it was introduced, and based on evidence in three studies, the Collaborative Reanalysis (CR), the Women's Health Initiative (WHI) and the Million Women Study (MWS), it is claimed that causality is now established (Shapiro, 2011). One aspect of WHI (Women's Health Initiative randomized controlled trial) study was discussing the increased incidence of breast cancer in the group receiving HRT (Rossouw, 2002). There are also other studies evaluated the association between the incidence of breast cancer and using HRT. Some of them approved a positive link between using HRT and increased incidence of breast cancer among women (De, 2010). In contrast, some other studies couldn't find any relationship between using HRT and breast cancer (Antoine, 2011; Stanford, 1995). With regard to these controversies, we conducted a study to analyze the relationship between using HRT and occurrence of breast cancer in Iranian population.

2. Material and Methods

In a descriptive analytical study, 1000 women older than 40 years old without any clinical symptoms who came to a radiology center in Tabriz (capital of East Azerbaijan province in Iran) were selected. They were referred to a radiology center for a screening mammography. By using a questionnaire the information about using HRT was gathered .the screening technique included physical examination of breasts by an experienced physician before taking mammograms and then performing screening mammography in two standard views: craniocaudal (CC) and mediolateral-oblique (MLO) view.
A radiologist read the mammograms and any kind of abnormal findings were recorded. If there was any need, the patients were referred for further evaluation or to a surgeon for a biopsy. The association between the HRT therapy and breast cancer occurrences was analyzed.

Ethical considerations:

This study was in perfect compliance with privacy protection, and all patients' information is completely confidential and their name and specifications have never been revealed.

3. Results

1000 women between ages 40-77 years old and without any clinical symptoms were evaluated. The frequency of age groups in the sample is shown chart 1.

In this sample, 167 cases (16.7%) were referred for a checkup because of using HRT. 381 cases (38.1%) were referred for a checkup before initiating HRT and 452 cases (45.2%) were referred for a general checkup.16.7% of cases was using HRT and 83.3% had no history of using HRT. Among 1000 cases, 13 mammograms had signs of malignancy. In these cases 7.7% was using HRT and 92.3% didn't have any history of using HRT. Among the cases that were using HRT, 93.4% had normal mammograms, 6% had signs of benign mass in mammograms and 1.8% had calcification in their breast.

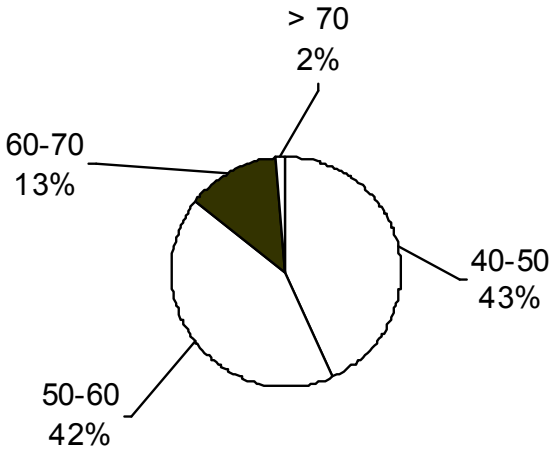

Chart 1. Frequency of age groups in the sample

4. Discussions

In this study we couldn't find any significant association between the development of breast cancer and using HRT (P=0.604). Würtz et al in one case control study in 2012 on 348 eligible cases among 20,861 postmenopausal women reported that there is Modest direct associations between estrogen levels and breast cancer incidence among both never and baseline HRT users. Estrone and estrone sulfate were more consistently associated among both groups than estradiol. They concluded that higher serum estrogen levels were associated with a higher risk of breast cancer among both never and baseline HRT users (Würtz, 2012).

Turkoz et al in one cross-sectional study that consisted of 1884 invasive breast cancer cases in 2012 reported an increased risks for postmenopausal women with HER-2 over expressing (OR 2.20, 95% CI 0.93-5.17; p=0.04) and luminal A (OR 1.87, 95% CI 0.93-3.90, p=0.02) breast cancers, who used hormone replacement therapy for 5 years or more (Turkoz, 2012).

