

BLOOD HISTAMINE LEVELS IN PATIENTS WITH LYMPHOPROLIFERATIVE DISORDERS

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Blood histamine levels (BHL) in patients with malignant lymphomas - Hodgkin's disease (HD) and non-Hodgkin's lymphomas (NHL) as well as with chronic lymphocytic leukemia (CLL) were studied in the active phase of the diseases and during remission after treatment. BHL were significantly decreased by 2,5-fold in HD patients in the active phase as compared to the controls. After treatment and during remission BHL normalized. It was found out that according to the calculated correlation R and determination (D) coefficients of BHL with the obligatory indices for biological activity in HD (ESR, fibrinogen, serum iron, α_2 -protein fraction), the most informative criterion for the active phase was ESR ($R=0,99$, $D=98\%$) followed by BHL ($R=-0,89$, $D=79\%$), and BHL during remission ($R=0,87$, $D=75\%$). In NHL patients, no significant differences in BHL in comparison to clinically healthy persons were established independently of the process activity and grade of malignancy. In patients with CLL, however, BHL were statistically significantly ($p < 0,01$) elevated by 45,8 % during the active stage compared with the control group. A significant correlation was found between the BHL and leukocyte counts in the active phase of the disease ($r_s = 0,71$, $p < 0,001$). BHL normalized during remission. Therefore, BHL can be used as an additional criterion for the evaluation of the biological activity and remission in HD patients.

Key-words: Histamine, Hodgkin's disease, non-Hodgkin's lymphoma, chronic lymphocytic leukemia

Changes in blood histamine levels have been established in a number of stem cell - myeloproliferative disorders such as chronic myelogenous leukemia (2-6,12) and polycythemia vera (1,2,6,7,11). However, the studies of blood histamine levels in

lymphoproliferative disorders are scarce. To our best knowledge, such studies related to Hodgkin's disease (HD) have not been reported in the specialised literature available, and there are only a few related to non-Hodgkin's lymphomas (NHL) (8). There are also very few reports on chronic lymphocytic leukemia (CLL) in which, however, the disease phase when the studies are conducted is not specified (3,11).

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In this study we aimed at examining the clinical significance of blood histamine level in patients with HD, NHL and CLL in the active phase of the diseases and during remission following the respective treatment as well as at seeking for a correlation of this index with biological and haematological indices of biological activity in the above diseases.

MATERIAL AND METHODS

Forty-three patients with HD (mean age of 41,8 years), 30 patients with NHL (mean age of 36,6 years), and 35 patients with CLL (mean age of 45,2 years) were included in this trial. The patients were treated according to the conventional regimens. They were investigated in the active phase of the disease and during remission after the corresponding treatment for the following indices: blood histamine in all patients, spectrofluorimetrically after Lorenz et al. (9); indices for biological activity in patients with HD: ESR (after

Westergren); fibrinogen (after Podmor DA); alpha₂-protein fraction (electrophoretically); serum iron (by bathophenanthroline method); leukocyte count in CLL. The same indices were investigated monitored in 30 age- and sex-matched healthy persons (mean age of 35,5 years).

In order to measure the data objectively the variation, correlation, and regression statistical analyses were used.

RESULTS AND DISCUSSION

Blood histamine levels in patients with HD in the active phase were about 2,5-fold lower than in the group of healthy controls ($0,030 \pm 0,002 \mu\text{g/ml}$ vs $0,072 \pm 0,002 \mu\text{g/ml}$). During remission after treatment the histamine levels increased reaching up to $0,077 \pm 0,006 \mu\text{g/ml}$. We used the probability assessment method for the permission ability of a criterion to determine the differentiation value of blood histamine index for the states of activity and re-

Table 1

Mean values of the indices for biological activity in HD patients

Indices	HD patients		Controls
	active phase	remission	
ESR (mm)	$66,54 \pm 4,95^*$	$24,67 \pm 3,36^*$	$8,60 \pm 0,94$
Fibrinogen	$6,93 \pm 0,66^*$	$3,09 \pm 0,14$	$2,93 \pm 0,14$
α 2-fraction (g/l)	$0,19 \pm 0,01^*$	$0,13 \pm 0,05$	$0,09 \pm 0,01$
Serum iron (μl)	$8,66 \pm 1,14^*$	$13,57 \pm 0,99$	$15,27 \pm 1,26$
BHL (μml)	$0,030 \pm 0,002^*$	$0,077 \pm 0,006$	$0,072 \pm 0,002$

*p < 0,001

■ission in HD - 0,040 µg/ml.

In patients in active phase out of the obligatory indices for biological activity (10) we found out that as compared to the control group the following values were statistically significantly increased: ESR, fibrinogen and alpha₂-protein fraction, and the values of serum iron were significantly decreased. During remission only the ESR values remained significantly higher (Table 1). By means of regression models the coefficients of correlation and determination were calculated. The cor-

relation coefficients provide information about the normal relation and dependence of the values of the respective index on the disease phase. The correlation coefficient is a measurement of the interaction power between phenomena and ranges from 0 to 1. The calculation of the correlation coefficients indicate that during the active phase ESR is the most informative (R1 = 0,99, p < 0,001) followed by the histamine level (R1 = 0,89, p < 0,001). For remission the histamine level is the most informative ((R2 = 0,87, p < 0,01) (Table 2).

