Study of Erythrocyte δ-Aminolevulinic Acid Dehydratase Activity in Porphyria Cutanea Tarda

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Summary. The erythrocyte δ-aminolevulinic acid dehydratase activity was studied in porphyria cutanea tarda patients, compared to healthy controls, in an attempt to resolve the contradictions in the relevant literature data. In an in vitro experimental system, a study was also made of how the erythrocyte δ-aminolevulinic acid dehydratase activity varies on the action of the activators –SH and Zn²⁺.

It was found that, compared to the healthy controls, the erythrocyte δ-aminolevulinic acid dehydratase activity of porphyria cutanea tarda patients is significantly decreased, but it is restored to the original activity level on the addition of –SH and Zn²⁺.

Since there is a general –SH requirement of δ-aminolevulinic acid dehydratase, the most obvious explanation for the decrease of the activity in the case of the patients is the shift of the natural redox systems of the erythrocytes, and the decrease of the reduced glutathione/oxidized glutathione ratio.

Key words. Erythrocyte δ-aminolevulinic acid dehydratase activity – Porphyria cutanea tarda – –SH activator

Porphyria cutanea tarda-Kranken die Verschiebung der natürlichen Redox-systeme der Erythrocyten, die Verringerung des Quotienten reduziertes Glutathion/oxydiertes Glutathion.

**Schlüsselwörter:** Erythrocyten-δ-Aminolävulinsäure-Dehydrase-Aktivität — Porphyria cutanea tarda — —SH-Aktivator

Studying the enzymes of haem biosynthesis is of basic importance in human porphyrinopathic diseases. One such enzyme is δ-aminolevulinic acid dehydratase (EC 4.2.1.24.) (ALAD). This catalyzes the condensation of two molecules of δ-aminolevulinic acid (ALA) to yield one molecule of porphobilinogen (PBG), a direct precursor of various tetrapyrrole compounds.

Thus, porphyria cutanea tarda (PCT) has been recorded as a disease of hepatic origin. We chose the study of the erythrocyte ALAD enzyme easy of access instead of impracticable hepatic enzyme study.

Since the relevant literature data are fairly sparse, and at the same time contradictory, the aim of the present work was to study the erythrocyte ALAD activity in porphyria cutanea tarda (PCT) patients. Our own earlier examinations in this respect [13] clearly demonstrated an activity decrease in PCT patients. However, Kaufman and Marver did not observe a significant alteration in the ALAD activity of the liver tissue compared to healthy controls [8]. Schuppli found an enhanced erythrocyte ALAD activity in experimentally induced porphyria, but did not observe this in human porphyria [14].

In the present work a study was also made of how the in vitro erythrocyte ALAD activity of our PCT patients responds to the activators —SH and Zn²⁺.

It must be noted that ALAD no longer functions in the circulating erythrocytes, and thus the in vitro activity can only be an indicator of the physiological changes in the erythrocytes.

The results permit only cautious conclusions.

**Materials and Methods**

**Individuals**

1. Control group. This consisted of 43 in-patients of our Department who were not suffering from porphyrinopathy.

2. PCT patients. The patients were outpatients, 34—75 years of age; 15 were male and 2 female. Both fresh cases (disease of a few months’ duration) and patients who had the disease for several years featured in the group. All of them had previously participated in the blood-letting therapy proposed by Ippen [7]. A number of our patients regularly consume alcohol by their own account. It was forbidden for them to have any drink 12 h before the assay. The results of the liver function tests (SGOT, SGPT, LAP, γ-GT) and the liver biopsy examinations were taken into account for every patient. All of our patients display the liver changes characteristic of PCT (increased liver function tests, in 5 cases hepatic cirrhosis).

**Measurement of Erythrocyte ALAD Activity.** The Mitchell et al. [11] modification of the Coleman [2] determination was employed. All blood necessary for the examinations was obtained by venipuncture. (Heparin was used as anticoagulant.) The samples were cooled and stored until measurement, which was performed on the same day. We modified the method reported by Mitchell et al. [11] insofar as cysteine, in a concentration of 50mmol/l, was used as —SH activator instead of reduced glutathione. Enzymatic