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The Prognostic Values of Interleukin-1 Beta and Cortisol in Iraqi Women with Breast Cancer

Janan M. Al-Akedi*, Aqeel S. Mahmood

College of Pharmacy, University of Baghdad, Iraq

Abstract Cytokines such as IL-1 beta and cortisol have an important role in the prognosis of breast cancer disease. Prediction of survival for patients with breast cancer is often inaccurate and may be helped by new biological parameters. This study was designed to investigate the clinical significance of cortisol and IL-1 beta, measured in 36 patients with fully documented patient having breast cancer using an enzyme-linked immunoassay. All patients have detectable levels of IL-1beta,whereas no significant elevation in cortisol values. Iraqi women in this study showed that cortisol have no role in breast cancer disease that could be attributed to their adaptation to the external environment.

Keywords IL-1 Beta, Cortisol, Breast Cancer

1. Introduction

Inflammation within the tumor micro-environment was correlated with an increased invasiveness and poor prognosis in many types of cancer including breast cancer[1]. It is well established that chronic inflammation that is driven by extrinsic factors promotes several types of cancer. However inflammation has also been correlated with the development of cancers that are typically associated with chronic inflammatory states such as breast cancer[2].

IL-1beta produced by macrophages as apoprotien which is proteotically processed to its active form by caspase 1. It is important mediator of inflammatory response and is involved in a variety of cellular activities including cell proliferation, differentiation, and apoptosis[3].

Different cellular signaling may operate in response to varying levels of IL-1 beta leading to genotoxic damage, cell apoptosis or cell growth[4].

Cortisol is a glucocorticoid hormones released by the hypothalamic-pituitary- adrenal (HPA) axis in response to inflammation[5]. Stress and other stimuli serves as an important regulator of metabolic function. In healthy individuals, cortisol secretion follows a diurnal rhythm characterized by elevated levels in the morning which decline over the afternoon and evening and reach a nadir during the first half of the night[6].

Dysregulated patterns of cortisol secretion often characterized by elevated nocturnal cortisol, which have been noted in diverse populations of breast cancer patients including breast, ovarian and cervical cancers and lymphoma [7].

The specific effects of abnormal diurnal cortisol patterns on tumor physiology in humans are not known. Although disruption of cortisol rhytms resulting in a flattened cortisol slope but it has been associated with shortened survival time in breast cancer patients[8]. Cortisol dysregulation has been linked with quality of life of cancer patients and accelerate tumor growth[9].

2. Materials and Methods

2.1. Patients

A total of thirty six Iraqi patients who were Attending the National Center for Early Detection of Cancer and Baghdad Teaching Hospital, Medical City, Iraq. Patients were divided into two clinical subgroups: (28) are the breast cancer patients and (8) patients are a control group. Samples serum were taken from each case stored at (-20C).

2.2. Evaluation of IL-1 Beta and Cortisol in Serum Samples Using ELISA Technique

The micro titer plate provided in this kit has been pre-coated with an antibody specific to IL-1β. Standards or samples are then added to the antibody preparation specific for IL-1β and Avidin conjugated to Horseradish Peroxidase (HRP) is added to each microplate well and incubated. Then a TMB (3,3',5,5' tetramethyl-benzidine) substrate solution is added to each well. Only those wells that contain IL-1β, biotin-conjugated antibody and enzyme-conjugated Avidin will exhibit a change in color. The enzyme-substrate reaction is terminated by the addition of a sulphuric acid solution and the color change is measured by spectrophotometer at a wave

* Corresponding author:
lyrebird2008@yahoo.com (Janan M. Al-Akedi)
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length of 450 nm ± 2 nm. The concentration of IL-1β in the samples is then determined by comparing the O.D. of the samples to the standard curve. The procedure was applied according to Cusabio company.

2.3.Cortisol Detection

Blood samples obtained in post surgical visit. They were generally obtained before 12 p.m and they were stored at -20º c, then analyzed by ELISA method**[0]**

2.4. Statistical Analysis

Statistical analyses of data were performed by using SAS program (2000). Data were subjected to more than one test (homogeneity and normality) to determine the proper test for detecting the significant differences between parameters used in this study.

