Lysossomal acid lipase activity in dried blood spots - preliminar results

Paulo Gaspar1, Sandra Alves2, Laura Vilarinho1

1 – Unidade de Rastreio Neonatal, Metabolismo e Genética, Departamento de Genética Humana, Instituto Nacional de Saúde Dr. Ricardo Jorge (INSA), Porto, Portugal; 2 – Departamento de Investigação e Desenvolvimento, Departamento de Genética Humana, Instituto Nacional de Saúde Dr. Ricardo Jorge (INSA), Porto, Portugal

Lysosomal storage diseases (LSDs) are a group of heterogeneous and multisystemic disorders caused by defects in enzymes responsible for the intralysosomal degradation of particular compounds. One of them is Lysosomal Acid Lipase Deficiency (LALD) that is caused by the deficiency of the enzyme Lysosomal Acid Lipase (LAL), which is responsible for the hydrolysis of cholesterol esters and triglycerides in the lysosome. Historically, LALD has been reported as one of two major clinical presentations: Wolman disease (WD), the early onset form characterized by hepatosplenomegaly, adrenal calcification and cytopenia, in which death occurs within the first 6 months of age; and Cholesterol Ester Storage Disease (CESD), the late onset form characterized by an heterogeneous phenotype and unpredictable progression with hepatomegaly as the most common manifestation. With the development of enzyme replacement therapy for LALD, the early diagnosis of LALD patients became imperative, in order to start the treatment before the appearance and/or progression of the most deleterious symptoms. The major aim of this work was to establish an accurate and feasible method to measure LAL activity in dried blood spots (DBS). This assay will be used for the early diagnosis of LALD patients, allowing a quick intervention, and preventing the progression of the disease, especially in the case of WD, where the progression is very rapid. The measurement of LAL activity was done in DBS samples obtained from healthy controls with different ages, LALD patients and patients with other lysosomal disorders. A specific substrate marked with the fluorescent 4-methylumbelliferyl (4-MU), together with 3,4-disubstituted thiadiazole carbamate, as a selective inhibithor of Lysosomal Acid Lipase were used to determine the enzymatic activity of LAL through a modified version of the method originally described by Hamilton et al (1). The results obtained proved that this assay is suitable for the biochemical diagnosis of LALD even in very young patients. Once DBS samples are easy to collect and to ship, the implementation of this methodology will also contribute to the better knowledge of the LALD prevalence in Portugal. Finally, the early diagnosis of LALD is fundamental for directing the patients to a more efficient treatment as well as for the prevention of the disease.

1 - Clin Chim Acta. 2012 Aug 16;413(15-16):1207-10