

Detection of Xanthine Oxidase IN Breast Cancer

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Abstract:

Thirty two females with breast cancer were studied .in this study xanthine oxidase levels were compared with normal females .Results obtained in the present study showed that high levels of xanthine oxidase in older age than in lower age . High level of xanthine oxidase was detected in patients having breast cancer and Diabetes Meilltus ,heart diseases, and anemia ,but no change in xanyhine oxidase was detected in breast cancer with hyperytension .

key words: *xanthine oxidase ,breast cancer.*

Introduction:

Breast cancer is a type of cancer originating from breast tissues, most commonly from the inner lining of milk ducts or the lobules that supply the ducts with milk(1).The size, stage, rate of growth and other characteristic determine the kind of treatment (2.) Breast cancer may be invasive or noninvasive. Invasive means it has spread from the milk duct or lobule to other tissues in the breast. Noninvasive means it has not yet invaded other breast tissue(3).

Xanthine oxidase (XO) is the final enzyme in the degradation of purines. It converts hypoxanthine to xanthine and subsequently to uric acid. Unlike other oxidases.

Immunohistochemical location of XO has been reported its presence in various tissues from various animal species(4) .Other researcher demonstrated the ubiquitous localization of this cytosolic enzyme in human tissues, such as tongue,esophagus, trachea, sweat glands, mammary glands, small and large intestine, renal tubules skeletal muscle, lung, spleen and liver. It was found that human blood or serum contains XO activity, since high concentration of XO antibodies are present in human sera (5).XO may play a beneficial role by producing superoxide radicals (6). Previous studies suggested a role of XO as an antimicrobial agent (7).. Moreover, it was reported that uric acid, in its normal range,serve as an antioxidant. Therefore, XO serves as a defense mechanism by generating uric acid as well(6).

Subjects and methods:

This study was conducted in Iraqi center for cancer research and medical genetic. Thirty two With age range 40-73 years, had breast cancer diagnosed by history, clinical and laboratory findings, and twenty controls with range age 30-75 years old, had no evidence of diseases of diseases. Blood was collected from a forearm vein.Blood samples were allowed to clot at room temperature and serum was separated by centerfugation at 1500g for 10 min.

Xanthine Oxidase Assay: Xanthine Oxidase(XO,EC 1.17.3.2). In this assay XO oxidizes xanthine to hydrogen peroxide which reacts with stoichiometrically with OxiRed™ probe to generate color(at lambda=570nm).Since the color intensity is proportional to XO cotent,the XO activity can be accurately measured.

1-Standard curve preparations:

It has been added 0, 10, 20 , 30 , 40 , 50 ul of the 0.1mM H2O2 standard,to generate 0 ,1 ,2 ,3 ,4 ,5 nmol/ well H2O2 standard.

2- Sample preparation: 44 ul buffer , 2ul substrate, ,2 ul enzyme mix , 2ul probr.

3-It has been measured the plate immediately (O,D=570 nm) for colorimetric assay.

$4 - XO \text{ activity} = \frac{B}{(T2-T1) \times V} \times \text{Sample Dilution Factor} = \text{nmol} / \text{min/ml} = \text{mU/ml}$

Where; B is the amount of H2O2 Generated by XO from standard curve(in nmol).

T1 is the time of first reading(A1) (in min)

T2 is the time of second reading (A2)(in min)

V is the pretreated sample volume added into the reaction well (in ml).

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Results:

Table (1): Results of xanthine oxidase in breast cancer patients according to age compared with control

patients	Xanthine oxidase Mean \pm SD) mU/ml	% of patients
40-49	341 \pm 155.19	21.87%
50-59	369.71 \pm 271.06	21.87%
60-69	399.46 \pm 361.06	40.62%
70-79	507.8 \pm 190.99	15.62%
Control(30-40)	462 \pm 207.25	100 %

Table (2) xanthine oxidase in breast cancer patients with others diseases

Diseases other than breast cancer	Xanthine oxidase (Mean \pm SD) mU/ml	% Of patients
Hypertension	468 \pm 321.02	28.1%
Diabetes	724 \pm 203.4	18.75%
Anemia	540 \pm 210.6	6.25%
Heart diseases	500 \pm 190.6	6.25%
smoking	331.5 \pm 258.81	18.75%
No other diseases	236 \pm 94.79	21.87%

