Erythrocyte 2,3-Diphosphoglycerate as Related to Diabetes and Obesity

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2,3-Diphosphoglycerate was determined in the erythrocytes of 17 diabetic and 18 obese patients. Results for obese subjects were significantly ($P < .01$) different from those obtained for 21 healthy subjects. Results for obese and diabetic patients also differed significantly ($P < .01$), but not those for diabetic and healthy subjects. Hemoglobin, hematocrit, or bicarbonate measurements did not differ among the three groups.

2,3-Diphosphoglycerate (2,3-DPG) is apparently the most important regulatory factor in erythrocyte metabolic activity, as judged from its close relation to the function of hemoglobin and its concentration in these cells, which is more than three times greater than that of ATP (1). On the other hand, a relationship exists between 2,3-DPG and the activity of certain enzymes in a number of hereditary disorders (2, 3).

A marked increase in 2,3-DPG has been described in erythrocytes in cases of hypoxia of different causes (4–6) and this increase is thought to be of physiological importance for the release of oxygen to peripheral tissues.

There are contradictory reports on 2,3-DPG in diabetic patients (7–9) — who, as it is generally known, suffer from severe tissue hypoxia. Moreover, obesity is associated with respiratory insufficiency followed by secondary polycythemia, which is an indication of hypoxia (10–12). These facts have motivated us to measure 2,3-DPG in the erythrocytes of groups of obese and diabetic patients and to compare the results with those found for healthy individuals.

Materials and Methods

Blood samples were drawn early in the morning from the antecubital vein of fasting individuals and transferred into siliconized tubes. In the case of diabetic patients, these were drawn before their usual insulin dose.

The diabetic patients were not obese, had no ketoadidosis, and did not manifest any signs of cardiac, pulmonary, or renal insufficiency or any other complicating disease.

In the group of diabetics, 16 to 56 years old (mean, 35.7 ± 10.9), one was a man and 16 were women. In the group of obese patients, 20 to 48 years old (mean, 29.4 ± 5.6), three were men and 15 women. Their weight ranged from 114.5 to 88.6 kg (mean, 102.5 kg). A control group of 21 healthy subjects, with ages ranging from 18 to 54 years (mean, 32.6 ± 7.8), consisted of three men and 18 women.

Samples were kept at −20 °C for not longer than 4 h. Bicarbonate was estimated according to Jørgensen and Astrup (13). 2,3-DPG was determined enzymatically as described by Krimsky (14). Conventional methods were used for hemoglobin and hematocrit estimations. All analyses were performed in duplicate and Student’s t-test was used to evaluate the results statistically.

Results

Our results are presented in Table 1. Hemoglobin, hematocrit, and serum bicarbonate did not show any statistically significant differences between healthy controls and either diabetic or obese patients, nor did the latter two groups differ from each other.

The mean value for 2,3-DPG in controls was 0.94 ± 0.13 mmol/mol of hemoglobin tetramer (Hbt); in diabetic patients it was lower, 0.90 ± 0.10, although the difference was not significant ($P > 0.02$). Between controls (0.94 ± 0.13) and obese patients (1.05 ± 0.16) the difference was significant ($P < 0.01$), as it also was ($P < 0.01$) between the diabetic and obese groups.

It must be added that our sample population was mostly female and therefore no attempt was made to examine possible sex-related differences.

Discussion

We selected two pathological conditions in which the glycolytic pathways of the erythrocyte might conceivably be disturbed, with the aim of interpreting any alterations in the concentration of 2,3-DPG on the basis of a similar pathogenetic mechanism.

Studies on the metabolism and function of erythrocytes, and especially studies of their glycolytic pathways, have shown the importance of 2,3-DPG in affecting the affinity of hemoglobin for oxygen. In addition, changes in the function of hemoglobin...
caused by changes in 2,3-DPG concentrations are probably related to alterations in the consumption of glucose by the cell. In normal individuals, this indication is well documented by quantitative estimations of 2,3-DPG in erythrocytes (4, 15, 16), but under pathological conditions the available evidence is sometimes conflicting. Hemoglobin and 2,3-DPG in normal subjects is inversely related to that in patients with various types of anemia (4, 6, 15).

Our failure to find any statistically significant differences between diabetics and healthy controls agrees with previous observations (8, 9, 17), but contrasts with the findings of Ditzel (7).

The high negative correlation between 2,3-DPG and hemoglobin concentrations might be the factor determining changes in the metabolic activity of the erythrocyte when hemoglobin is in its reduced form. In this case, most of the 2,3-DPG is conjugated with hemoglobin. The opposite is true of oxyhemoglobin, thus allowing the release of larger volumes of oxygen to the tissues.

The difference observed between healthy individuals and obese patients could be the result of hypoxia, because obesity is frequently associated with respiratory disturbances.

Although many suggestions have been offered to explain significant changes in oxygen transport in whole blood in vivo (18--20), we believe that the most likely one is related to large variations in the 2,3-DPG content of pathological erythrocytes. On the other hand, 2,3-DPG variably affects those enzymes that play an important role in glucose metabolism, but the reports are not always in accord (21--25).

References

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