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Erythropoietin level in acute leukemia

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Abstract

Background: Acute leukemia is a proliferation of immature bone marrow-derived cells (blasts) that may also involve peripheral blood or solid organs. Erythropoietin, is a glycoprotein hormone that controls erythropoiesis, or red blood cell production also has other range of actions including vasoconstriction-dependent hypertension, stimulating angiogenesis,and inducing proliferation of smooth muscle fibers.

Objective: to evaluate serum level of erythropoietin in patients with acute leukemia.

Research design and methods: In this case-control study, serum level of erythropoietin measured in 22 patients with Acute leukemia and 22 apparently healthy subjects using ELISA. Statistical analysis was performed using SPSS 17.0 .

Results: There was a significant increment in level of erythropoietin in patients with acute leukemia compared to apparently healthy subjects ($P < 0.001$) independently to other parameters.

Conclusion: Erythropoietin concentrations may predict adverse outcomes, and their measurement may facilitate risk estimation in leukaemic patients.

Keywords: Acute leukemia, erythropoietin.

Abbreviations: **EPO:** erythropoietin, **AML:** acute myloid leukaemia **ALL:** acute lymphocytic leukaemia ,**KD:** kilodalton, **ELISA:** enzyme linked immunosorbent assay, **SD:** standard deviation.

مستوى الإريثروبويتين في سرطان الدم الحاد

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مدرس

الخلاصة

الخلفية : سرطان الدم الحاد هو انتشار الخلايا المشتقة من نخاع العظم غير الناضجة التي قد يشتمل أيضا على الدم المحيطي أو الاعضاء الصلبة. الإرثروبويتين ، هو هرمون بروتين سكري والذي يسيطر على انتاج الكريات الحمر وعمليات اخرى بما في ذلك تضيق الأوعية وارتفاع ضغط الدم ، وتنشيط الأوعية الدموية ، و يحفز انتشار ألياف العضلات الملساء .

الهدف من الدراسة: لتقييم مستوى الإرثروبويتين في المصل من المرضى الذين يعانون من سرطان الدم الحاد .
طريقةالعمل: في هذه الدراسة تم قياس الإرثروبويتين في ٢٢مريض الذين يعانون من سرطان الدم الحاد و ٢٢ شخصا على ما يبدو اصحاء باستخدام تقنية الاليزا . تم إجراء التحليل الإحصائي باستخدام SPSS 17.0 .

النتائج : كان هناك زيادة كبيرة في مستوى إرثروبويتين في المرضى الذين يعانون من سرطان الدم الحاد مقارنة مع الأصحاء ($P < ٠.٠٠١$) .
الاستنتاج : تركيزات إريثروبويتين قد يتوقع نتائج سلبية ، وقياسها قد يسهل تقدير المخاطر في المرضى
الكلمات المفتاحية: سرطان الدم الحاد ، الإريثروبويتين .

Introduction

The acute leukemias are the result from abnormality in clonal proliferation of progenitor cells which in turn caused by mutations that block the maturation process, leading to an accumulation of immature cells. The expansion of the abnormal clone leads to decrease other elements in the marrow, often producing clinical bone marrow failure and

making the patient gravely ill (1). Rapid therapeutic intervention is required in acute leukemia because the progression and accumulation of the malignant cells is aggressive, which then spill over into the bloodstream and spread to other organs of the body resulting in metastasis (2). The diseases are subdivided according to the kind of blood cell which affected into lymphoblastic or lymphocytic leukemias and myeloid or myelogenous leukemias:

In lymphocytic leukemias, lymphocytes giving marrow cell undergo the cancerous change, which are infection-fighting immune system cells. Most lymphocytic leukemias involve a specific subtype of lymphocyte, the B cell.

In myeloid leukemias, the cancerous change takes place in a type of marrow cell that normally form red blood cells, some other types of white cells, and platelets(3).

Erythropoietin (EPO) is a 30.4 kD glycoprotein consisting of 165 amino acids and four carbohydrate groups (4).Human EPO produced by interstitial fibroblasts in the kidney in close association with peritubular capillary and tubular epithelial tubule. It is also produced in perisinusoidal cells in the liver (5).

The principal physiological function of EPO is red blood cell production by activating red bone marrow progenitor cells (6) .It has been reported that EPO may have not only erythropoietic (7) but also neuroprotective (8) anti -apoptotic and anti-oxidative and angiogenic (9) properties.

In healthy subjects blood level of EPO is low, where as erythropoietic stress, such as hypoxia or anemia, can stimulate a dramatic increase in EPO production in the kidney, leading to a significant increment in hormone concentration and subsequently increased erythropoiesis (10), EPO also stimulates red blood cell production by binding and activating a

high affinity receptor EPOR that is expressed predominantly on the surface of immature erythroid cells (11). Over the last decade it has become clear that EPO acts as growth and survival factors for multiple tissues expressing the EPOR (12).

