
δ-Aminolevulinic Acid in Plasma by Free Amino Acid Analysis, Charles J. Hannan, Jr.,1 Thomas Kettler,1 Irwin Dabe,2 and Timothy Clark3 (Depts. of 1 Clin. Investigation (Box 454), 2 Medicine, and 3 Psychiatry, Madigan Army Medical Center, Tacoma, WA 98431-5454)

Toxicity of heavy metals and the genetic porphyrias (most commonly acute intermittent porphyria, AIP) produce increased concentrations of δ-aminolevulinic acid (δ-ALA) or porphobilinogen in plasma and urine. The quantitative test for δ-ALA or porphobilinogen in urine described by Mauzerall and Granick (1) involves column separation and is recommended (2). For monitoring patients more closely, it would be desirable to measure concentrations of δ-ALA or porphobilinogen in blood. The only published method available for this requires synthesis of internal standards, multiple extractions, and gas chromatography with flame ionization (3).

Because δ-ALA is an amino acid, we evaluated its behavior in our system for assaying free amino acids in plasma (Pico-Tag method; Waters Chromatography, Milford, MA). This technique involves alkaline derivatization of ultrafiltered serum with phenylisothiocyanate, gradient separation on a reversed-phase column, and detection at 254 nm. The δ-ALA peak appeared at 6.5 min (with a retention time ratio to alanine of 0.316), which, in our standard mixture, was in a "window" between a-aminoacidic acid (5.5 min) and hydroxyproline (7.1 min). Examination of computer-stored amino acid chromatograms for normal subjects revealed the occasional presence of an unidentified peak at this time, corresponding to an δ-ALA concentration of about 1 μmol/L. [The reported normal value for δ-ALA in plasma is <1 μmol/L (2, 3).]

Our patient with an acute episode of AIP had three blood samples collected during the first day of her admission and before treatment was initiated. Serum δ-ALA was increased in all samples, to 7.6, 9.2, and 9.7 μmol/L at 0800, 1200, and 1700 h, respectively. Treatment with hematin was started; blood collected 1 h later contained a tinge of brown-black pigment, probably from the hematin, which was removed by ultrafiltration. The patient's metabolic response to the treatment was prompt, and the δ-ALA concentration decreased to 1.8 μmol/L (Figure 1). Pain and other symptoms slowly resolved over the next four days.

The only other peak that changed after the treatment with hematin was phosphoethanolamine (PEA). The increase in PEA from undetectable (small shoulder on the hydroxyproline peak) to 23 μmol/L is unexplained but may be of platelet origin (4), induced by the infusion of hematin. The finding of δ-ALA in a free amino acid profile of plasma has not to our knowledge been reported (5, 6). This approach for determining δ-ALA in serum should be considered with other amino acid analysis systems and could be used in management of the porphoric or lead-poisoned patient.

The opinions or assertions contained herein are the private views of the authors and do not necessarily reflect the views of the Department of the Army or the Department of Defense.

References

Ranitidine and High Concentrations of Phenylpropanolamine Cross React in the EMT Monoclonal Amphetamine/Methamphetamine Assay, Gregory F. Grinstead (Marshfield Medical Center Laboratory, 611 St. Joseph Avenue, Marshfield, WI 54449)

A urine specimen submitted to our laboratory tested positive in the EMT (Syva Co., Palo Alto, CA 943-3-0847) monoclonal amphetamine assay, negative in the EMT polyclonal amphetamine assay. We analyzed the specimen by a sympathomimetic amine differentiation procedure (Toxi-Lab, Inc., Irvine, CA 92718) and found no evidence for phenylpropanolamine, ephedrine, pseudoephedrine, phenetermine, amphetamine, or methamphetamine. Gas chromatographic–mass spectrometric analysis (sensitivity 25 μg/L for both amphetamine and methamphetamine) was negative (1). TOXI-LAB A analysis of the specimen revealed a spot with relative migration and color characteristics that suggested the presence of ranitidine. The patient's physician confirmed that the patient was taking ranitidine.