Alteration in Lipid Metabolism of Children with Medium-Chain Acyl-CoA Dehydrogenase Deficiency: Evidences from Plasma Lipidomics Analysis

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Medium-chain acyl-CoA dehydrogenase deficiency (MCADD) is the most prevalent mitochondrial fatty acid β-oxidation disorder characterized by the accumulation of medium-chain acylcarnitines (CAR) and fatty acids (FA). The therapeutic approach for MCADD involves avoiding prolonged fasting and maintaining a lifelong low-fat, high-carbohydrate diet. Despite dietary restrictions, specific changes in the profiles of CAR, FA, and the presence of oxidized phosphatidylcholine (PC), and isoprostanes have been reported in the plasma of MCADD patients. However, the molecular-level understanding of the modulation of circulating lipids in MCADD remains unclear. In this study, we aimed to assess the variability of the lipid profile in children with MCADD compared to control subjects. We used gas chromatography-mass spectrometry to analyse esterified fatty acids and high-resolution C18-liquid chromatography-mass spectrometry to analyse lipid species in blood plasma samples. Through this approach, we identified 251 lipid species belonging to 15 different lipid classes. Principal component analysis revealed a separation between the MCADD and control groups. Univariate analysis identified 126 lipid species that exhibited significant differences between the two groups. The lipid species showing the most significant variation included triacylglycerols (TG) and phosphatidylcholine (PC) containing saturated and monounsaturated fatty acids, specifically 14:0, 16:0 and 16:1, which were found to be more abundant in MCADD. This observation may be related to the accumulation of these fatty acids in individuals with MCADD. It is noteworthy that higher levels of TG and PC containing saturated and monounsaturated fatty acids, such as 14:0, 16:0, and 16:1, have previously been associated with an increased risk of cardiovascular diseases. This study highlights for the first time that the plasma lipidome of children with MCADD is changed compared to controls. Further investigations with larger cohorts are necessary to determine whether these alterations are exclusive to MCADD individuals and whether they are associated with the development of potential clinical outcomes.

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