Effects of Butyrate Against Pediatric Obesity: the BAPO randomized-controlled trial

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Objectives and Study: Butyrate, a short chain fatty acid, may have beneficial effects against obesityand related comorbidities. We aimed to test whether oral butyrate could be effective in adjuvating thestandard care for pediatric obesity.

Methods: The Butyrate Against Pediatric Obesity (BAPO) trial (trial identifier: NCT04620057) was a randomized, double-blind, parallel-group, placebo-controlled trial aimed at testing the effect of butyrateon childhood obesity. Children/adolescents aged 7 to 16 years with a Body Mass Index (BMI)>95th percentile for gender and age were enrolled at a tertiary care center. Patients were randomly assigned to standard care plus sodium butyrate (20 mg per os/kg body weight/day) or standard care plus placebo. The primary outcome was the decrease of at least 0.25 SDS in BMI at 6 months, which is considered the minimal clinically important difference. The secondary outcomes werethe changes in waist circumference, glucose, insulin, HOMA-IR, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, serum ghrelin, mi-RNA 221, interleukin-6 (IL-6). Other outcomes were the changes in dietary habits and metagenomics of the gut microbiota (GM).

Results: 27 patients were randomized to butyrate and 27 to placebo. 48 children/adolescents (89%)completed the study. At intention-to-treat analysis, assuming that all patients lost to follow-up had reached the primary outcome, the absolute benefit increase for butyrate vs. placebo arm was 40% (95%CI 21% to 61%, $p<0.001$, $N = 54$), corresponding to a number needed to treat of 2 (95%CI 2 to5). A significant reduction of waist circumference, insulin, HOMA-IR, serum ghrelin, mi-RNA 221 expression and IL-6 was observed in the butyrate arm. The changes in the energy content and composition of the diet were similar across arms. GM signatures at baseline predictable of the metabolic response to the intervention have been identified.

Conclusions: Obese pediatric patients treated with oral butyrate showed beneficial effects on nutritional status, glyco-lipid metabolism, GM composition and inflammation. These beneficial effectsmay be partly mediated by a synergistic modulation of microbiome, epigenetic mechanisms and hormonal regulation of food intake.

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