Materials and methods:

This case –control study included (44) subjects, (22) patients with acute leukaemia; both subtypes and (22) apparently healthy persons act as a control group.

Five milliliters of blood were collected, part in plane tube (without anticoagulants) which centrifuged and the obtaining serum was stored for measuring EOP using ELISA kit (Creative diagnostics-USA) (13) and the other part used for direct measuring of haemoglobin.

The standard curve for estimation of erythropoietin concentration was represented in figure (1).

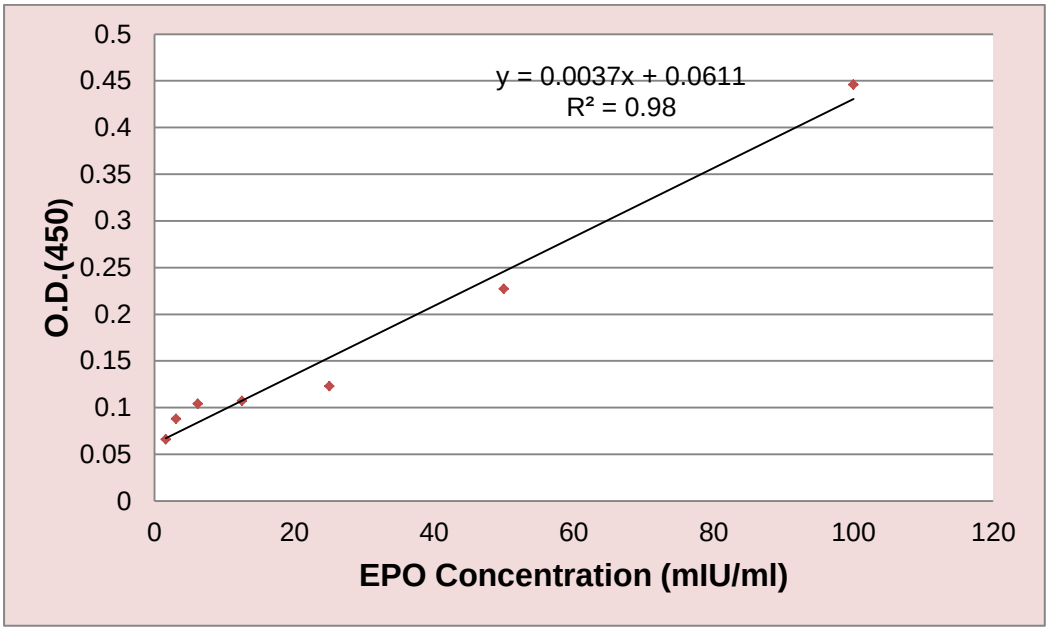

Figure (1): Standard curve of erythropoietin.

Statistical Analysis

Statistical analysis were performed using SPSS 17.0 (SPSS Inc, Chicago, IL, USA) . Data were expressed as mean ± S.D, comparisons of means were performed using Student t-test. A value of $P < 0.05$ was considered statistically significant

Result

This study reveals that serum EPO concentration in leukemic patients is significantly higher than its level in apparently healthy subjects ($P<0.001$) as demonstrated in figure (2).

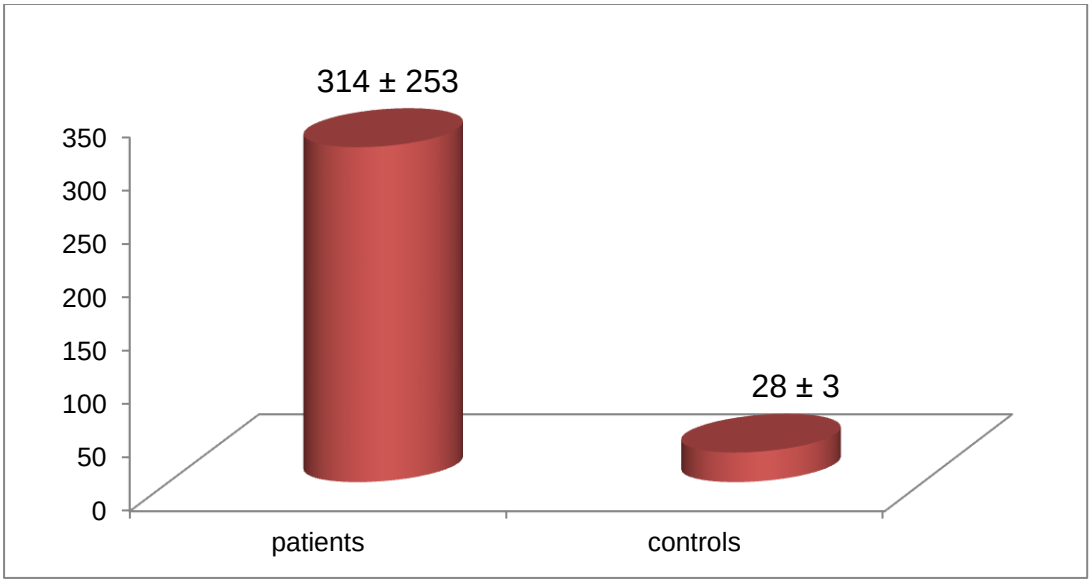

Figure (2): serum EPO concentration (mean± S.D).

