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Detection and clinical significance of serum EPO levels in patients with haematological tumours

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ABSTRACT

This experiment aimed to detect serum erythropoietin (EPO) levels in patients with haematological tumours and to investigate its clinical significance. For this purpose, 110 patients with haematological tumours admitted to our hospital between January 2019 and December 2020 were selected as the study population according to the inclusion and exclusion criteria, and they were included in the case group, and the clinical data of the patients were retrospectively analysed. 90 cases of people without hematological tumors who underwent physical examination during the same period were also included as a control group. The serum EPO levels of the two study groups were compared, and the clinical diagnostic value of EPO was analysed using the subject operating characteristic curve (ROC). Results indicated that of the 110 patients, 56 were leukaemia patients, 24 were multiple myeloma patients and 30 were malignant lymphoma patients. The differences in gender, age, disease history, alcohol consumption and smoking history between the two groups were not significant (P>0.05), while the EPO levels in the control group were significantly lower than those in the case group, with a statistical significant difference of P<0.05. The EPO levels in patients with leukaemia, multiple myeloma and malignant lymphoma were (165.43± 20.46) mU/mL, (28.14± 4.51) mU/mL and (86.25±10.33) mU/mL significantly higher than the control group, with a significant difference of P<0.05. Using the absence of haematological tumours as a control, the analysis yielded an area under the ROC curve of 0.995 for EPO diagnosis in patients with leukaemia, a 95% confidence interval of 0.987 to 1.000, a sensitivity of 97.80%, with a sensitivity of 98.2 %; the area under the ROC curve for patients with multiple myeloma was 0.910, with a 95% confidence interval of 0.818 to 1.000, with a sensitivity of 98.90% and specificity of 87.50%; the area under the ROC curve for patients with malignant lymphoma was 0.992, with a 95% confidence interval of 0.978 to 1.000, with a sensitivity of 96.70% and specificity of 96.70%. In conclusion, the serum EPO levels of patients with haematological tumours are significantly higher than those of the normal population, and the detection of serum EPO levels is valuable for the diagnosis of clinical haematological tumours.

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Introduction

Haematological tumours are malignant neoplasms that occur in the blood system, the most common of which include various types of leukaemia, multiple myeloma and malignant lymphoma etc.(1). For example, acute leukaemia is characterised by the abnormal proliferation of malignant leukaemia cells in the bone marrow, leading to the suppression of normal bone marrow haematopoiesis and subsequent severe anaemia, thrombocytopenia and infection. The most typical quadruple signs are elevated blood calcium, renal insufficiency, anaemia and bone pain(2-3). The impact of haematological malignancies on patients is obvious, especially in terms of the fatal damage to the immune system(4). Early diagnosis and prevention of haematological tumours is therefore particularly important. Anaemia is one of the most common clinical manifestations of haematological neoplasms and has a serious impact on the quality of life of patients, therefore more and more clinical treatment is focused on correcting tumour anaemia. Erythropoietin (EPO) is a glycoprotein hormone that regulates erythropoiesis and is mainly synthesized and secreted by cells near the proximal tubule of the kidney. Its basic physiological function is to stimulate the production and release of bone marrow erythrocytes, which in turn maintains a stable role for peripheral erythrocytes and haemoglobin(5-6). In order to investigate the clinical significance of EPO in patients with haematological tumours, this study was conducted to retrospectively examine the levels of EPO assayed in patients with haematological tumours and is reported below.

Materials and Methods

Clinical information.

One hundred and ten patients with haematological tumours admitted to our hospital between January 2019 and December 2020 were selected for the study, and they were included in the case group, and 90 people without haematological tumours who underwent physical examination during the same period were selected as the healthy control group. The study was approved by the hospital

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ethics committee.

Inclusion criteria.① Patients meet the clinical criteria for the diagnosis of leukaemia, multiple myeloma and malignant lymphoma. ② Have reached the age of 18 years.③ Subjects' general information is complete.

Exclusion criteria.① Concomitant other malignancies.② Persons with acute and chronic infections.③ Those with concomitant autoimmune disease.④ Women during pregnancy and lactation.

Research Methodology

3 ml of fasting venous blood was taken from the subject in the morning, left at room temperature for 1 h, centrifuged at 3 000 r/min for 10 min, and the serum was separated and stored at -30°C. Blood was collected on the same day or every other day for routine blood tests. Add 100 μl of diluent to each well of the enzyme plate, then add 100 μl of standard solution, control solution or specimen solution to each well, seal the plate, incubate for 2 h at room temperature (25°C), shake off the liquid in the plate wells, add 200 μl of EPO secondary antibody to each well, seal the plate and incubate for 2 h. Wash the plate four times with washing solution and shake off the plate, add 200 μl of substrate solution to each well (mixed with an equal amount of colour developing solution 15 min before use, avoid light). Incubate for 25 min at room temperature, add 100 μl of termination solution to each well, read absorbance (OD) at 450 nm within 15 min and obtain the control and sample EPO concentration (mU/mL) according to the standard curve.

