

BLOOD HISTAMINE LEVELS AS A POSSIBLE CLINICO-PHARMACOLOGICAL CRITERION IN CERTAIN BLOOD DISEASES

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The possible significance of blood histamine levels for diagnosing and treatment evaluation in patients with blood disorders such as malignant lymphomas - Hodgkin's disease (HD) and non-Hodgkin's lymphomas (NHL), and Schönlein-Henoch purpura (SHP) was studied. Histamine was established spectrofluorimetrically in the active phase of the disease as well as during remission after treatment. Blood levels of histamine were significantly decreased about 2,5-fold in patients with HD in the active phase as compared to healthy controls ($0,030 \pm 0,002 \mu\text{g/ml}$ versus $0,073 \pm 0,002 \mu\text{g/ml}$) and by 31,5 % in patients with active SHP ($0,050 \pm 0,004 \mu\text{g/ml}$ versus $0,073 \pm 0,002 \mu\text{g/ml}$). After treatment and during remission the histamine levels recovered to normal. Such a correlation between blood levels of histamine, on the one hand, and process activity and treatment efficiency, on the other, was not observed for NHL. These results indicated that blood levels of histamine could serve as an additional criterion for the process activity evaluation and for the therapeutic effectiveness in patients with HD or SHP but not NHL. Furthermore, blood histamine levels might be considered as a possible clinico-pharmacological criterion for the evaluation of new drugs anticipated for the treatment of HD or SHP.

Key-words: Histamine, Hodgkin's disease, non-Hodgkin's lymphoma, Schönlein-Henoch purpura, diagnosis

Certain blood disorders such as malignant lymphomas - Hodgkin's disease (HD) and non-Hodgkin's lymphomas (NHL) as well as Schönlein-Henoch purpura (SHP) are usually associated with major immunological alterations (1,5,7).

Knowing that histamine can act as a modulator of various immune functions (2,8), we have been interested in the possible changes of blood histamine levels in patients with malignant lymphomas and SHP in the active phase of the disease and during remission due to treatment. The aim of the present study was to compare the levels of histamine in blood of patients with HD, NHL, and

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SHP in the active phase and after treatment in order to assess the possible significance of blood histamine levels as an additional criterion for the diagnosis of HD, NHL, and SHP and for the evaluation of treatment.

MATERIAL AND METHODS

Blood samples from 97 age and sex mixed patients with malignant lymphomas - HD and NHL, or SHP were tested. Fifty-three of them presented with HD. Eleven of the patients were registered as NHL. The other 33 patients were with diagnosis of SHP. Blood samples were taken during the active phase of the disease before the start of treatment and during remission due to therapy. Blood samples from 45 clinically healthy persons served as control. Blood histamine levels were assayed spectrofluorimetrically. All values are presented as means \pm S.E.M. Differences were assessed with Student's *t*-test.

RESULTS AND DISCUSSION

The mean blood concentration of histamine in controls was $0,073 \pm 0,002$ $\mu\text{g/ml}$. In patients with HD blood histamine concentrations were $0,030 \pm 0,002$ $\mu\text{g/ml}$ in the active phase of the disease. This is significantly lower ($p < 0,001$) by

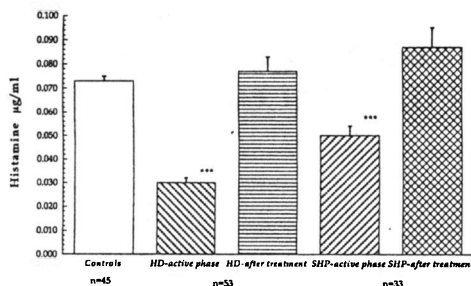


Fig. 1. Blood histamine levels in patients with HD and SHP in the active phase of the disease and after treatment. Values are means \pm S.E.M. *** $p < 0,001$ versus controls

2,5-fold compared to control. After treatment blood histamine concentrations became $0,077 \pm 0,006$ $\mu\text{g/ml}$ thus approaching control values (Fig. 1). Blood histamine levels never reached control value in patients without any improvement after treatment. The mean concentration of histamine in blood of patients with active SHP was $0,050 \pm 0,004$ $\mu\text{g/ml}$, which was significantly lower ($p < 0,001$) by 31,5 % compared to control. After a course of heparin treatment histamine levels ($0,087 \pm 0,008$ $\mu\text{g/ml}$) became slightly higher but not significantly different from the normal, healthy group (Fig. 1). In patients with NHL blood histamine levels were $0,068 \pm 0,014$ $\mu\text{g/ml}$ during the active phase and $0,050 \pm 0,007$ $\mu\text{g/ml}$ during remission. There were no significant differences compared to control.

The results from the present study reveal that blood levels of histamine are decreased below normal in patients with HD or SHP during the

active phase of the disease and revert to normal after treatment. These findings suggest that the assay of blood histamine might be helpful for monitoring disease activity or for prediction of treatment failure in patients with HD or SHP but not in patients with NHL. The observed changes in blood histamine concentration in patients with active HD or SHP might be related to the immunological alterations typical of these diseases. There is evidence that certain immunological factors such as interleukin-2 receptor serum levels could serve as prognostic indicators in patients with HD (3). Histamine itself plays an immune modulatory role by both augmenting or

suppressing the immune response depending on the type of receptors or the cells present in a given circumstance (6). The observation that in patients with NHL the activity of the process was not associated with changes in blood histamine concentrations could be due to the histological and immunological diversity of the different types of NHL (4).

The elevation of blood histamine levels close to the normal range as a result of adequate drug therapy might be useful as a possible clinico-pharmacological criterion for the evaluation of new drugs anticipated for the treatment of HD or SHP.

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Нива на хистамина в кръвта като възможен клиничко-фармакологичен критерий при някои кръвни заболявания

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Резюме: Проучено е значението на нивото на хистамина в кръвта за диагнозата и за преценка на ефективността от лечението при пациенти с малигнени лимфоми - болестта на Ходжкин (БХ) и не-Ходжкинови лимфоми (НХЛ), и с пурпурата на Шьонлайн-Хенох (ПШХ). Хистаминът в кръвта е определян спектрофлуориметрично в активна фаза на заболяванията, както и в ремисия, настъпила след лечение. Установено е, че нивата на хистамина в кръвта са значимо по-ниски в активна фаза в сравнение с тези при здрави контроли - около 2,5 пъти при пациенти с БХ ($0,030 \pm 0,002 \mu/ml$ спрямо $0,073 \pm 0,002 \mu/ml$) и с 31,5 % - при пациенти с ПШХ ($0,050 \pm 0,004 \mu/ml$ спрямо $0,073 \pm 0,002 \mu/ml$). След лечение и при ремисия съдържанието на хистамин се възстановява до нормални стойности. При НХЛ не се наблюдава подобна корелация между нивата на хистамина и активността на процеса, от една страна, както и ефективността на лечението, от друга. Резултатите показват, че нивото на хистамина в кръвта може да бъде използвано като допълнителен критерий за преценка на активността на процеса и на ефективността от лечението при пациенти с БХ и ПШХ, но не и при тези с НХЛ. Наред с това нивото на хистамина може да се обсъжда като възможен клиничко-фармакологичен критерий при оценката на нови лекарствени средства, предлагани за лечение на БХ или ПШХ.