P-145 - INVESTIGATION OF THE ROLE OF C26: 0-LYSOPHOSPHATIDYLCHOLINE IN THE OXIDATIVE STRESS INDUCTION IN X-LINKED ADRENOLEUKODYSTROPHY

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INTRODUCTION: X-linked adrenoleukodystrophy (X-ALD) is caused by mutations in ABCD1 gene and is characterized by very long-chain fatty acids (VLCFA) accumulation. It is clinically heterogeneous, however male patients are at high-risk to develop adrenal insufficiency and/or cerebral demyelination. Since untreated adrenal insufficiency can be life-threatening and considering the possibility of cure when hematopoietic stem cell transplantation is performed in an early stage of the disease, prompt diagnosis is crucial for a good prognosis. Thus, an increasing interest has arisen in the neonatal screening of X-ALD, which is possible through the analysis of C26: 0-lysophosphatidylcholine (C26: 0-LPC). Although a considerable number of studies has demonstrated the importance of this new biomarker for the diagnosis of X-ALD, its role in the pathophysiology of this disease has not been investigated.

OBJECTIVES: Considering that oxidative stress is a well described mechanism of damage in X-ALD, our objective was to investigate if this mechanism could be related with C26: 0-LPC accumulation in X-ALD patients.

MATERIALS AND METHODS: We measured blood C26: 0-LPC concentrations in five patients with X-ALD (2 children, one with CCER and the other with AMN; and 3 adult heterozygous women) by liquid chromatography tandem mass spectrometry. Oxidative stress was investigated in these patients through the measurement of the reactive species formation by the 2',7'-dichlorofluorescin oxidation assay (DCF) in plasma and by determination of plasma sulphydryl groups, whose reduction reflects protein oxidation.

RESULTS: Our results showed a significant increase of C26: 0-LPC in blood of X-ALD patients when compared with healthy controls of similar ages, being higher in the male X-ALD patients in relation to the X-ALD female carriers. We also verified a strong inverse correlation between plasma sulphhydryl groups and C26: 0-LPC (r=-0,817, p=0,091) and a positive correlation between C26: 0-LPC and DCF (r=0,611, p=0,274).

CONCLUSIONS: The correlations verified in this study between oxidative stress parameters and C26: 0-LPC probably could be significant whether the number of analyzed patients was higher, which would make it possible to separate the patients according their phenotypes. Even so, preliminary data from this study suggest that C26: 0-LPC may be involved in the induction of oxidative imbalance in X-ALD, deserving further investigation.