Observation indicators

The general information of the two groups of patients was counted, including age, gender, history of the disease, history of alcohol consumption and smoking, etc. The tumour types of the patients in the case groups were also counted, and the EPO levels of patients with different tumour types and the control group were compared.

Statistical analysis

SPSS 21.0 software was used for statistical analysis statistics, and the measures were tested for normality, data that conformed to a normal distribution were expressed mean±standard error, and one-way group comparisons were made using the independent samples t-test. Data that did not conform to a normal distribution were expressed using the median (quartiles), and comparisons between groups were made using the Mann-Whitney U test. Categorical counts were expressed as percentages, and unordered categorical data were compared between groups using the χ^2 or Fisher exact test; ordered categorical data were compared between groups using the Mann-Whitney U test. The diagnostic value of EPO in patients with haematological tumours was evaluated using the Receiver Operating Characteristic curve (ROC). $p<0.05$ was considered a statistically significant difference.

Results

Comparison of general information between the case group and the control group

Of the 110 patients, 56 were leukaemia patients, 24 were multiple myeloma patients and 30 were malignant lymphoma patients. The differences between the two groups in gender, age, history of the disease, history of alcohol consumption and history of smoking were not significant ($P>0.05$), while the EPO levels in the control group were significantly lower than those in the case group, with statistically significant differences, $P<0.05$. See Table 1.

Comparison of EPO levels between the case and control groups

The results showed that the EPO levels of (165.43± 20.46) mU/mL, (28.14± 4.51) mU/mL and (86.25± 10.33) mU/mL were significantly higher in patients with leukaemia, multiple myeloma and malignant lymphoma respectively than in the control group, with a significant difference at $P<0.05$. See Figure 1.

ROC curve analysis of EPO clinical diagnosis

ROC curves were plotted based on the EPO levels of

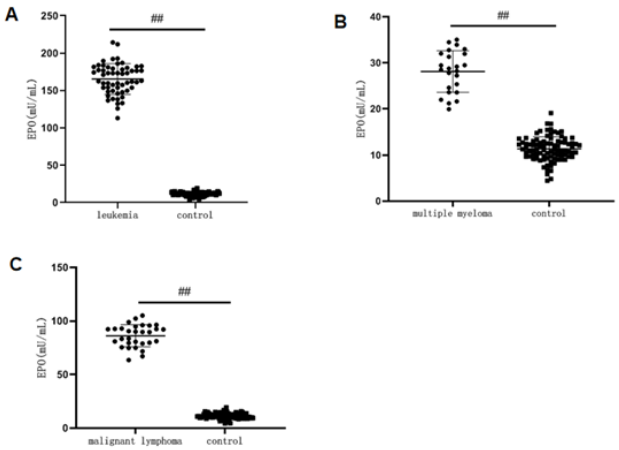

Figure 1. Comparison of EPO levels in the case and control groups. (Note: A. Comparison of EPO levels in leukemia patients and controls; B. Comparison of EPO levels in multiple myeloma patients and controls; C. Comparison of EPO levels in malignant lymphoma patients and controls. $^{\#\#}P<0.05$).

Table 1. Comparison of general information between the haematological tumour group and the control group.

General information		Case group (n=110)	Control group (n=90)	X^2 /T	*P*
Gender (cases)	Male	67	42	1.339	0.247
	Female	43	38		
Mean age (years,± s)		57.62 4.89	57.28± 4.62	0.501	0.617
Disease history (cases)	High blood pressure	28	18	0.832	0.362
	Diabetes	25	20	0.007	0.932
History of alcohol consumption (cases)		41	26	1.562	0.211
Smoking history (cases)		26	20	0.056	0.813
EPO (mU/mL, s)		113.88± 58.64	11.35± 2.62	16.566	0.000

