Evaluation of Estradiol and Prolactin Serum Levels "In Premenopausal; and Postmenopausal" Women with ((Breast Cancer)) In Baghdad City

تقويم مستويات هرموني الاسترادايول والبرولاكتين في مصول النساء(قبل وبعد انقطاع الطمث)المصابات بسرطان الثدي في بغداد

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المستخلص:

الهدف: تقويم مستويات هرموني الاسترادايول والبرولاكتين في النساء المصابات بسرطان الثدي في مدينة بغداد .

المنهجية: الدراسة الحالية تم اجرائها على ٦٠ من مرضى سرطان الثدي و ٤٠ حالة صحية لغرض تقييم مستويات هرموني الاسترادايول والبرولاكتين في مصول العينات(ماقبل وبعد انقطاع الطمث) في النساء المصابات والسليمات من مرض سرطان الثدي. تم قياس الهرمونين لكل الحالات بواسطة استخدام تقنية حديثة جدا وهي طريقة البريق الكيميائي بواسطة جهاز IMMULITE2000،و تم تحليل البيانات احصائيا بواسطة النظام الاحصائيSPSS.

النتائج:. اظهرت النتائج ارتفاع لامعنوي (**P>0.05**) في متوسط مستوى هرمون الاسترادايول لمجموعة المرضى (ماقبل وبعد انقطاع الطمث) (54.0 + 22.8 pg/ml),(31.6 + 9 pg/ml) على التوالي مقارنةمع النساء السليمات(ما قبل وبعد انقطاع الطمث) على التوالي (47.0 ± 22.3 pg/ml) ,(28.4 + 10.7 pg/ml) بينما اظهرت الدراسة ارتفاع معنوي عالي(P<0.01) عند قياس هرمون البرولاكتين في مصل النساء المصابات (ما قبل وبعد انقطاع الطمث) على التوالي (30.9 + 18.5" ng/ml") (20.9 +15.2 "ng/ml"), مقارنة مع النساء السليمات(ما قبل وبعد انقطاع الطمث) على التوالي (11.7 ± 10.4" ng/ml"),(8.7 ± 5.1 "ng/ml")

التوصيات: توصي الدراسة إلى التأكيد على ضرورة التعاون بين وزارة الصحة ووزارة التجارة وحمايتهم من السلوك الخطر بتوفير الدعم والإرشاد الكافي لهم بالابتعاد عن المنتجات الهرمونية ، والتركيز على البرامج الارشادية في حماية المجتمع من خلال تثقيفهم ببرامج التوجيهه.

ABSTRACT:

Objective: To Evaluate of Estradiol and Prolactin hormones levels for Breast Cancer women in Baghdad City.

Methodology: The current study was conducted on 60 breast cancer women and 40 apparently healthy subjects to evaluate the levels of estradiol and prolactin "hormones in the serum" of ({premenopausal & postmenopausal}) breast cancer and healthy controle women. Estradiol and prolactin hormones estimated for all cases by using the IMMULITE 2000 instrument that performs chemiluminescent immunoassays results are calculated for each sample.Data were analysed using SPSS-18.data of two groups was comparison by the student's t-test.

Results: The results showed a non significant""(**P>0.05**) elevation in the –mean- serum estradiol level of the study (premenopausal &postmenopausal) group (54.0 ± 22.8 pg/ml),(31.6 ± 9 pg/ml) respectively compared to that of control (pre& postmenopausal) group (47.0 ± 22.3 pg/ml), (28.4 ± 10.7 pg/ml) respectively.while a highly significant (**P<0.01)** elevation of serum prolactin (30.9 ± 18.5 ng/ml) ,(20.9 ±15.2 ng/ml) respectively was found in study (premenopausal &postmenopausal) group compared to healthy control (premenopausal &postmenopausal) group (11.7 ± 10.4" ng/ml"),(8.7 ± 5.1 "ng/ml") respectively.The results of this study indicate that the elevation of estradiol and prolactin hormones may implicate these hormones in the aetiology of" breast cancer"..

