



➤ Product Review ◀

March 2023 #368

NEW PRODUCT IN DEVELOPMENT

ELEMENTAL SELECT™ – PART III:

THE IMPACT OF ENTERAL

NUTRITION ON GUT

MICROFLORA AND BILE ACIDS

INTRODUCTION

In part I of this series, I briefly introduced research that suggested enteral nutrition, in addition, to leading to clinical improvement with inflammatory bowel disease, can have a positive impact on gut microflora populations. In this installment of this series, I would like to examine this facet of **Elemental Select™**, the upcoming enteral nutrition product from Moss Nutrition, in more detail by reviewing the paper “The impact of exclusive enteral nutrition on the gut microbiome and bile acid metabolism in pediatric Crohn’s disease” by Lv et al (Lv Y et al, *Clin Nutr*, Vol. 42, pp. 116-128, 2023).

THE IMPACT OF ENTERAL

NUTRITION ON GUT

MICROFLORA AND BILE ACIDS – IN DETAIL

The first quote I would like to feature from this paper addresses a point that, surprisingly, is still somewhat controversial among many health care practitioners, particularly those who are more traditional allopathic practitioners. In fact, more and more research supports the hypothesis that disturbances in gut microfloral populations can play a role in creating inflammatory bowel syndrome:

“Mounting evidence supports that intestinal dysbiosis plays an important role in the disease pathogenesis of pediatric Crohn’s disease. The gut microbiome as the largest symbiotic ecosystem with the host are able to regulate intestinal physiology and immune function.”

Of course, as you probably noticed, the Lv et al paper not only considers the gut microbiome but also bile acid metabolism. Why? The authors point out:

“...one of the main modes that the gut microbiota interacts with the host is by means of metabolites, among which bile acids (BAs) are critical signaling metabolites to the gut inflammation and immune functions in Crohn’s disease. BAs are synthesized in the liver and bio-transformed by gut microbiome in the intestine. The size and compositions of the BA pool can be modified by the gut microbiota, in turn, BAs can regulate the microbial community structures.”

Next, the authors discuss the fact that the signaling actions of BAs are regulated by sensor receptors such as farnesoid X receptor (FXR) and Takeda G protein-coupled receptor (TGR5). As you will see in the following quote, BAs promote the action these receptors:

“Two primary BAs chenodeoxycholic acid (CDCA) and cholic acid (CA) are the most potent FXR agonists, and the secondary BAs lithocholic acid (LCA) and deoxycholic acid (DCA) are the main TGR5 agonists.”

In turn, as you will see, FXR regulation pathways are inhibited in Crohn’s disease:

“It had been confirmed that FXR regulation pathways were impaired in Crohn’s disease, and the FXR played an important role in the preservation of the intestinal barrier and

inhibition of inflammatory immune responses of Crohn's disease."

With this relationship in mind, understanding how gut microflora and BAs interact can help us better understand how enteral nutrition therapy may be beneficial:

"...exploring the mechanistic cross-talk between gut microbiome and BAs will help us to better understand the mechanism of enteral nutrition therapy."

Study construction

To ascertain the relationship between enteral nutrition, gut microflora, and bile acids Lv et al conducted the following study:

"This was a prospective single-center cohort study in the Children's Hospital, Zhejiang University School of Medicine which is one of the major referral centers for children with inflammatory bowel disease (IBD) in China. We enrolled aged from 6 years to 18 years, newly diagnosed, therapy naïve pediatric patients with Crohn's disease from September 2019 to January 2021...based on endoscopic, biopsies, clinical manifestations, and/or radiological findings. Patients received enteral nutrition treatment as initial therapy for 2 months..."

Study results

As you will see, the results of the study were quite impressive:

"After 2-months of enteral nutrition treatment, 12 out of 13 patients reached clinical remission as indicated by The Pediatric Crohn's Disease Activity Index (PCDAI) ≤ 10 . Their calprotectin levels were reduced significantly in stools after enteral nutrition treatment."

There were also improvements with several blood chemistry analytes:

"...RBC, hemoglobin, ALT, AST and creatinine were significantly reduced with platelets and total bile acids increased in the patients with Crohn's disease."

What about gut microflora and bile acids, the primary subjects of investigation in the study?

First, Lv et al state the following about gut microflora:

"Firstly, the microbial community structures were significantly different between patients and the healthy controls at the phylum level. *Firmicutes* and *Bacteroidetes*, were two dominant phyla in the healthy control group, in comparison, *Proteobacteria* was the most dominant one in the patients with Crohn's disease upon diagnosis. After enteral nutrition treatment, *Firmicutes* increased significantly in the patients. At the genus level, we observed that the *Escherichia* and the *Klebsiella* were increased in patients. The disrupted balance of gut microbial community was recovered after enteral nutrition therapy."

