SERUM OESTRADIOL IN WOMEN WITH CARCINOMAS OF THE BREAST AND UTERINE CERVIX

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ABSTRACT

Endogenous oestrogens are thought to be involved in breast cancer, but few studies could show the direct relationship between hormones and pathological process of the disease. In the present study, oestradiol was estimated in the serum of pre-and postmenopausal breast cancer patients along with normal healthy controls and patients with carcinoma of the uterine cervix which is not dependent on oestrogens. Premenopausal patients with breast cancer showed higher levels of oestradiol as compared to premenopausal control women as well as cervical cancer patients. Whereas, no statistically significant differences were observed in serum oestradiol levels amongst postmenopausal groups of breast cancer, cervical cancer and normal women. The result of the study reflects the association of oestradiol as well as its difference in the pathological events of pre and postmenopausal breast cancer.

KEY WORDS: Oestradiol, menopausal status, breast cancer, cervical cancer.

INTRODUCTION

Carcinomas of the uterine cervix and breast are the commonest malignancies among Indian females. Numerous studies have implicated the human papilloma-virus (predominantly HPV16) in carcinoma of the uterine cervix (1). Breast cancer is the second most common female cancer in India (2). There is an increasing trend in the incidence of breast cancer in the recent past. The biological properties of breast cancer and its associated risk factors suggest that oestrogens are involved in the carcinogenic process (3). However, studies on the levels of oestrogen in blood and urine of breast cancer patients as well as normal controls have provided inconsistent and mostly inconclusive results (4-7). On the contrary, cervical cancer, the commonest cancer among Indian women, is not dependent on endogenous hormonal factors.

Interestingly, several risk factors for cancer of the uterine cervix appear to be of inverse relationship as those for carcinoma of the breast (4). Therefore, between these two commonest malignancies (of the

breast and uterine cervix among Indian women), a comparative study on levels of oestradiol was undertaken to comprehend the oestrogen related pathological process of breast cancer.

MATERIALS AND METHODS

In the present study, 31 premenopausal breast cancer patients, 43 premenopausal cervical cancer cases and 28 premenopausal normal healthy women were included. Postmenopausal group consisted of 25, 32 and 20 breast cancer cases, cervical cancer cases and normal healthy women respectively. All the incident cases of breast carcinoma and cervical carcinoma of stages I and II were randomly selected from the Radiotherapy Department of Maulana Azad Medical College and associated Lok Nayak Hospital, New Delhi. Only histopathologically proven cases with infiltrating duct carcinoma of the breast and squamous cell carcinoma of the uterine cervix were included in this study. Normal healthy women who accompanied the patients were selected and requested to donate 2ml. of blood. Clinical and epidemiological informations were also collected using a pretested proforma. No case with the history of familial breast cancer was included.

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After an overnight fast, peripheral venous blood samples were collected from controls and cases before initiation of any systemic treatment and/or radiotherapy. For premenopausal women, blood samples were collected during the first week of the follicular phase of their menstrual cycle. The serum was separated within 6 hours of collection of the blood and was stored at -20°C until the samples were analysed.

The estimation of the oestradiol- 17β was done by radioimmunoassay (RIA) technique using the reagents from the Orion Diagnostica Spectria (Finland). Serum samples and ^{125}I -labelled oestradiol were added to tubes coated with anti-rabbit second antibody raised in goat and a primary polyclonal antibody raised in rabbit. After incubation for 2 hours at 37°C , the tubes were decanted and washed. Their radioactivity was then measured using ^{125}I gamma counter (EC-India). A standard curve was produced on a semi-logarithmic scale by calculating the binding of standards (containing 0, 50, 150, 500, 1500, 5000 and 15000 p mol oestradiol/L). Using the standard curve of RIA test, oestradiol levels were estimated for each patient's and control's serum.

Statistical analysis : Mean and S.D. for oestradiol- 17β were estimated for each group of women. Kruskal-Wallis one way analysis of variance followed by Mann-Whitney's test of significance were employed to test for statistical significance in the mean values amongst the above groups.

RESULTS

The mean age of the premenopausal patients of

breast cancer ($n=31$), cervical cancer ($n=43$) and normal premenopausal healthy controls ($n=28$) were $38.6 (\text{SD}\pm 7.08)$, $41.5 (\text{SD}\pm 7.18)$ and $35.3 (\text{SD}\pm 7.46)$ years respectively. The mean age of the postmenopausal subjects with breast cancer ($n=25$), cervical cancer ($n=32$) as well as normal healthy controls ($n=20$) were $60.4 (\text{SD}\pm 7.33)$, $57.6 (\text{SD}\pm 5.32)$ and $58.8 (\text{SD}\pm 5.34)$ years respectively.