Discussion:

Xanthine oxidase (XO:EC1.2.3.2) is implicated in the formation of free radical and in cyclic episodes of tissue damage or oxidative stress with degenerative disease symptoms largely characterized by the local of the initial, inflammatory event (7). As a central generator of reactive oxygen species (ROS) during inflammation, XO is linked to as many as 50 illnesses from Alzheimers and Arthritis to diabetes and cancer(8). It catalyzes the conversion reactions of hypoxanthine to xanthine and xanthine to uric acid, the last reaction in the purine catabolism, with byproduct of toxic superoxide radical. In this regard, it is a key enzyme between purine and free radical metabolism. It was reported that XO is an endogenous source of ROS and reactive nitrogen species (RNS) that can induce oxidative stress and inflect tissue injury 9). There is growing evidence that superoxide radicals generated by XO are primarily responsible for the cellular deterioration associated with several conditions (10).

In table 1 patients with older age have XO level higher than other ages 507.8 \pm 190.99 mU/ml these results, indicate that Late menopause may increases the risk of breast cancer. Women who have undergone the menopause have a lower risk of breast cancer than pre-menopausal women of the same age and childbearing pattern. Risk increases by almost 3% for each year older at menopause (natural or induced by surgery), so that a women who has the menopause at 55 rather than 45, has approximately 30% higher risk(11). In this study XO of Diabetes patients as shown in table 2 are(724 \pm 203.4) mU/

ml, higher than the control 462 \pm 207.25 mU/ml. These finding have been in agreement with the finding reported before by Khandwala who suggested that the link between diabetes or hyperglycaemia and cancer rely on biological, particularly hormonal, mechanisms involving insulin-resistance. Indeed, in the genesis of type 2 diabetes, reduced insulin sensitivity plays a key role, induce in compensatory hyperinsulinism with an increased level of circulating Insulin-like Growth Factors (IGF), well known to stimulate cell proliferation in many organs ,including the liver, pancreas, colon, ovary, breast (12). Also in table 2 anemic patients had XO activity(540 \pm 210.6) mU/ml, higer than control(462 \pm 207.25) mU/ml. The pathophysiological origins of anemia can be grouped into different categories :blood loss ,increased destruction of red blood cells and decreased production of functional red blood cells(13). In this study,XO in heart diseases patients as shown in table 2 are (500 \pm 190.6) mU/ml compared with the control(462 \pm 207.25) mU/ml. These finding have been in agreement with the finding before reported by Jennifer who suggest that the Women with heart diseases are less likely to be treated or may be more likely to experience adverse effects of therapy and not complete their treatment regimens(14).XO activity for Hypertension patients were(468 \pm 321) mU/ml compared with control (462 \pm 207.25) mU/ml,so there no association between breast cancer and hypertention these finding agreement with (15). Patients had XO activity there is some evidence that exposure to tobacco smoke is most problematic

between puberty and first childbirth. The reason is that breast tissue appears most sensitive to chemical carcinogens breast cells not fully differentiated until lactation(16). The likely reason that the older studies of active smoking did not detect risks associated with smoking was that they compared active

smokers to all nonsmokers (which includes many passive smokers). The newer studies, which exclude passive smokers from the control group, generally show elevated risks associated with active as well as passive smoking(17).

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الكشف عن أنزيم الكزانثين أوكسيداز في سيرم مرضى سرطان الثدي

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الخلاصة:

درس تأثير انزيم الكزانثين أوكسيداز للمصابات بسرطان الثدي. أظهرت النتائج ارتفاع نسبة الانزيم لدى الاعمار الكبيرة مقارنة بالاعمار الصغيرة كما أوضحت الدراسة ارتفاع نسبة الانزيم للمصابات بداء السكري والمصابات بأمراض القلب وفقر الدم. ليس هناك تأثير لارتفاع ضغط الدم والتدخين على مستوى الانزيم