Streszczenie w języku angielskim

In recent years, there has been a steady increase in the incidence of gallstones in children. Known causes of cholesterol stone formation include genetic factors, female gender, older age or obesity. Despite the known risk factors for cholesterol stones, the pathomechanism of the disease is complex and has still not been thoroughly elucidated, especially in the pediatric population.

It is now believed that adipose tissue is not only a source of spare substances, but is also an endocrine organ that produces numerous protein substances, such as: adipokines. The liver also influences lipid and carbohydrate metabolism by releasing hepatokines into the circulation. Changes in their concentration have been described in obesity, non-alcoholic fatty liver disease, atherosclerosis or type 2 diabetes. To date, the concentrations of adipokines and hepatokines have not been analyzed in children with gallstones. Lipidomics is a branch of science that deals with the study of lipids in various biological materials. To date, there are no data on the profile of sphingolipids in patients with gallstones.

The aims of the studies included measuring the concentrations of: chemerin, vaspin, progranulin, fine retinol-4 (RBP-4), fibroblast growth factor 21 (FGF21) and selected sphingolipids (C16:0-Lactosylceramide (C16:0-LacCer), C18:0-lactosylceramide (C18:0-LacCer), C18:1-lactosylceramide (C18:1-LacCer), C24:0-lactosylceramide (C24:0-LacCer), C24:1-lactosylceramide (C24:1-LacCer) , C14:0-Ceramide (C14:0-Cer), C16:0-Ceramide (C16:0-Cer), C18:0-Ceramide (C18:0-Cer), C18:1-Ceramide (C18:1-Cer), C20:0-Ceramide (C20:0-Cer), C22:0-Ceramide (C22:0-Cer), C24:0-Ceramide (C24:0-Cer), C24:1-Ceramide (C24: 1 -Cer), sphingosine (Sph) and sphinganine (SPA)) in the serum of children with cholelithiasis compared to a control group without gallstones, then evaluating the correlation of the markers with anthropometric parameters and laboratory results. A generalized multivariable linear model was created to determine the association between sphingolipid levels and the presence of cholelithiasis.

The study included children who were admitted to Department of Paediatrics, Gastroenterology, Hepatology, Nutrition, Allergology and Pulmonology of the University Children's Clinical Hospital in Bialystok. The control group included children without any somatic organ. The protocol was approved by the Bioethics Committee of the Medical University of Bialystok prior to patient recruitment. All patients had body mass index (BMI) calculated based on the World Health Organization (WHO). The measurements of chemerin, vaspin, progranulin, RBP-4 and FGF-21 were determined using enzyme-linked immunosorbent assay systems. The content of sphingolipids was measured using ultra-high performance liquid chromatography–tandem mass spectrometry.

The first publication showed significantly higher concentrations of chemerin, FGF21 and RBP-4 in patients with gallstones compared to the control group. Then, the study group was divided according to BMI into group I with normal BMI and group II with overweight and obesity. Significantly higher values of triglycerides (TG), insulin resistance index (HOMA-IR) and RBP-4 were observed in group II compared to group I, however, the concentration of chemerin was comparable in both groups. On the other hand, significantly higher concentrations of chemerin were recorded among patients in group I with respect to the control group, indicating higher levels of chemerin in children with cholelithiasis regardless of body weight. These data may indicate a potential role for this adipokine in the development of cholelithiasis in children

and adolescents. Moreover, in the group with gallstones, positive correlations were observed between: chemerin and TG, HOMA-IR and FGF21, and vaspin and high-density lipoprotein (HDL).

Another study found significant differences in total cholesterol (TC), SPA, C14:0-Cer, C16:0-Cer, C18:1-Cer, C18:0-Cer, C18:0-Cer, C20:0-Cer, C24:1-Cer, C16:0-LacCer, C18:0-LacCer, C18:1-LacCer, C24:0-LacCer and C24:1-LacCer in children with cholelithiasis compared to controls. The following significant positive correlations were observed in the study group: BMI and C16:0-Cer, TG and C14:0-Cer, TG and C24:1-Cer, TG and C24:0-LacCer, TC and C14:0-Cer, TC and C16:0-Cer, TC and C24:1-LacCer, TC and C24:0-LacCer, and negative correlations: BMI and C20:0-Cer, BMI and C24:1-Cer, TC and C18:1-LacCer. The best diagnostic values in differentiating patients with cholelithiasis from controls were obtained for C16:0-Cer and C14:0-Cer. In a multivariate analysis of the effect of sphingolipid levels after accounting for age, gender, presence of obesity, and levels of triglycerides and total cholesterol on the presence of cholelithiasis in children, the best differential values were recorded for reduced levels of SPA, C14: 0-Cer, C16:0-Cer, C24:1-LacCer, C24:0-LacCer and increased values of C20:0-Cer, C24:1-Cer, C16:0-LacCer, C18:1-LacCer.

The aim of the review is to present the latest research on the etiology of gallstone disease in children.

Based on the conducted research, the following conclusions were drawn:

• The concentrations of selected adipokines, FGF21 and sphingolipids differ in patients with gallstones compared to healthy controls.

• Among the analyzed adipokines, significantly higher chemerin concentrations were found in patients with gallstones, regardless of BMI.

• The best diagnostic values in differentiating patients with gallstones from healthy controls were obtained for C16:0-Cer and C14:0-Cer.