

Evaluating Association of Tissue Selenium Level and Estrogen Receptor and Progesterone Receptor Expression in Breast Cancer

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ABSTRACT

Background and Objectives: Recently, the incidence of breast cancer has increased drastically worldwide. Therefore, the identification of novel diagnostic biomarkers is essential for improving treatment outcomes and prognosis. Estrogen receptor (ER) and progesterone receptor (PR) are routinely available in breast cancer specimens. Semi-quantitative assessment of ER and PR is important for prognosis. Even with the development of genomic tests, hormone receptor status remains the most significant predictive and prognostic biomarker. Selenium is known to protect mammary epithelial cells against oxidative DNA damage and early carcinogenic events. Since overexpression of ER and PR is common in breast cancers, we aimed to evaluate association of tissue selenium level and ER and PR expression in breast cancer.

Methods: Sixty tissue samples (30 tumors and 30 tumor margins) were collected from patients with breast cancer. Selenium level was measured using graphite furnace atomic absorption spectroscopy and ER/PR expression was evaluated using immunohistochemistry.

Results: About 60% of the samples were positive for ER/PR expression. Mean level of tissue selenium was 209.54 $\mu\text{g/L}$ in tumors and 185.04 $\mu\text{g/L}$ in tumor margins that were ER/PR positive. In addition, mean selenium level was 243.39 $\mu\text{g/L}$ and 168.06 $\mu\text{g/L}$ in ER/PR-negative tumors and tumor margins, respectively. There was no significant association between selenium level and ER/PR expression ($P>0.05$).

Conclusion: There is no association between tissue Se level and ER/PR expression in breast cancer.

Keywords: Selenium, Estrogen receptor (ER), progesterone receptor (PR), breast cancer.

INTRODUCTION

Recently, the incidence of breast cancer has increased drastically worldwide (1). Estrogen receptor (ER) and progesterone receptor (PR) are routinely available in breast cancer specimens. Semi-quantitative assessment of ER and PR is important for breast cancer prognosis. Even with the development of genomic tests, hormone receptor status remains the most valuable predictive and prognostic biomarker (2, 3). Therefore, identification of reliable biomarkers for predicting the effectiveness of specific therapies and understanding the respective molecular mechanisms that enhance treatment efficacy are urgently needed (4). ER and PR are expressed in approximately 75–80% of breast cancer cases, but nearly 40% of the cases fail to respond to the current treatment strategies and eventually die from the disease (1, 4).

Selenium (Se) is a trace element that plays an essential role in many biological processes. It possesses anti-carcinogenic properties that can protect mammary epithelial cells against oxidative DNA damage and early carcinogenetic events (5). The anticancer effects of supplemental Se were first demonstrated over forty years ago (6).

It has been shown that Se can reduce mortality rates in prostate, lung, pancreatic and colorectal cancer patients by 39-52% (7, 8). A number of mechanisms have been proposed for the preventative effects of Se, including stimulation of apoptosis, induction of cell cycle arrest, inhibition of tumor cell invasion, and alteration of estrogen and androgen receptor expression (9-11).

Almost all breast cancer patients are female and usually have persistently elevated blood estrogen levels, a known breast cancer risk factor (12). Hence, hormonal assessment must be considered in breast cancer studies.

The growth of breast cancer cells is regulated by binding of estrogen or progesterone to their respective receptors that induces cell proliferation and prevents apoptotic cell death (4, 13). Most breast cancer patients exhibit overexpression of ER and PR. In this study, we aimed to evaluate association of tissue selenium level and ER and PR expression in breast cancer.

MATERIALS AND METHODS

Sixty tissue samples (30 tumors and 30 tumor margins) were collected from the Imam Khomeini hospital in Tehran, Iran. A pathologist performed histopathological evaluations. Tumors containing less than 50% tumor cells in total cell mass as well as tumor margins containing any tumor cell were excluded from the study. The tissue specimens were stored at -80 °C until analysis. The samples were cut, weighed (0.02-0.03 g), washed with PBS (pH 7.2-7.4) and rapidly frozen with liquid nitrogen. After melting at 2-8 °C, 200 µl of 0.2M PBS (pH 7.4) were added and the samples were homogenized, vortexed and centrifuged at 13000 rpm for 20 min. The supernatant was used for analysis.

Measurement of Se in both tissue liquid and serum was carried out at the Kavosh Laboratory in Gorgan (Iran), using graphite furnace atomic absorption spectroscopy with longitudinally-heated graphite atomizer (Agilent-AA240) and Zeeman-effect background correction. In brief, 50 µl of sample were diluted with 450 µL of aqueous solution of Triton, ascorbic acid and nitric acid. The aqueous solution was prepared by diluting 600 µL Triton X-100 (Merck), 5 mg ascorbic acid (Sigma) and 2.5 ml nitric acid in 500 ml of water. After diluting the samples and the calibration standard materials, 30 µl of the diluted samples and 20 µl of the freshly prepared matrix modifier (500mg/L palladium chloride) were injected into the furnace with an auto-sampler (Varian-PSD120). Se hollow cathode lamp (Agilent Technologies) was used.

A pathologist determined the status of ER and PR using immunohistochemistry tests.

Statistical analysis of data was performed using IBM SPSS Statistics (version 25).

RESULTS

About 60% of the samples were positive for ER/PR expression. We found no significant difference in the mean Se level in both ER/PR-positive and -negative tissue and tissue margin samples (Table 1). There was no significant association between tissue Se level and ER/PR expression.

Table 1- Mean Se level in tumor and tumor margin samples from breast cancer patients

ER/PR expression	Type of tissue	Mean level of Se (µg/L)
Positive	Tumor	209.54
	Tumor margin	185.04
Negative	Tumor	243.39
	Tumor margin	168.06

DISCUSSION

We found no association between tissue selenium level and ER/PR expression in breast cancer. In this regard, Zhang et al. reported that low Se-binding protein 1 expression in ER-positive breast cancer patients was significantly associated with poor survival, and its expression progressively declined with clinical progression of cancer ($P>0.05$)(14). Contrary to our results, a study suggested that organic Se supplementation may reduce/delay breast cancer metastasis (15), and another study reported the chemopreventive and therapeutic potential of Se for women at high risk for breast cancer and those with ER-positive breast cancer (16). Estrogens exert their proliferative effect on hormone-dependent breast cancer cells by preventing apoptotic cell death. Se can cause growth arrest and apoptosis by disrupting estrogen signaling in ER-positive breast cancer cells (11). Wei et al. observed that Se could

significantly reduce the risk of breast cancer in premenopausal women but not in postmenopausal women, which may be explained by the fact that premenopausal women have higher estrogen levels than postmenopausal women (17).

CONCLUSION

There is no association between tissue Se level and ER/PR expression in breast cancer.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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