Plasma Apolipoprotein-A1 as a Prognostic Indicator for Pediatric Crohn Disease

Katelyn Gordon[1], Yael Haberman[1], Phillip Minar[1], Lee A. Denson[1]

[1]*Gastroenterology, Hepatology, and Nutrition, Department of Pediatrics, Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine*

Introduction: Apolipoprotein-A1 (Apo-A1) regulates both lipid metabolism and immune function, and Apo-A1 mimetics suppress mucosal inflammation in murine colitis. Our prior studies demonstrated that higher ileal levels of Apo-A1 at diagnosis are associated with increased rates of steroid-free remission (SFR) in pediatric CD after accounting for clinical and mucosal severity and infliximab therapy. Whether plasma Apo-A1 levels would also be associated with SFR in pediatric CD was not known.

Hypothesis: Plasma Apo-A1 levels will be associated with ileal Apo-A1 expression and steroid-free remission in newly diagnosed pediatric CD.

Methods: Apo-A1 and soluble CD64 (sCD64) as an inflammatory marker were quantified by ELISA in plasma samples obtained at diagnosis from a sub-group of pediatric CD patients enrolled in the multi-center CCFA sponsored RISK inception cohort study. The association between plasma Apo-A1 concentration and ileal Apo-A1 gene expression was tested using a Spearman correlation, and differences in rates of SFR six months after diagnosis between patients with high versus low plasm Apo-A1 were tested by chi2 test.

Results: Plasma levels of Apo-A1 were found to be significantly inversely associated with mucosal levels of Apo-A1 ($p<0.001$) and sCD64 ($p=0.003$) at diagnosis. A plasma level of Apo-A1 greater than 250 mcg/mL was correlated to reduced ileal Apo-A1 expression. Plasma Apo-A1 levels above this cut-point point were associated with lower rates of 6m SSFR, 18% versus 52%, $p=0.05$. The populations of patients above and below this plasma Apo-A1 level had no significant differences in age, gender, or clinical and mucosal severity at diagnosis, but did differ for subsequent infliximab exposure.

Conclusions: Plasma Apo-A1 was found to be inversely related to intestinal Apo-A1 expression in murine models, supporting our findings. This can be attributed to coordinate liver Apo-A1 expression, which accounts for the majority of plasma Apo-A1. Our findings support the use of plasma Apo-A1 as a prognostic tool to determine the likelihood that a patient will achieve steroid and surgery free remission. While murine models of colitis have shown the benefit of supplementation with Apo-A1 mimetic peptides in reducing disease severity, there is potential therapeutic benefit in patients with CD reduced gut Apo-A1 expression.

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