
δ-AMINOLEVULINIC ACID DEHYDRATASE IN BLOOD AS A BIOMARKER FOR LOW-LEVEL LEAD EXPOSURE

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Introduction: Lead (Pb) poisoning at both low and high concentrations adversely affects haematopoietic, vascular, nervous, renal, and reproductive systems. Recent research has indicated that even blood Pb concentrations below 10 µg/dl (0.48 µmol/l) may be associated with negative health outcomes especially in children. Determination of lead in blood, serum/plasma, urine, hair, bone, teeth, nail, milk etc., is used in epidemiological studies. However, not all mentioned indicators equally reflect exposure/dose and internal dose/effects relationship.

Objective: The aim of our research was to review recent literature related with studies of δ-aminolevulinic acid dehydratase, and to evaluate whether it could be used as a biomarker of low-level lead exposure.

Materials and methods: We searched PubMed/MEDLINE and Google Scholar for relevant publications using the headings “aminolevulinic acid dehydratase”, “ALAD AND lead”. The headings matched 5330 hits for “ALAD”, and 2270 hits “ALAD AND lead”, dated from the year 1986. We selected 70 articles based on the selection criteria and keywords presented below.

Results and discussion: One of the primary detectable parameters of lead exposure is inhibition of haeme synthesis and the decrease of the δ-aminolevulinic acid dehydratase (ALAD) activity in erythrocytes. Lead inhibits three enzymes in the haeme biosynthesis pathway – ALAD, coproporphyrinogen oxidase, and ferrochelatase – but its effects on ALAD are most profound. At the molecular level, lead displaces a zinc ion at the metal binding site, producing inhibition through a change in the enzyme’s quaternary structure. The ALAD inhibition results at blood lead levels less than 10 µg/dl while there are indications that ALAD activity is not proper measure of lead exposure at high (>50 µg/dl) blood lead levels. The differences in susceptibility to lead toxicity could be explained by ALAD G177C polymorphism, which yields two co-dominant alleles, ALAD-1 and ALAD-2. The rarer ALAD-2 allele, predominant among Caucasians, has been associated with high blood lead levels and has been thought to increase the risk of lead toxicity by generating a protein that binds lead more tightly than the ALAD-1 protein. Studies also imply that carriers of the ALAD-2 allele who are exposed to lead might then retain it in their blood and tissues longer, increasing the chance of an adverse effect due to inhibition of ALAD and consequent build-up of δ-aminolevulinic acid (ALA) or perhaps due to lead itself.

Conclusions: It is suggested that the critical dose of blood lead, causing the increased levels of ALA in plasma and urine is below 10 µg/dl. The degree of erythrocyte ALAD inhibition has been used clinically to gauge the degree of lead poisoning. Thus, the ALAD activity may be used as one of the earliest and sensitive diagnostic biomarkers of low-level lead exposure. Moreover, it is essential to take into account an ALAD genotype when studying lead kinetics and adverse health effects.