Recommendations: This learn lines recommends emphasizing the necessity of cooperation between the Ministry of Health and the Ministry of Commerce and protecting them from dangerous behavior by providing them with sufficient support and guidance to stay away from the hormonic products and focusing on the extension programs in the protection of the community through educating them with the guidance programs.

Key Words: Breast Cancer ,Prolactin ,Estradiol ,Risk factors, Premenopaus, Postmenopaus

Introduction

A "Breast cancer" was considered as the almost type of solid tumor diagnosed in females [1].It accounts for 16% of all kinds of cancer deaths globally {total mortality rate of cancer is 7,600,000, the total mortality rate of breast cancer is 460,000}, this according to the World Health Organization.According to the latest Iraqi Cancer Registry that found the breast cancer is the commonest type of women malignancy in Iraq and accounting for about one-third of the recorded women cancers[2]. There are several well-known "risk factors" for breast cancer involve female gender, age, earlier breast cancer, benign breast disease, hereditary (genetic) factors,for example, family history of breast cancer or other cancers types, females who have inherited mutations in the BRCA1 or BRCA2 genes have raised breast cancer risks [3].Moreover, early age at menarche, late age at menopause, late age at first full-term pregnancy, using of exogenous hormones or oral contraceptives, obesity, lack of exercise, diet, smoking, consumption of alcohol, low physical activity and exposure to high dose of ionizing radiation during early life, considered as risk factors for breast cancer[4].Nevertheless, all these risk factors have been shown to have different "associations" to breast cancer among various ethnic populations around the world [5] .An endocrine system is a group of glands that produce various types of hormones. This system is made up of the pituitary gland, gonads (ovaries and testes), adrenal glands, hypothalamus glands, thyroid, parathyroid, pancreas, pineal, and thymus gland. These glands secrete their hormones directly into the bloodstream [6].Principally, hormones can be divided into an amino acid, peptides and lipid derivatives, for example,(steroid hormones) [7] .

Estrogens are a family of hormones involve estrange "(E1)", estradiol "(E2)", and estriol (eE3) yield in a variety of tissues. Estradiol is the major estrogen of ovarian origin and plays a critical role in physiological function [8]. The serum estradiol levels are higher than the estrone levels throughout the reproductive years. Therefore, it is the predominant estrogen both in terms of absolute serum levels and in terms of estrogenic activity during reproductive years. Throughout menopause, estrone is the main circulating estrogen but during pregnancy, the major circulating estrogen is estriol[9].

The estrogens synthesis begins in near internal cells in the ovary, through the synthesis of androstenedione from cholesterol. Androstenedione is a substance of moderate androgenic activity. This compound traverses the basal membrane into the surrounding granulosa cells, where it is transformed to estrone or estradiol, either directly or through testosterone. The conversion of testosterone to estradiol, and of androstenedione to estrone, is transformed by the aromatase enzyme.Major amounts of estrogens are made by the peripheral aromatization of androgens [10,11]. The biological effects of estrogen are mediated by its binding to one of the structurally and functionally distinct Estrogen Receptors (ERs) ("ERα and ERβ") [12].Estrogens exist in the breast with relatively elevated concentrations, therefore they play a fundamental role in various breast cancers.However, estrogens can exert their effects on cells even at very low concentrations. They act through entering cells and connecting to specific proteins called estrogen receptors (ERs), subsequently can bind to specific DNA sequences in the nucleus of the cells causing fast cell proliferation and differentiation. The rapid growth of cell leads to reduced time for DNA repair, which results in DNA damage and mutations. The products of estrogen breakdown also contribute to the risk of breast cancer, through binding to DNA and generate mutations in genes These changes are identified as (epigenetic changes) that have the same importance to genetic that initiate a breast tumor [13]. Furthermore, estrogens can cause fluctuations which do not affect the primary DNA sequence of a gene but change its properties. changes in their latent effects[14]. Further to estrogen hormone prolactin hormone also induces breast cancer, which is a neuroendocrine polypeptide hormone that produced principally by lactotrophs that located at the anterior pituitary gland of human[15,16]. However, it has been found in many other extra-pituitary sites, involving reproductive, immune, neural, integumentary tissues and other sites, for example, lacrimal glands, adipose tissue, blood endothelial cells, and kidney [17]. The role of prolactin and its receptor in the growth of tumor stays controversial. In addition to prolactin produced by lactotrophs in the anterior pituitary, it produced locally and could induce tumorigenesis in an autocrine manner in breast cancer [18]. However, cellular, molecular, and epidemiological studies discovering the role of prolactin in breast cancer have yielded conflicting results. This observation could be due to prolactin has a different role in the pathogenesis of breast cancer [19,20].

