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SELENIUM AS A BIOMARKER IN PRE AND POSTMENOPAUSAL BREAST CANCER PATIENTS – AN UPDATE

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ABSTRACT

In the present study we determined the selenium content in different clinical stages of pre and postmenopausal breast cancer patients. A total of 72 breast cancer patients were included in this study. Patient's tumor tissues were separated as pre and postmenopausal along with their respective non tumors. The selenium metal content was estimated by acid digestion method using atomic absorption spectroscopy. In the present investigation we observed that selenium content was significantly decreased from stage I to stage III tumor tissues of both pre and postmenopausal women. However in comparison of pre and postmenopausal breast tissues in each stage it was also found that selenium content was lower in postmenopausal women in all stages. This study provides compelling evidence for the first time that the selenium content was decreased in both pre and postmenopausal tumor tissues. This indicates that selenium might be considered as a valuable biomarker to evaluate breast cancer stage progression.

Keywords: Atomic Absorption Spectroscopy, Breast Cancer, Menopausal Women, Biomarker, Selenium

INTRODUCTION

Breast cancer is a common malignant tumor in females. The incidence of breast cancer increases with age, certain environmental, lifestyle factors and inherited mutations in BRCA1, BRCA2 oncogenes [1]. Studies also suggested the etiology and pathogenesis of this malignancy implying genetic, hormonal and environmental factors [2]. Trace metals play a vital role in a number of biological processes by activating or inhibiting various enzymes [3]. Selenium (Se) is a non-metallic, essential nutrient for humans being necessary for activity of Glutathione peroxidase (GSH-Px). The effective form of selenium in the body is selenocysteine, a component of selenoproteins and has important structural, enzymatic roles and also exhibits antioxidant activity. Low content of Se protects cells from oxidative stress induced DNA damage by scavenging free radicals in breast cancer causing epithelial cells [4]. Selenium also inhibits carcinogenesis by reduction of oxidative stress and inflammation, improvement of immune response, activation of DNA repair genes and also acts as an antitumor agent [5]. In the present study, we aimed to evaluate the selenium content in different clinical stages of pre and postmenopausal breast cancer women.

MATERIALS AND METHODS

Experimental Source

Seventy two clinically diagnosed pre and postmenopausal breast carcinoma patients (infiltrating ductal cell carcinoma) of 29-74 years age were selected for the present study and were categorized into the clinical stages of I, II and III. Infiltrating ductal cell carcinoma (IDCC) tumor samples were collected along with non tumor samples. Subjects with the history of breast cancer, breast surgery and taken exogenous hormones (Tamoxifen, Raloxifene, thyroid hormones and oral contraceptives); and also patients suffering from myocardial infarction, liver disease, polycythemia, diabetes mellitus and pancreatic disease, rheumatic fever and tuberculosis were excluded from the study.

Estimation of Se Content by Acid Digestion Method

Selenium metal level in non tumor and breast tumor tissues was estimated according to the method of Ebdon *et al*., [6] on a flame atomic absorption spectrophotometer (Perkin-Elmer model No. 2380, USA) and the values were expressed as µg/gr wet weight of tissue.

Statistical Analysis

The data was represented as mean ± standard deviations of 72 replicates and was analyzed using SPSS, version 17.0. $P<0.05$ was

considered as a significant versus control (Non tumor tissues).

RESULTS

Selenium Content in Premenopausal Women

The mean index of Se content in premenopausal non-tumor tissues in all three clinical stages was found to be 14.9 ± 0.4, 14.6 ± 0.35 and 14.8 ± 0.39 μg/gr wet weight of tissue which is statistically insignificant ($p<0.05$). However a significant ($p<0.05$) decrease in Se content was seen as 8.2 ± 0.32, 7.92 ± 0.37 and 6.99 ± 0.42 in premenopausal breast tumor tissues with stage progression (**Table 1**). The per cent decrease in Se content was observed as 55.3 ± 2.73, 54.1 ± 2.87 and 47.6 ± 3.09 (**Figure 1**) in stage I, II and III breast cancer tissues in comparison with their respective non tumor tissues ($p<0.001$).

Selenium Content in Postmenopausal Women

The mean index of Se content in postmenopausal non-tumor tissues in all three clinical stages was found to be 14.5 ± 0.34, 14.9 ± 0.39 and 14.5 ± 0.4 μg/gr wet weight of tissue (**Table 2**) which is statistically insignificant ($p<0.05$). However a significant ($p<0.05$) reduction in Se content was seen as 7.09 ± 0.3, 6.58 ± 0.4 and 5.39 ± 0.38 in premenopausal breast tumor tissues with stage progression. The per cent decrease in Se

content was seen as 48.9 ± 2.65, 44.16 ± 3.13 and 37.17 ± 2.71 in stage I, II and III breast cancer tissues in comparison with their respective non tumor tissues ($p<0.001$) (**Figure 2**).

DISCUSSION

Selenium is a nutritionally important trace metal in humans at lower content whereas, it is potentially toxic at higher concentrations. It is well documented that selenium shows anti-carcinogenic property in various cancers [7]. 'Se' is an integral part of the enzymes such as glutathione peroxidases, type I iodothyronine deiodinase, metalloprotein, thioredoxin reductase and selenoprotein P, which plays a potential role in protecting DNA and other cellular components from oxidative damage [8]. It has been suggested that low intake of selenium improves the antioxidant defense system [9]. In the present study, significant decrease in Se content was observed in pre and postmenopausal breast tumors than non tumors. Previous studies of patients with malignancies showed a lower level of selenium in serum of various cancers, including colonic cancer [10, 11]. A decreased level of selenium has been associated with a higher risk of cardio-vascular diseases as well as cancer in humans [12]. Earlier it has been reported that higher selenium intake through diet, may act as a

protective agent against cancers in humans **[13]**. Studies of Chen *et al.,* **[14]** suggested that the decreased Se content was related with the increase in telomerase activity and apoptotic process. A strong relationship between low serum Se concentration and increased risk of breast cancer has been documented **[15]**. Moreover, *in vitro* studies reported that selenium compounds were proficient to inhibit oxidative stress, induce the apoptosis and inhibit cell growth in transformed cells **[16]**.

