BRIEF COMMUNICATION

Intraerythrocytic Adaptation (2,3 DPG, $P_{50}$) in Thalassemia Minor

By Howard A. Pearson, Etsuro Motoyama, Myron Genel, Michael Kramer, and Charlene J. Zigas

$P_{50}$ and 2,3 DPG content of erythrocytes were determined in 25 patients with heterozygous $\beta$ thalassemia minor to assess the adaptive mechanisms to anemia. 2,3 DPG levels were appropriately elevated for the degree of anemia. However, $P_{50}$ values were not proportionately increased. No correlations were noted between hemoglobin level, 2,3 DPG, or $P_{50}$ and the presence of symptomatic complaints of fatigue or weakness in these heterozygous patients.

HETEROZYGOUS $\beta$ THALASSEMIA (thalassemia minor) is a hypochromic, microcytic anemia characterized by hemoglobin levels 1-2 g/dl lower than found in normal individuals of the same age and sex. Most persons with thalassemia minor have no symptoms that can be attributed to their anemia; others, however, have subjective complaints of chronic fatigue and weakness.

One of the important compensatory mechanisms mounted as a response to anemia involves alterations in the affinity between hemoglobin and oxygen. This adaptation is largely mediated by changes in the levels of organic phosphate intermediates, chiefly 2,3 diphosphoglycerate (2,3 DPG) within the red cell. In order to assess this intraerythrocytic compensatory mechanism, 2,3 DPG levels and whole blood $P_{50}$ values have been measured in 25 heterozygous adults with thalassemia minor.

MATERIALS AND METHODS

The Coulter Model S electronic counter was used to measure red blood cell count, hemoglobin, mean corpuscular volume, and derived values. Hb A$_2$ was determined by starch block electrophoresis. Hb F was measured by the one minute alkali denaturation method. Red cell 2,3 DPG was determined using a commercial Sigma kit based on the reduced NADP method. Whole blood $P_{50}$ was measured, using the mixing technique of Edwards and Martin. Twenty-five adults with heterozygous $\beta$ thalassemia were studied.

RESULTS

The data from the 25 subjects with thalassemia minor are listed in Table 1. All had a moderate hypochromic, microcytic anemia, and hemoglobin A$_2$ levels elevated above 3.4%. The mean hemoglobin in seven men was 12.8 g/dl. None had symptoms attributable to anemia. Eighteen women with thalassemia minor...
were divided into symptomatic or normal groups on the basis of whether they believed that they were more fatigued, weaker, or required more rest than normal. 2,3 DPG levels were appropriately elevated for the degree of anemia. However, the P₅₀ level did not show the expected shift to the right for the degree of anemia or the increased level of 2,3 DPG. No significant differences of hemoglobin, 2,3 DPG, or P₅₀ levels were noted between groups of symptomatic and normal women.

DISCUSSION

As an intraerythrocytic, compensatory mechanism, a “shift to the right” of the oxygen dissociation curve occurs in most anemic states. This shift, mediated primarily by increases in red cell 2,3 DPG, results in more oxygen being unloaded to the tissues at a given arteriovenous difference in oxygen tension.

The individuals with thalassemia minor that we studied had appropriate increases in 2,3 DPG, but their P₅₀ levels were not shifted. Oski has suggested that 2,3 DPG levels can be expected to increase approximately 430 μmoles/ml RBC for a decrease in hemoglobin level of 1 g/dl. The mean increase above normal of 2,3 DPG in this group of individuals with thalassemia minor was approximately 1000 μmoles/ml, an increase predicted for an approximately 2 g/dl decrease below normal in mean hemoglobin. The observed increased 2,3 DPG level would have been expected to result in an increase of P₅₀ of about 2 mm Hg, and this increase was not observed. The reason for the failure of the P₅₀ value to be increased in the presence of increased 2,3 DPG is not certain.

None of the men with thalassemia minor reported symptoms which could be attributed to anemia. When women with thalassemia minor were categorized on the basis of complaints of fatigue and weakness, no differences were observed between the two groups in mean hemoglobin level, 2,3 DPG, or P₅₀. Therefore, such symptoms in individuals with thalassemia minor did not result from a more severe degree of anemia or a failure of the intraerythrocytic adaptive mechanisms that were studied. The possible effects of circulatory adaptive mechanisms remain to be studied.

REFERENCES

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HA Pearson, E Motoyama, M Genel, M Kramer and CJ Zigas