Methodology

This prospective study was conducted at two main medical facilities in Baghdad City: The Main Training Center for Early Detection of

Breast Tumours/Oncology Teaching Hospital and poisoning consultation center/specialized surgeries hospital during the period from November/2016 to March/ 2017.
A total of 100 subjects were enrolled in this study and divided into two groups.The first group included 60 patients women aged between 30-60 years, this group divided into subgroups 31 premenopausal breast cancer women and 29 postmenopausal breast cancer women.The second group included 40 (20 pre & 20 postmenopausal) healthy women that have normal breast tissue and without any previous history of any systemic diseases.Estradiol and prolactin hormones are estimated for all cases by using the IMMULITE 2000 instrument that performs chemiluminescent immunoassays. This instrument uses assay – specific antibody or antigen was coated polystyrene beads as the solid phase. After the sample is incubated with an alkaline phosphatase –labeled reagent then quantified using the dioxetane substrate to produce light that is emitted when the chemiluminescent substrate reacts with the alkaline phosphatase label bound to the bead.The amount of light emitted is proportional to the amount of hormone originally present in the sample.This light emission is detected by the Photomultiplier Tube (PMT) and results are calculated for each sample.Data were analyzed using SPSS-18.data of 2 groups was compared by the student's t-test;p >0.05 was taken as non- significant, p<0.05 was taken as significant and p<0.01 was taken as highly significant.

Results

TABLE (1) : Comparison of Serum Estradiol Concentration (pg/ml) among (Premenopaus and Postmenopaus) of the Study and Control Groups

Groups	Pre-M (Mean± SD.) (n=50)	Post-M (Mean± SD.) (n=50)	t-test	P-Value	Sig.
Control (n=40)	47.0 ± 22.3	28.4 ± 10.7	0.708	0.488	P>0.05(NS)
Study (n=60)	54.0 ± 22.8	31.6 ± 9.6	2.624	0.017	P< 0.05(S)
t-test	1.291	1.356			
P-Value	0.212	0.191			
Sig.	P>0.05(NS)	P>0.05(NS)			

Pre-M = Premenopausal, Post-M = Postmenopausal , Sig=Significance ,S= Significant ,NS=not significant , n= sample size, P-value = Probability value , SD= Standard Deviation.

Results in the table (1) are expressed as mean ± SD and represented the mean value of serum estradiol in (pre & postmenopausal) control and study groups .The results showed a non significant elevation in the mean serum estradiol level of the study (premenopausal &postmenopausal) group (54.0 ± 22.8 pg/ml),(31.6 ± 9 pg/ml) respectively compared to that of control (pre& postmenopausal) group (47.0 ± 22.3 pg/ml), (28.4 ± 10.7 pg/ml) respectively (p>0.05). And showed significantly increased in mean serum estradiol of premenopausal study group (54.0 ± 22.8 pg/ml) compared to that of postmenopausal study group (31.6 ± 9 pg/ml) (p<0.05).In control group the comparison between (pre &postmenopaus) showd non significant elevation in mean serum estradiol level (47.0 ± 22.3 pg/ml),(28.4±10.7)pg/ml respectively (p>0.05) .