Table 2

Correlation coefficients (R) of criteria for biological activity in HD

Indices	active phase R ₁	remission R ₂
ESR (mm)	0,99	- 0,45
Fibrinogen	0,81	- 0,79
α 2-fraction (g/l)	0,89	- 0,41
Serum iron (µ/l)	- 0,79	0,53
BHL (µ/ml)	- 0,89	0,87

Determination coefficients indicate what percentage of the changes in the investigated parameters is determined by the disease process. The established values show that the highest

degree of informativeness in the activity phase is borne by the indices ESR (D1 = 98,01 %) and histamine level (D1 = 79,21 %) and for remission - histamine level (D2 = 75,69 %) and with fibrinogen (D2 = 62,41 %) (Table 3).

Table 3

Determination coefficients (D) of criteria for biological activity in HD

Indices	active phase D ₁ (%)	remission D ₂ (%)
ESR (MM)	98,01	20,35
Fibrinogen	66,23	62,41
α 2-fraction (g/l)	78,51	17,08
Serum iron (µ/l)	51,84	28,09
BHL (µ/ml)	79,21	75,69

The mean blood histamine levels in patients with NHL in relapse was $0,087 \pm 0,012 \mu\text{g/ml}$. The difference in comparison to the control group is not statistically significant. No difference in blood histamine levels was established in patients with high grade NHL malignancy ($0,086 \pm 0,023 \mu\text{g/ml}$) and those with low grade NHL ($0,087 \pm 0,008 \mu\text{g/ml}$). After treatment the mean blood histamine levels in patients with NHL was $0,073 \pm 0,01 \text{ mkg/ml}$ which approximated closely the control values.

In patients with CLL during active disease phase the blood histamine level was $0,110 \pm 0,015 \mu\text{g/ml}$. The elevation by 45,8 % as compared to the healthy control group was statistically significant ($p < 0,01$). During remission as a result of the treatment the mean histamine values decreased to $0,079 \pm 0,011 \mu\text{g/ml}$. The mean leukocyte count in patients with CLL in the active phase was $89,7 \pm 15,0 \times 10^9/l$ which was by about 17 times higher than the mean values in the control group - $5,3 \pm 0,15 \times 10^9/l$.

In patients during remission the leukocyte count decreases, the mean value of $19,8 \pm 6,9 \times 10^9/l$ being statistically significantly ($p < 0,01$) lower than that in the active phase. Nevertheless, it is about twice as high as of the refer-

ence values for this index. During the active phase of the disease a strong statistically significant correlation (Spearman's rank correlation coefficient $r_s = 0,71$; $p < 0,001$) was established between blood histamine levels and the leukocyte count. During remission this correlation is not statistically significant.

The results obtained point to the following conclusions:

1. In patients with HD the blood histamine levels can be used as an additional criterion for assessing the states of biological activity and remission resulting from effective treatment.

2. In patients with CLL the changes in the leukocyte count which indicate the disease activity affect the changes in histamine levels which suggests that blood histamine level can be used as an additional criterion for disease activity assessment.

3. In patients with NHL blood histamine levels are a not an informative index neither for process activity assessment, nor for the grade of disease malignancy.

Acknowledgements:

The indices for biological activity in HD and the leukocyte count in CLL were investigated in the Clinic of Haematology at the Medical University of Varna for which I would like to express my thanks.

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Ниво на хистамина в кръвта при болни с лимфопролиферативни заболявания

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Резюме: Нивото на хистамина в кръвта (НХХ) при болни с малигнени лимфоми - болест на Ходжкин (БХ) и не-Ходжкинови лимфоми (НХЛ), и с хронична лимфоцитна левкемия (ХЛЛ) е проследено в активна фаза на заболяванията и след лечение. Данните показват, че НХХ при болни с БХ в активна фаза е статистически значимо намалено 2,5 пъти в сравнение с това при контролна група здрави лица. След лечение и в ремисия НХХ се нормализира. Изчислените коефициенти на корелация (R) и детерминация (D) на НХХ със задъжителните показатели за биологична активност при БХ (СУЕ, фибриноген, серумно желязо, 2-протеинова фракция) показват, че най-информативен за активност на процеса е СУЕ (R = 0,99, D = 98 %), следван от НХК (R = -0,89, D = 79 %), а за ремисия - НХК (R = 0,87, D = 75 %). НХК при болни с НХЛ не се различава значимо от това на контролната група, независимо от активността на процеса и степента на малигненост. При болни с ХЛЛ нивото на хистамина е с 45,8 % ($p < 0,01$) по-високо от това при здравите лица. Установена е значима корелативна зависимост на НХК с броя на левкоцитите ($r_s = 0,71$, $p < 0,001$). При ремисия НХК се нормализира. Предлага се НХК като допълнителен критерий за преценка на състоянията на биологична активност и ремисия при болни с БХ.