Also study finds that high level of EPO independent of Hb level despite of its low level in all patients mean± S.D. is (6.4±1.4 g/dl).

There is no significant difference in EPO level between types of acute leukaemia (AML and ALL), ($P>0.05$) as figure (3) shows

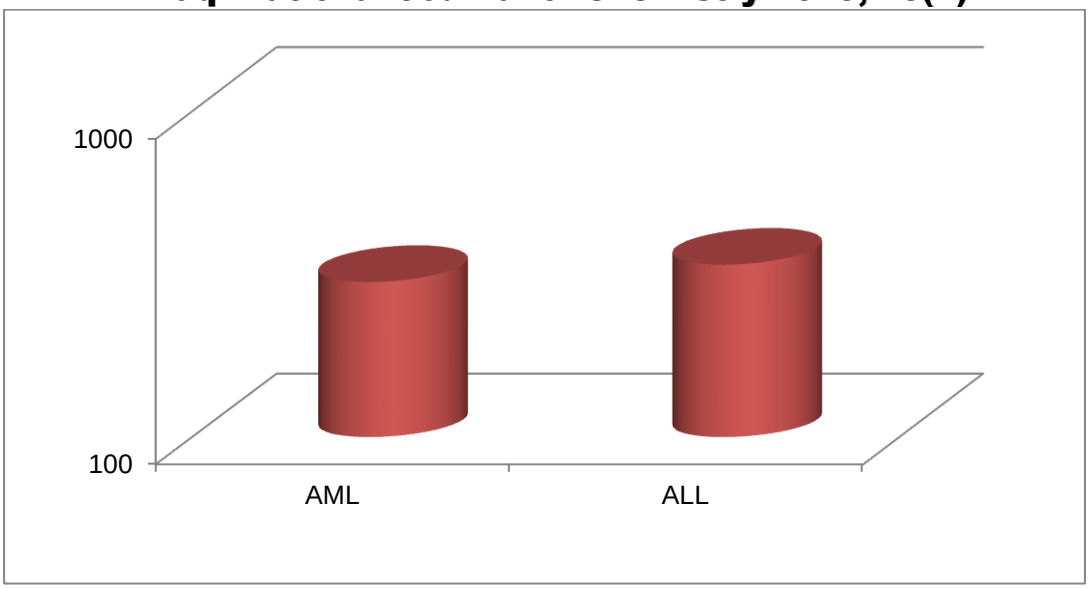

Figure (3): serum EPO concentration and type of leukemia.

There is non significant negative correlation between age, sex and EPO (P>0.05).

Discussion

This study reveals that serum EPO concentration in leukemic patients is significantly higher than its level in apparently healthy subjects this finding consistent with study done by xing Ming et al. (14).

The clinical presentation of leukemia result from the abnormal proliferation of leukemic clone cells, which tends to interfere with the development of normal blood cells in the bone marrow(15) which in turn leads to neutropenia, anemia, and thrombocytopenia. The symptoms are often due to the suppression of these normal blood elements and consequent anemia, which can stimulate a dramatic increase in EPO production in the kidney, leading to a significant rise in circulating hormone amounts this may be the main cause for obtained result other possible cause is that EPO consider as angiogenic factor (9) and leukaemia is abnormal clonal proliferation of mutated progenitor cells which need more blood supply so more blood vessels (angiogenesis) and

so stimulate angiogenic factor and in turn increase EPO level and if this confirmed so EPO supplementation for leukaemic patients is critical .

Non significant difference in EPO level between types of acute leukaemia (AML and ALL) may belong to that both types have same pathological pathway that stimulate EPO production.

Elderly persons have an inadequate erythropoietin response due to many factors such as decline renal excretory function with age (16) due to occult interstitial renal dysfunction without a change in glomerular filtration so that EPO production (17) or the set point for secretion is lowered and anaemia developed in patient with normal serum creatinine (18) and this may explain negative correlation between age and EPO that obtained in this study. bone marrow responsiveness or erythropoietin production may be reduce by cytokine dysregulation (19).

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