It is an important step to conduct two tests for the data before analyzing: test of homogeneity and test of normality, especially when the data include a few observations such as our data. Levens test was used to test the homogeneity whereas Shapiro-Wilk test was used to test the normality. When the data were not follow the normal distribution, the t-test becomes invalid test and in such case, using non parametric tests is more suitable. Difference between means of parameters was performed using Wilcoxon – Mann - Whitney test which is analog to t-test.

3. Results

Table (1) shows that the Levens test for homogeneity of IL-1beta variance was not significant (P=0.58) and same result was found for cortisol (P=0.60) (Table 2).

Table (1). Test of homogeneity for IL-1 beta (Levens test)

Source of Variation	Mean square	F value	P
TRT	3.475E13	0.3023	0.5861
Error	1.15E14		

Table (2). Test of homogeneity for cortisol

Source of Variation	Mean square	F value	P
TRT	8.961E11	0.2734	0.6045
Error	3.278E12		

Results of Shapiro-Wilk test (Table 3) revealed that all groups have no normal distribution except in IL-1 beta of control group, thus the significant differences between parameters were tested by using Wilcoxon-Mann-Whitney test.

Table (3). Test of normality for two parameters (cortisol & IL-1 beta (Shapiro-Wilk test)

Groups	Control W statistic	P	Patients W statistic	P
Cortisol	0.79	0.05	0.45	0.01
IL-1 beta	0.90	N.S	0.46	0.01

There are an increase in the level of IL-1 beta in breast cancer patients as compared with control group (Table 4). The difference between means was significant (P=0.011) (Table 5). On the other hand the difference between means for cortisol was not significant (Table 5).

Table (4). Means±SE for the two parameters

Groups	No.	Mean± SD Cortizol	Mean± SD IL-1 beta
Control	8	514.12±251.27	97.62±6.20
Patients	28	488.85±671.44	160.92±26.83

Table (5). Test of differences using Wilcoxon-Mann-Whitney test

Parameter	Z value	P
Cortisol	1.08	0.278
IL - Beta	-2.53	0.0114

In regards to cortisol, the results of this study was disagree with some studies which confirmed the significant differences between breast cancer patients and control group [5, 6]. These inconsistencies could be attributed to the variation in the size of samples and the nature of country.

4. Discussion

Several inflammatory interleukins have been linked with tumorigenesis, so inflammation is associated with cancer development. The study shows an increase in the level of IL-1beta in the patient group as compared to the control group. Statistically, the difference was significant (p= 0.011). IL-1beta promotes growth & induces angiogenic factors from tumor and stromal cells that promotes tumor growth through hypervascularization. In the pathogenesis of estrogen-dependent cancers particularly breast cancer, the role of IL-1beta is implicated in the pro-tumorigenic insults, cell proliferation angiogenesis, and cell adhesion. It appears that it is concentration of peptide IL-1 beta which determines its stimulatory or inhibitory paracrine and or autocrine signals that regulate the growth of estrogen- dependent tumors. The IL-1 beta over expressing by MCF7 cell secreting high level of IL-1 beta[11] and elevation level of P53 protein is detected in these cells.

IL-1beta has also been found to stimulate the local production of chemotactic factors of PMNs in tumors. On the other hand other studies found that IL-1 beta was promote tumor growth[12]. Furthermore, the inflammatory cytokines such as IL-1 beta and other mediators of inflammation have been linked to breast cancer formation & recurrence[13].

IL-1 beta acts on the mammary epithelial cells to contribute to induction of hyperplastic lesions. It act cooperatively with another oncogenic stimulus to promote tumorigenic changes[14]. The relationship between stress and cancer development has not been firmly established. This study was demonstrated that no relationship between cortisol and IL-1 beta.

Iraqi women with breast cancer in this study even they have more than one child but their cortisol level didn't

influenced, this may be due to the adaptation of these women to the external environmental factors. The potential biological mechanism for cancer related fatigue may come from changes in the immune system induced by cancer or cancer treatment including releasing of pro-inflammatory cytokines IL-1beta[15]. Cortisol was secreted by the breakdown of protein & fat to provide metabolites that can be converted to glucose in liver & it activates anti-stress and anti-Inflammatory pathways[16].

