Bile Acids Influence on Gut Microbiota and Metabolism Regulation in Patients with Glycogen Storage Disease: A Metabolomic Approach

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Glycogen storage disease (GSD) is an inborn error of metabolism, a rare hereditary disorder in which a deficiency of an enzyme affects the processing of glycogen synthesis or its breakdown into glucose in the muscles and liver, resulting in glycogen accumulation and a lack of energy for the body. This can lead to severe hypoglycemia, potentially causing seizures, coma, and death. Therefore, patients must adhere to a strict dietary regimen. Additionally, to maintain blood glucose levels, they require the constant use of raw cornstarch solution, day and night, varying according to each person\'s metabolic needs. The dysbiosis of the gut microbiota is affected by this genetic metabolic disorder, directly impacting the balance of bile acid production by the liver and the synthesis of secondary bile acids by the gut microbiota. In this project, we use fecal metabolomics as a strategy to investigate a genetic metabolic disorder, glycogen storage disease, through non-targeted and targeted analyses by LC-MS, quantifying bile acids and searching for a potential biomarker that signals this pathology. To establish the analytical method, urine and fecal samples were subjected to extraction procedures such as sonication, agitation, centrifugation, and concentration. Twenty-five bile acids were quantified, including primary bile acids, conjugated primary bile acids, and secondary bile acids. Then, the untargeted strategy by liquid chromatography coupled to high-resolution mass spectrometry was applied and the respective data was processed by the MSDial and MetaboAnalyst platforms . The influence of glycogen storage disease patients and control health group on bile acid expression was observed. In the qualitative non-targeted analysis a strong trend of separation between the studied groups was observed using supervised and unsupervised analysis methods, such as PCA and PLS-DA. The chemical annotation of metabolites is making it possible to identify factors that are being affected in the disease and their correlation with the gut microbiota.

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