Table (2): Comparison of Serum Prolactin Hormone Concentration (ng/ml) among (Premenopausal and Postmenopausal) of the Study and Control Groups

Groups	Pre-M (n=50) (Mean± SD.)	Post-M (n=50) (Mean± SD.)	t-test	P-Value	Sig.
Control (n=40)	11.7 ± 10.4	8.7 ± 5.1	4.968	0.000	P<0.01(HS)
Study (n=60)	30.9 ± 18.5	20.9 ± 15.2	2.543	0.020	P<0.05(S)
t-test	6.413	4.204			
P-Value	0.000	0.000			
Sig.	P<0.01(HS)	P<0.01(HS)			

Pre-M = Premenopausal, Post-M = Postmenopausal , Sig=Significance ,S= Significance ,NS=Not Significance , n= sample size , P-value =Probability value , SD= Standard Deviation

Table (2) presents the distribution of study and control (premenopausal &postmenopausal) groups according to serum prolactin level . The results in the previous table showed that the mean serum prolactin in the study (premenopausal &postmenopausal) group (30.9 + 18.5 ng/ml) ,(20.9 +15.2 ng/ml) respectively was highly significant elevation compared to the control (premenopausal &postmenopausal) groups (11.7 + 10.4 ng/ml),(8.7 + 5.1 ng/ml) respectively (p< 0.01).Also showed highly significant elevation in the mean serum prolactin in both (study & control) premenopausal groups (30.9 + 18.5 ng/ml) , (11.7 + 10.4 ng/ml) respectively , compared to that of the postmenopausal (study & control) groups (20.9 +15.2 ng/ml) ,(8.7 + 5.1 ng/ml) respectively , (p< 0.01).

4.Discussion

The previous study has recorded an increased breast cancer risk with elevated serum estradiol levels in premenopausal women [(21)]. However, the fluctuating level of hormones through the menstrual cycle confuses hypothesis analysis in premenopausal women [(22)].Also in postmenopausal females have evidence for the same relationship [(23,24)]. Premenopausal women undergo alterations in their serum estrogen levels during their menstrual cycle and this affected the results of the current study.Previous Studies on postmenopausal women have been more reliable in their results, due to the absence of the variability of hormone levels during the menstrual cycle.Estrogens act as a proliferative factor to the breast tissue, are possibly associated with rising mitotic activity and are thought to be a stimulating effect rather than an initiating influence. The cells proliferation is important for carcinogenesis because the risk of errors during replication of deoxyribonucleic acid (DNA) is raised through cell division, which can lead to cancer when not corrected [(25)]. Change in hormone levels influences carcinogenesis of breast via several mechanisms.Therefore, the exposure to higher levels of estrogen primarily is the causing factor to the breast cancer risk [(26)]. Also may contribute to carcinogenesis by increasing the rate of cell division and proliferation, so permitting for an increase in the accumulation of random genetic errors. Another theory is that the continued cell division and proliferation coming from many ovulatory cycles, mainly between menarche and first birth, high susceptibility of breast tissue to carcinogenic environmental and abuses for hormonal therapy as (endogenous and exogenous estrogen) which is directly correlated to the risk of breast cancer development [(27)]. The association between serum prolactin and breast cancer risk has been studied previously [(28,20)]. Levels of serum prolactin differ by menopausal status

[29] . Therefore, the means were marked separately for premenopausal and postmenopausal women.These results are agreement with the finding of study [30].They observed a significant positive association between serum prolactin levels and the risk of breast cancer, as well as with the finding of studies [31,32]. They showed that higher levels of prolactin were related to an increased breast cancer risk in both premenopausal and postmenopausal women. However, these finding disagreed with the finding of study [33] which showed that there was no significant relationship between the prolactin hormone levels and the risk of breast cancer in both premenopausal or postmenopausal women. The complex and different biological and molecular mechanisms by which prolactin may elevate the risk of breast cancer are not clear. Certainly suggested mechanisms involve its proliferative influences on malignant breast cells, mitogenic activity, and apoptosis depression through signaling via the prolactin receptor [34]. Moreover, prolactin also functions to improve angiogenesis and cell migration, that may contribute greatly to metastases of cancer[30].As well as the endocrine concentrations, prolactin is also locally produced that may induce cancer development via autocrine and paracrine effects [35].

5.Recommendations

The study recommends emphasizing the necessity of cooperation between the Ministry of Health and the Ministry of Commerce and protecting them from dangerous behavior by providing them with sufficient support and guidance to stay away from the hypnotic products and focusing on the extension programs in the protection of the community through educating them with the guidance programs.

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