In the present investigation, the decreased content of selenium in pre and postmenopausal women is associated with increased risk of breast cancer and it might be utilized as an antioxidant to compensate oxidative damage against free radicals. Whereas the decrease in Se levels in postmenopausal women compared to premenopausal women might be correlated with decreased antioxidant defense at an older age, wherein Se might be utilized by the body efficiently as an antioxidant. Therefore, it is suggested that the lower Se content may play an important role in breast carcinogenesis and it may be plausible to monitor the prognosis of breast tumors by measuring Se as a biomarker.

CONTRIBUTORS

All the authors contributed equally to the work

CONFLICT OF INTERESTS

We declare that we do not have any conflict of interest.

ETHICAL ASPECTS

The study protocol and ethical aspects were approved by Institutional Ethics Committee Review Board, Vydehi Institute of Medical Sciences and Research Centre, Bangalore, India (Resolution No: IERB/MISC/2010). A written informed consent was taken from all studied patients to carry out the study.

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Table 1: Selenium Content in Different Clinical Stages of Premenopausal Breast Cancer Patients. Each Value is Mean ± S.D of 12 Individuals. Mean Values That do Not Share Same Superscript Represented as a,b,c Differ Significantly from Each Other at p< 0.05

Stages	Samples	Se content(µg/gr wet weight of tissue)
Stage I (n=12)	Non tumor	$14.9^a \pm 0.4$
	Tumor	$8.2^b \pm 0.32$
Stage II (n=12)	Non tumor	$14.6^a \pm 0.35$
	Tumor	$7.92^b \pm 0.37$
Stage III (n=12)	Non tumor	$14.8^a \pm 0.39$
	Tumor	$6.99^c \pm 0.42$

Table 2: Selenium Content In Different Clinical Stages of Postmenopausal Breast Cancer Patients. Each Value is Mean ± S.D of 12 Individuals. Mean Values that do not Share Same Superscript Differ Significantly From each other at p< 0.05

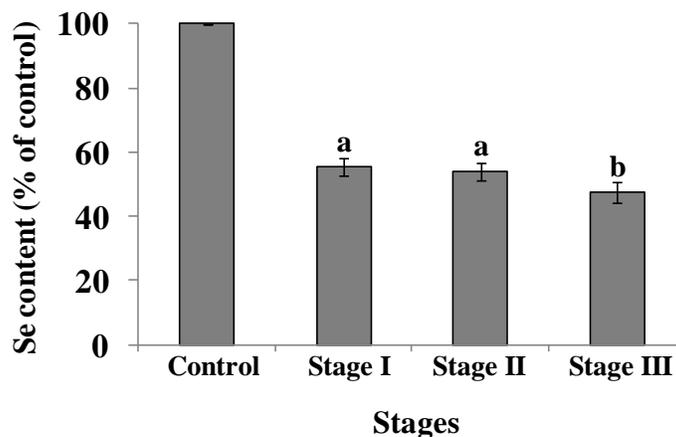| Stages	Samples	Se content (µg/gr wet weight of tissue)
Stage I (n=12)	Non tumor	$14.5^a \pm 0.34$
	Tumor	$7.09^b \pm 0.3$
Stage II (n=12)	Non tumor	$14.9^a \pm 0.39$
	Tumor	$6.58^b \pm 0.4$
Stage III (n=12)	Non tumor	$14.5^a \pm 0.4$
	Tumor	$5.39^c \pm 0.38$

Figure 1: Percentage Selenium Content in Different Clinical Stages of Premenopausal Breast Cancer Patients. Each Stage is Mean ± S.D of 12 Individuals. Mean Values are Represented as a, b and c that Differ Significantly From Each Other at p< 0.001
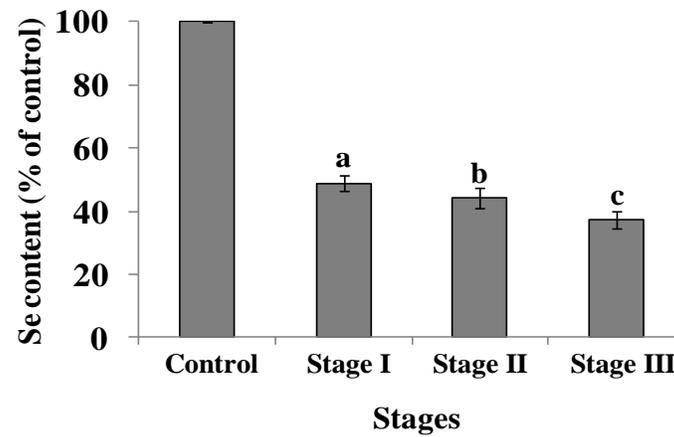
Figure 2: Percentage Selenium Content in Different Clinical Stages of Postmenopausal Breast Cancer Patients. Each stage is mean ± S.D of 12 individuals. Mean Values are Represented as a, b and c That Differ Significantly From Each Other at $p < 0.001$