Gut Inflammation in the Pediatric Patient with Cystic Fibrosis

Patients with cystic fibrosis (CF) have associated gastrointestinal (GI) inflammation, and such inflammation is associated with worsening pulmonary outcomes. The authors of this study evaluated clinical markers of GI inflammation in pediatric patients with CF to see if specific markers were helpful in determining clinical outcomes. Pediatric patients with CF who were between 1 and 21 years of age were recruited from a single, tertiary children's hospital. These patients did not have any alternative cause for intestinal inflammation such as inflammatory bowel disease or celiac disease, did not have a colostomy or ileostomy, and were not on total parenteral nutrition. The pediatric study patients were compared to 20 control patients under 21 years of age who had a prior esophagogastroduodenoscopy demonstrating no GI inflammation.

Study patients with CF had blood and stool samples obtained at study entry and then 2 weeks and 3 months later. Questionnaires about GI symptoms were also obtained at these time points. Body mass index (BMI) and forced expiratory volume in 1 second (FEV1) were obtained in study patients who were 4 years of age or older. It should be noted that 90% of control patients had blood and stool samples available for analysis. Intestinal permeability on all patients was measured by testing serum *E. coli* anti-core lipopolysaccharide (LPS) and lipopolysaccharide-binding protein (LPB). Intestinal inflammation on all patients was measured by stool biomarkers, including fecal calprotectin (FC), fecal lipocalin-2 (FL2), and fecal neopterin (FN).

A total of 26 patients with CF completed the entire study, and these study subjects were compared to the 18 control patients who had existing blood and stool samples available.The control group was noted to be older than the study group with CF. FL2 and FN levels in patients with CF were significantly higher compared to control patients based on age-matched controls. Patients with CF who were on CF transmembrane conductance regulator (CFTR) modulators had less intestinal inflammation compared to patients with CF not on CFTR modulator therapy although the inflammation occurring with those patients on CFTR therapy was still increased compared to control patients. Increased FC and increased FL2 appeared to correlate with decreases in FEV1% predicted. No biomarker correlated with changes in BMI z-scores or weight-for-length z-scores after model adjustments for age and presence of pancreatic insufficiency. FL2 levels had statistically significant correlation with FC and FN levels, and LPS levels had statistically significant correlation with LPB levels. However, no other correlations between biomarkers were present.

This study demonstrates that FL2 may prove eventually to be a reliable marker for GI dysfunction in patients with CF. FL2 levels were increased in patients with CF compared to controls suggesting GI inflammation in the setting of CF, and FL2 levels were inversely correlated to FEV1 function while simultaneously having correlation with other serum and stool biomarkers. Further studies should look for specific microbiome signatures associated with increased FL2 levels in patients with CF while also looking for a correlation of such levels with other aspects of lung disease seen in CF.

Duckworth L, Sutton K, Shaikh N, Wang J, Hall-Moore C, Holtz L, Tarr P, Rubenstein R. Quantification of Enteric Dysfunction in Cystic Fibrosis: Inter- and Intraindividual Variability. J Pediatr 2024; 265: 113800.