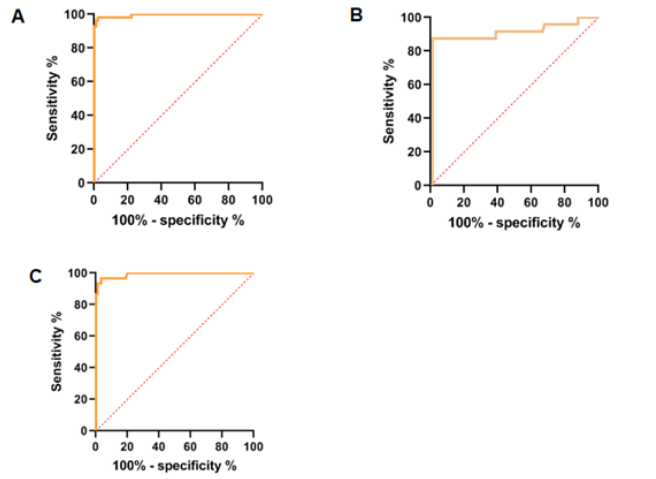

Figure 2. ROC curve for clinical diagnosis of EPO in patients with haematological neoplasms. (Note: A. ROC curve for clinical diagnosis of EPO in leukaemia patients; B. ROC curve for clinical diagnosis of EPO in multiple myeloma patients; C. ROC curve for clinical diagnosis of EPO in malignant lymphoma patients).

patients in the control and haematological tumour groups. Using the absence of haematological tumours as a control, the analysis yielded an area under the ROC curve of 0.995, with a 95% confidence interval of 0.987 to 1.000, a sensitivity of 97.80% and a sensitivity of 98.2 % for patients with leukaemia diagnosed by EPO; an area under the ROC curve of 0.910, with a 95% confidence interval of 0.818 to 1.000, for patients with multiple myeloma. The area under the ROC curve for patients with malignant lymphoma was 0.992, with a 95% confidence interval of 0.978~1.000, a sensitivity of 96.70% and a specificity of 96.70%. See Figure 2.

Discussion

Anaemia is the most common complication in haematological tumours, however, the mechanisms by which anaemia in haematological tumours arises are complex(7), and Musio (8) found that 50 out of every 100 patients with haematological malignancies are also anaemic. And in related studies, it has been found that the presence of anaemia in patients with haematological neoplasms may be related to a decrease in red lineage cells in the bone marrow, a reduced ability of the kidney to synthesise EPO, impaired iron utilisation, shortened red blood cell lifespan and radiotherapy(9-10). EPO is the first cytokine to be used clinically and consists of a 166 amino acid glycoprotein, with the gene encoding EPO located on the long arm of human chromosome 7(11). The main target cells in the bone marrow are late erythroid progenitor cells (CFU-E), which bind to the receptor, stimulate DNA and RNA synthesis and promote the proliferation and differentiation of young erythrocytes(12-13). EPO is mainly regulated in the body by negative feedback from anaemia and hypoxia (14).

In recent years, the prevalence of haematological malignancies has been increasing, and if not treated promptly, the survival of patients can be significantly shortened. The aim of this study was to investigate the diagnostic value of serum EPO levels in haematological tumours for clinical diagnosis. Several studies have shown that the correlation between serum EPO levels and gender and age is not significant(15-18). However, the correlation between EPO and anaemia in haematological malignancies has not been clearly reported. In the present study, a comparison of data from haematological tumour patients and the healthy population revealed that the difference in basic information between the two was not significant, while haematological tumour patients had significantly higher EPO levels than the healthy population. This suggests that EPO levels are significantly altered in haematological tumours, staging which may be due to the fact that the bone marrow of haematological tumour patients is infiltrated by malignant cells and normal haematopoietic cells are suppressed, leading to a reduction in EPO utilisation, which may also account for the elevated EPO levels in haematological tumour patients but still associated with anaemia. Also, in this study, it was found that the 110 haematological tumour patients selected could be divided into leukaemia patients, multiple myeloma patients and malignant lymphoma patients, and all of these patients had higher serum EPO levels than the control group, and the leukaemia patients had the highest EPO levels (19). The reason for this may be due to the proliferation of a large number of leukaemic cells in the bone marrow of leukaemia patients and the crowding out or suppression of normal red blood cells, resulting in anaemia and hypoxia in patients, which further leads to a feedback increase in EPO in the body. Based on the above findings, it can be considered that EPO levels have some diagnostic value for haematological neoplasms (20). In the current study, ROC curves were plotted by plotting serum EPO levels in control and different haematological tumour patients. The results showed that the area under the ROC curve was 0.995, 0.910 and 0.992 for patients with leukaemia, multiple myeloma and malignant lymphoma respectively, and it is generally accepted that an area under the ROC curve above 0.9 is indicative of a high screening value. These results suggest that serum EPO levels are highly specific for the diagnosis of haematological tumours and have a high diagnostic value (20).

In summary, serum EPO levels are significantly higher in patients with haematological tumours than in the normal population, and the measurement of serum EPO levels is of some value in the diagnosis of clinical haematological tumours. However, this study only investigated the diagnosis of patients, but not the changes in EPO during the treatment of patients, and the therapeutic effect of EPO in tumour patients has not yet been explored, so further investigation is needed at a later stage.

Data Availability

The experimental data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declared that they have no conflicts of interest regarding this work.

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