Table 1. shows the mean, standard deviation (S.D.) and median values as well as range of values of oestradiol for various groups. It was observed that the mean (149.0 p mol/L) and median (140.0 p mol/L) levels of oestradiol among premenopausal patients with breast cancer were found to be higher as compared to premenopausal cervical cancer patients and control women. The differences in mean values between breast cancer patients vs. normal women, and breast cancer vs. cervical cancer patients were found to be statistically significant ($p<0.01$). Premenopausal patients with cervical cancer have shown a low median (68.8 p mol/L) and mean (80.4 p mol/L) levels of serum oestradiol as compared to the patients with breast carcinoma and normal healthy controls.

Interestingly, amongst postmenopausal women, no statistically significant differences were observed in serum oestradiol levels between different study groups. The mean (55.2 p mol/L) value of postmenopausal breast cancer patients did not alter significantly in comparison to postmenopausal normal controls (mean= 64.3 p mol/L) or postmenopausal patients with cervical cancer (mean= 67.5 p mol/L).

Table 1. Mean, Median, S.D. and Range of oestradiol- 17β level amongst pre and postmenopausal women with carcinomas of the breast and uterine cervix as well as normal healthy control women.

Groups	No.	Premenopausal				Postmenopausal				
		Mean	S.D.	Median	Oestradiol (p mol/L) Range	No.	Mean	S.D.	Median	Range
Breast cancer	31	149.0*	43.47	140.0	70-225	25	55.2**	19.55	50.0	26-94
Cervical cancer	43	80.4*	40.87	68.8	35-205	32	67.5**	23.85	64.0	33-115
Normal controls	28	130.2*	61.75	115.0	40-250	20	64.3**	27.33	49.0	30-110

* Kruskal-Wallis $H=31.70$, $p<0.001$ (Significant), **Kruskal-Wallis $H=3.86$, $p=0.145$ (Not significant) Statistical significance between the Premenopausal groups, (a) Breast cancer vs Normal controls: $p<0.001$, (b) Breast cancer vs Cervical cancer: $p<0.001$, (c) Cervical cancer vs Normal controls: $p<0.01$

DISCUSSION

Oestradiol and oestrone are the major oestrogens circulating in the blood, but oestradiol is by far, the oestrogen which is the most biologically active in breast tissue (8). Aromatization of androgens into oestrogens occurs either in the granulosa cells of the ovary or in the adipose tissue and other tissues. Therefore, peripheral oestrogen biosynthesis is the important process among postmenopausal women. Although, there is a general agreement that oestrogens are involved in the aetiology of breast cancer (9,10), there is no general consensus on precise oestrogen environment that defines risk in this cancer. The data of the present study have shown an increase in the serum level of oestradiol among premenopausal patients with breast cancer. Contrary to this, oestradiol level among premenopausal women of cervical cancer was lower even than healthy premenopausal women. Thomas et al (11) and Key (12) reported higher level of oestradiol in breast cancer patients. However, this difference in levels of oestradiol concentration could be important from aetiological point of view.

Several investigators (13-17) have observed higher oestradiol concentrations in peripheral blood of patients with breast cancer. Toniolo et al (18) and Zeleniuch-Jacquotte et al (19) reported a positive

association between postmenopausal serum levels of total oestradiol as well as percentage of free oestradiol and breast cancer risk. However, the present study on postmenopausal group of women did not reveal any significant alteration in the oestradiol level of breast cancer patients in relation with cervical cancer patients and healthy controls. Further, serum levels of total oestradiol amongst postmenopausal women with breast cancer and cervical cancer as well as postmenopausal normal subjects in the present study did not show any appreciable change. Our observation in postmenopausal breast cancer cases supports the findings of Helzlsouer et al (5), Recchione et al (20) and Mady (17). Although, Recchione et al (20) found significantly higher oestradiol concentration in breast cancer tissue than in blood among postmenopausal cases.

The result of our study reflects different pathological events among pre and postmenopausal breast cancer, which are possibly associated with an altered oestrogen hormone metabolism. Sex-steroids could be taken up from plasma, and thus there could be a storage of the steroid hormones inside the breast tissue and/or perhaps some alterations in their local metabolism (21,22). The uptake process of oestrogen by breast tissue may play differently between premenopausal and postmenopausal women in relation to the circulating levels of oestrogen.

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