Antoine et al in 2012 in the study on Belgium reported that There is a significant association between the invasive BC incidence rate and estimated rate of HRT users in the previous year: p-value<0.001.and concluded that Although this study is hampered by a number of limitations, these data support the idea that the drop in BC incidence can be partly attributed to the decrease in HRT use. Since HRT remains the most used medication for climacteric symptoms, we encourage the creation of a prospective registry in Europe, collecting detailed data in various European countries, in order to assess the adjusted increase in BC risk associated with HRT, which may be population and regimen dependent (Antoine, 2012).

Ritte and et al in 2012 Within the European EPIC cohort reported that Current use of HRT is significantly associated with an increased risk of receptor-negative (HRT current use compared to HRT never use HR: 1.30 (1.05 to 1.62) and positive tumors (HR: 1.74 (1.56 to 1.95)), although this risk increase was weaker for ER-PR- disease (Phet = 0.035) (Ritte, 2012).

Cerne and et al in 2012, in a case control study reported that in postmenopausal women using HRT, the KRAS variant might lead to HER2 over expressed and poorly-differentiated breast tumors, both indicators of a worse prognosis (Cerne, 2012).

Calvocoressi and et al in 2012, in a population-based case-control study on 1179 post-menopausal women (603 controls and 576 cases) reported that no association between DCIS and ever use of any HT (adjusted odds ratio (OR) =0.85, 95% confidence interval (CI): 0.65-1.11); of estrogen alone (adjusted OR=0.93; 95% CI: 0.68-1.29) or of estrogen and progesterone (adjusted OR=0.75; 95% CI: 0.52-1.08). There was also no association between DCIS and current use of these hormones. In addition, estimated risk of DCIS did not increase with duration of use of these preparations (Calvocoressi, 2012).

Shapiro and et al in 2012, Using generally accepted causal criteria, in one study, evaluate the findings in the MWS (Million Women Study) for E+P and for ET. They reported that despite the massive size of the MWS the findings for E+P and for ET did not adequately satisfy the criteria of time order, information bias, detection bias, confounding, statistical stability and strength of association, duration-response, internal consistency, external consistency or biological plausibility. Had detection bias resulted in the identification in women aged 50-55 years of 0.3 additional cases of breast cancer in

ET users per 1000 per year, or 1.2 in E+P users, it would have nullified the apparent risks reported and concluded that HRT may or may not increase the risk of breast cancer, but the MWS did not establish that it does (Shapiro, 2012).

Shapiro and et al in 2011, Using generally accepted causal criteria; evaluate the findings in the WHI (Women's Health Initiative) for estrogen plus progesterone. For estrogen plus progesterone the findings did not adequately satisfy the criteria of bias, confounding, statistical stability and strength of association, duration-response, internal consistency, external consistency or biological plausibility and concluded that HRT with estrogen plus progesterone may or may not increase the risk of breast cancer, but the WHI did not establish that it does(Shapiro, 2011).

Shapiro and et al in 2011, Using generally accepted causal criteria; evaluate the findings in the Collaborative Reanalysis (CR) for hormone replacement therapy cause breast cancer? The findings in the CR did not adequately satisfy the criteria of time order, bias, confounding, statistical stability and strength of association, dose/duration-response, internal consistency, external consistency or biological plausibility they concluded that HRT may or may not increase the risk of breast cancer, but the CR did not establish that it does(Shapiro, 2011).

Despite our result in Iranian women, in other studies on Caucasian women almost there is association between HRT and occurrence of breast cancer.

Conclusion:

In this survey, by using statistical analysis, it seems there isn't any statistically significant association between the development of breast cancer and using HRT (P=0.604) in our study on Iranian women in contrast with another studies, it can due to our people different races with other studies (on Caucasian) in this study or another effective factors in breast cancer as same as gen and environment or maybe to our small no of samples. Further studies with large no of samples may be needed to investigate the association in our population.

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