

SUMMARY

We measured in the blood samples of 72 adults leprosy patients who were ingesting 100 mg of dapsone/day, the levels of erythrocytes, hemoglobin, methemoglobin, sulfone and reticulocytes. NADH-methemoglobin reductase was measured in the hemolysate and ghost cells. All subjects were inpatients of Instituto Lauro de Souza Lima - Baum S.P. Brazil.

Identical tests, except sulfone were applied in the blood samples of 72 healthy individuals that not ingested oxidant drugs.

The means of the erythrocytes, hemoglobin, hematocrit and hematological indexes were among patients lower than healthy individuals, what is due to the hemolytic effect of dapsone. An important mechanism for oxidant drug-induced hemolysis is because some of these drugs generate hydrogen peroxide by their reaction with hemoglobin¹⁷.

The mean level of methemoglobin in the leprosy patients was higher than in the control group, and it's also due to the action of dapsone, which has great potential to cause an increased methemoglobin level⁵⁰.

A balance between the oxidation and reduction of heme iron determines the level of methemoglobin in erythrocytes. The NADH cytochrome *b*₅ reductase of the erythrocytes reduced the ferric cytochrome *b*₅ generated from nonenzymatically reduction of methemoglobin by ferrous form of cytochrome *b*₅⁷².

In this work we measured NADH-reductase activity in hemolysate and intact ghost cell of the leprosy patients who were ingesting dapsone. The enzymatic activity was determined by spectrophotometric assays as previously described by Scott⁷³, with slight modifications. We incubated the washed erythrocytes for 30 minutes in a solution containing 1% (wt/vol) NaNO₂⁶⁷. The erythrocyte ghosts were prepared according to Dodge et al²¹.

The mean enzyme activity in the hemolysate of the leprosy patients and the healthy individuals has not differed significantly when expressed in UI/gr.Hemoglobin/1, but the mean enzyme activity in erythrocytes ghost from leprosy patients was significantly smaller than that erythrocyte ghosts from healthy individuals. The present observation may be explained by the increased level of methemoglobin in the erythrocyte cytoplasm of the patients.

The consumption of the NADH-reductase is increased and the erythrocytes did not produce more enzymes because that cell during the maturation stages develops extrusion of its nucleus and decrease it's number of ribosomes (cytoplasmic organelles) where this enzyme is likely produced⁶.

The NADH-methemoglobin reductase reduces cytochrome *b*₅, which converts non-enzymically methemoglobin into hemoglobin⁸³.

Hultquist et al, 1974, suggest the microsomal origin of this protein by comparing the trypsin-digest cytochrome *b₅* of erythrocytes with trypsin solubilized cytochrome *b₅* from human liver microsomes⁷².

The cytochrome *b₅* and NADH-cytochrome *b₅* reductase, which constitute the methemoglobin reducing system of mature human erythrocytes, originate from the endoplasmic reticulum of nucleated red cell precursors. The solubilizing agent is possibly a protease provided by lysosomes of the immature red cells⁷².

It's us therefore likely that leprosy patients, the consumption of erythrocyte membrane and soluble cytoplasmic NADH-reductase enzyme is increased due to raising of the methemoglobin level.

The membrane NADH-reductase enzyme is a precursor form of the soluble cytoplasm enzyme and both are regulated by a similar related genetic control mechanism⁴³.

Dapsone promotes the increase in enzyme activity in the supernatant of ghost suspension after treatment with the drug, and was dependent on Dapsone concentration⁴.