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Evaluation of sister chromatid exchange in patients with breast cancer in relation to clinical stage

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تقييم التبادل الكروماتيدي الشقيقي بين مريضات سرطان الثدي وعلاقتة مع المرحلة السريرية

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الخلاصة

تعكس المستويات العالية للتبادل الكروماتيدي ألشقيقي في مريضات سرطان الثدي عدم الثبات المجيني الذي يكون فعال في عملية التسرطن.دُرس تردد التبادل الكروماتيدي ألشقيقي في لمفاويات الدم المحيطي لمريضات سرطان الثدي وعلاقته مع المرحلة السريرية لهذا النوع من السرطان. أجريت الدراسة على ١٢ مريضة مصابة بسرطان الثدي في المرحلة السريرية الثانية للمرض و٥ مريضات مصابات بالمرض نفسه في المرحلة السريرية الرابعة. قورنت القيم الأساسية للتبادل الكروماتيدي ألشقيقي مع مجموعة التحكم التي تتكون من ١٢ من الإناث السليمات.كان الفرق معنويا عالياعند مقارنة المريضات قيد الدراسة مع مجموعة التحكم ($P<0.01$) . وازداد التبادل الكروماتيدي ألشقيقي بصورة معنوية في مريضات المرحلة السريرية الرابعة عند مقارنتها بنظيراتها في مريضات المرحلة السريرية الثانية ($P<0.05$) تُظهر نتائج هذه الدراسة زيادة في تردد التبادل الكروماتيدي ألشقيقي مع تقدم الحالة السريرية لسرطان الثدي.

Abstract

High levels of sister chromtid exchanges (SCE) in patients with breast caner reflects a genomic instability that may be operative in carcinogenesis.The frequency of sister chromatid exchanges in peripheral blood lymphocytes was analyzed in patients with breast cancer in relation to clinical stage in 12 stage II and 5 Stage IV untreated breast cancer patients.Moreover,SCE baseline values in patients were compared with a control group of 12 healthy women. A significant difference emerged between patients and control ($P<0.01$).SCE increased significantly in stage IV breast cancer patients compared with those patients of stage II ($P<0.05$).The results reveal that SCE frequency increases with the progression of clinical stage of breast cancer.

Introduction

Breast cancer dramatically impact the lives of affected women and further place a significant economic burden on both their families and the health care system(1).Sister chromatid exchange(SCE) can be used as a preclinical marker for early detection of cancer (2,3).High levels of SCE in breast cancer patients reflect a genomic instability that may be operative in carcinogenesis (4).In this study, the frequency of SCE was analyzed in patients with breast cancer in relation to disease stage.

Materials and Methods

Twelve untreated breast cancer patients in stage II (age:30-65years) and five untreated breast cancer patients stage IV (age: 32-60years) ,in addition to twelve healthy women (age:26-82)as a control were the subjects of this study. Patients were admitted to Baghdad teaching hospital and their clinical stages were determined according TMN system. The samples collected during summer 2008. .Whole blood was cultured in RPMI-1640 medium for SCE analysis.0.25ml of heparainized blood was inoculated in 2ml of RPMI-1640 medium (Serva) containing phytohemagglutenin (PHA) and 10% fetal calf serum (Sigma).Cultures were incubated at 37 for 72 hours .Colchicine 0.1ml (Serva) was added to each culture tube for the final two hours of incubation to harvest the cells. Cells then treated with hypotonic solution (0.075 KCl) for 20 minutes and fixed with methanol-acetic acid (3:1 vol/vol).Cells were dropped onto clean slides (5).SCE were scored using fluorescence plus Giemsa modified staining technique(6).SCE were scored in 25 well-spread second metaphase. Results were analyzed statistically using t-test.

Results and Discussion

Table 1 shows SCE (mean ±SE) of this study. The frequency of SCE in stage II and stage IV breast cancer patients revealed marked increase in their cells. The mean of SCE was higher in lymphocytes of stage II patients(5.62±0.89 SCE/cell versus 3.12±0.15 in control $P<0.01$).The mean of SEC of stage IV patients showed high significant value compared with control (6.89 ±87 SCE/cell versus 3.12±0.15 $P<0.01$).

Table 1:SCE (mean ±SE) in stage II ,Stage IV and control groups.

Study groups	SCE(Mean±SE)
Control	3.12±0.15
StageII	5.62±0.89[a]
StageIV	6.89 ±87 [a,b]

[a] P<0.01 vs. control group

[b] P<0.05 vs. stage II group

High levels of SEC in those patients reflects impairment of DNA systems and repair (7).Furthermore,BRCA1 and BRCA2 play important roles in the mechanisms that lead to the repair of DNA -double strand breaks (8).Thus, those patients may have mutated BRCA genes.

The results of this study reveal an increase in SEC/cell in patients with breast cancer with progression of disease. The SEC in stage IV patients was higher than SCE in patients with stage II disease. The significance difference was not highly ($P<0.05$), this may be due to the sample size. Our results were in agreement with Aristei et al.,2009 that their results showed increase in SEC frequency in 20 stage II breast cancer patients.

According to the results of this study ,we conclude that SCE levels increase with progression of clinical stage of breast cancer.

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