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2832646 - Whole-Food Enteral Nutrition but Not Standard Chemically-Defined Formulas Improves Outcomes and Prevents Gut Dysbiosis in a Murine DSS-Colitis Model.

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Purpose: Critically ill patients that cannot eat are almost universally fed with chemically-defined enteral formulas containing added sugar, additives such as emulsifiers, and a low fiber content. Such diets have been shown to promote gut dysbiosis that may worsen gut and systemic inflammation. Whole-food enteral formulas that are composed of natural ingredients may mitigate these effects and contribute to improved clinical outcomes. We hypothesize that whole-food enteral formulas will restore a healthy gut microbiota and reduce inflammation in critically ill patients. To test this hypothesis, we used a murine model of chemically-induced colitis as a surrogate for the gut inflammation seen commonly during critical illness.

Methods: C57BL/6 mice (3 randomized groups of 16 mice) received either chemically-defined formulas Vital (V) or Pediasure (P; Abbott Nutrition), or plant-based whole-food formula Liquid Hope (LH; Functional Formularies) for 7 days. Diets were isocaloric and available ad libitum. All mice were then given 4% dextran sodium sulfate (DSS) water or control water for 4 days, during which time they continued their experimental diets. Weights and disease activity indices (DAI) were measured daily. Upon sacrifice, plasma IL-6, fecal lipocalin-2, and colon length were measured. Fecal samples were collected from each group at three defined time points. Bacterial 16S rRNA gene sequences in each sample were amplified, sequenced on the Illumina MiSeq, and analyzed with QIIME. Cecal contents were analyzed for metabolites using ultra-performance liquid chromatography coupled with tandem mass spectrometry.

Results: The volume of consumed formula was not different across groups. After DSS exposure, weight loss was more severe ($p<0.01$) and DAIs were higher ($p<0.01$) in mice fed V or P compared to LH (Figure). Increased IL-6 plasma levels ($p<0.01$), decreased colon length ($p<0.01$), and a trend towards elevated fecal lipocalin-2 were observed in mice fed V and P compared to LH indicating more severe inflammation. The gut microbiome of mice fed V and P demonstrated reduced species diversity and altered species composition compared to LH ($p<0.05$). Specifically, LH mice compared to V and P contained a lesser abundance of *Enterobacteriaceae* ($p<0.05$), a family containing many Gram-negative pathogens and associated with gut inflammation, and higher abundance of Clostridiales ($p<0.05$), an order containing many commensal bacteria associated with immune homeostasis. The cecal contents of mice fed LH compared to V and P contained a significantly higher concentration of several beneficial anti-inflammatory compounds produced or metabolized by the microbiota, including lithocholic acid, a secondary bile acid, and hydroxycinnamic acid, a plant-derived polyphenol ($p<0.05$).

Conclusions: Mice fed LH in this model of gut inflammation had superior outcomes compared to mice fed V and P. LH maintained a healthy gut microbiota and stimulated production of anti-inflammatory metabolites in the gut. Future work will establish which microbiome alterations and metabolites resulting from whole-food nutrition protect against dysregulated inflammation, and whether the use of these diets can improve outcomes in critically ill or chronically ill tube-fed patients.

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