5. Conclusions

As Iraq has a specific condition, women were always under stress, so they have at most a high level of cortisol. Although, cortisol has been used as a suppressor of immune response, while the IL-1beta was unusual parameters used for predicting the breast cancer sequelae, our results revealed that it's not a case in all studies. In another words, the results showed that cortisol was inefficient predictor of breast cancer whereas IL-1beta was more efficient because of its action on the mammary epithelial cells which induce hyperplastic lesions and promote tumorgenic changes which are all related to the breast cancer formation and recurrence. In view of this it's an important to monitor the IL-1beta in patients with breast cancer after surgical operation to identify the prognosis of the disease.

REFERENCES

[1] Coussens LM.,Werb Z.,: Inflammation and cancer. Nature (2002):420:860-867.

[2] Allevena P., Sica A., Garlanda C, Mantovani A.,: The Yin-Yong of tumor associated macrophages in neoplastic progression and immune surveillance. Immunolo. Rev. (2008):222:155-161.

[3] Weber A., Wasiliew P. and Kracht M.,: Interleukin-1(IL – 1) pathway. Sci. Signal. (2010):3 (105). [DOI: 10.1126/ scisignal. 3105cm1]

[4] Auron PE, Webb AC, Rosenwasser LJ, Rich A, Wolff SM, Dinarell CA: Neuclotide sequence of human monocyte IL-1 precursor. Proc. Natl. Acad. Sci.USA (1984): 81(24): 7907-7911.

[5] Rhen T. and Cidlowski JA., : Anti-inflammatory action of Glucocorticoids new mechanisms for old drugs. N. Eng. J. Med. (2005) 353:1711-1723.

[6] Tsigos C. and Chrousos G.P.: Hypothalamic- pituitary - adrenal axis Neuroendocrine factors and stress. J. Psychosom Res. (2002): 534:865-871.

[7] Jhen CF., Kuhnhardt D., Bartholomac A., Pfeiffer S.,Schmid P., Possinger K., Flath BC., Luftner P.,: Association of hypothalamus Pituitary-adrenal axis function and depression in patients withCancer. Cancer therapy (2010):9:270-275.

[8] Sephton SE., Sapolsky RM., Kraemer HC. and Spiegel D.:Diurnal Cortisol rhythem as a predictor of breast cancer survival. JNCI (2000):92:994-1000.

[9] Filipski E., and Levi F.: Circadian disruption in experimental cancer process. Integr. Cancer. Therapy (2009):8:298-302.

[10] Kreamer HC., Glese-Davis J., Yutsis M., OHara R., Neri E. ,Gallagher- Thompson D., Taylor CB., and Spiegel D.: Design detections to optimize reliability of day time cortisol slopes In an older population. Am. J. Geriatr. Psychiatry (2006):14:325-333.

[11] Roy D., Sarker S., and Felty Q.: Levels of IL-1 beta control stimulatory /inhibitory growth of cancer cells. Fronont. Biosci. (2006) Jan 1:11:889-98.

[12] Liu J., Zhai X., Jin G., Hu Z., Wang S., Wang X., Qin J., Ma H., Wei Q., and Shen H.: Functional variants in the promoter of IL-1 beta are associated with an increased risk of breast cancer: a case-control analysis in Chinese population. Int. J. Cancer (2006):118: 2554-2558.

[13] Pantschenk AG., Pulikar I., Anderson KH., Wang Y., Miller LJ., Kurtzman SH., Barroos G., and Kreutzer DL.: The IL-1 family of Cytokines & receptors in human breast cancer implication. Int. J. Oncol (2003):23:269-284.

[14] Apte RN., and Voronov E.,: Its IL-1 a good or bad guy in tumor immunobiology & immunotherapy?. Imm. Rev. (2008): 222:222-241.

[15] Dantzer R.: Cytokine-induced sickness behavior: mechanism and implication. Ann. NY. Acad. Sci. (2001):933:222-234.

[16] Coderre L., Srivastava AK., and Chiasson JL: Role of glucocorticoid in the regulation of glycogen metabolism in skeletal muscle. Am. J. Physiol. (1991) 260:E927-32.