The authors also found that gut microflora diversity was initially low in Crohn's disease patients but recovered towards normal in Crohn's disease patients who used the enteral nutrition therapy and went into clinical remission.

What about bile acids? The authors state:

"The secondary unconjugated bile acids were dominant in the healthy control group. However, the bile acid compositions were significantly changed in the patients with Crohn's disease, which mainly consisted of primary and secondary unconjugated bile acids. After enteral nutrition therapy, the secondary unconjugated bile acids were increased towards the levels of healthy controls."

Finally, it should be noted that calprotectin levels, an inflammatory indicator, were reduced in Crohn's disease patients after enteral nutrition therapy:

"Most patients with Crohn's disease had reduced calprotectin levels after enteral nutrition therapy."

In the discussion section of their paper, Lv et al provide more detail on the relationship between gut microflora and bile acids as it relates to Crohn's disease and the impact of enteral nutrition on this relationship:

“The gut microbiota can deconjugate and convert primary bile acids into secondary bile acids in the gut. The altered bile acid transformation was associated with disease pathogenesis of Crohn’s disease. In this study, the primary bile acid concentrations were significantly higher in patients with active Crohn’s disease upon diagnosis, which was similar to previous work. Their bile acid profiles were improved after 2-months of enteral nutrition therapy, which were close to that of the healthy controls. There were 13 bile acids increased in the remission group, which were also associated with the alteration of fecal microbiota compositions.”

In the next quote the authors point out that levels of the phylum *Firmicutes*, which can be found on most modern, cutting-edge, DNA-based stool analyses available to clinicians today, are most closely correlated to both clinical improvement and levels of the inflammatory marker calprotectin:

“This study indicated that the phylum *Firmicutes* had the strongest correlation with both the PCDAI score and calprotectin, which may be used as potential biomarkers to predict the effects of enteral nutrition therapy for Crohn’s disease. *Firmicutes*, the most abundant human gut microbiota, play a key role in host nutrient metabolism, maintenance of integrity of the intestinal epithelial barrier, and immune defenses against pathogenic microorganisms.”

With all the above in mind, Lv et al conclude:

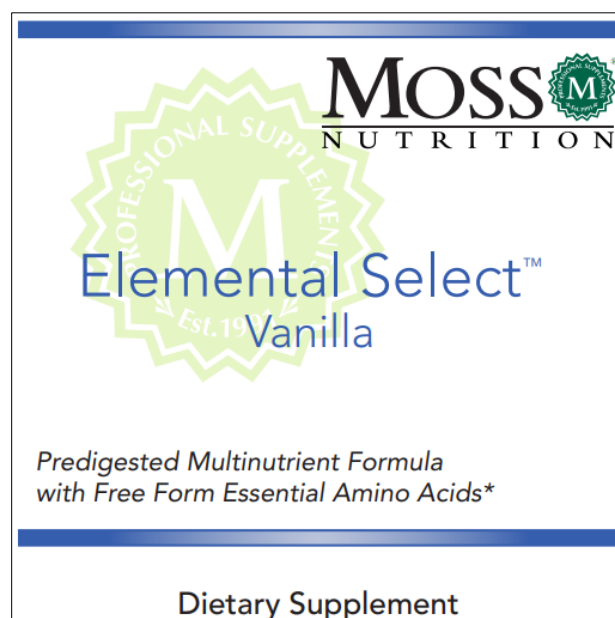
“The gut microbial community and bile acid compositions were associated with PCDAI score and calprotectin. The proportions of *Firmicutes*, and the balance of primary and secondary bile acid compositions in the gut may play an important role in the process of enteral nutrition treatment, serving as potential markers for clinical diagnosis and prognosis of Crohn’s disease.”

SOME FINAL THOUGHTS

In the first two installments of this series, it was my goal to establish a firm research basis for the efficacy of **Elemental Select™** with patients with ailments such as inflammatory bowel

disease. In this installment, though, I had two allied but distinctly different goals in mind. First, I wanted to provide a specific explanation as to why a product like **Elemental Select™** might benefit your patients with inflammatory bowel disease beyond the impact of its constituents. I feel that the Lv et al paper serves this need well by pointing out how enteral nutrition impacts both gut microflora and bile acids. Second, I wanted to provide an easy, fairly practical way that we can determine clinical success of **Elemental Select™** beyond symptomatic improvement. Since *Firmicutes* and calprotectin levels can easily be determined using stool analyses such as the GI-MAP from Diagnostic Solutions, follow-up stool analysis can be an excellent tool for providing clinical data to demonstrate that symptomatic improvements that might be gained from the use of **Elemental Select™** were more than just “placebo.”

In part IV of this series, I will review still another published paper that demonstrates why **Elemental Select™** can be a vital part of your supplemental repertoire when addressing the needs of patients with inflammatory bowel disease and related ailments such as irritable bowel syndrome.



A portion of the Elemental Select™ label.