Title

Altering the Gut Microbiome Through Oral Broad-Spectrum Antibiotics Influenced Colon and Liver Long-Chain Menaquinone Levels in Mice

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P27-028-24 Altering the Gut Microbiome Through Oral Broad-Spectrum Antibiotics Influenced Colon and Liver Long-Chain Menaquinone Levels in Mice

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Objectives: Long-chain menaquinones (LCMKs) are vitamin K forms produced by gut bacteria. In young male mice, antibiotic treatment altered LCMK concentrations in cecum and liver. However, the influence of antibiotic treatment on LCMK tissue concentrations in older mice is unknown. We sought to determine the response of tissue LCMK concentrations in older male and female mice to oral antibiotic-induced alterations in the gut microbiome.

Methods: Four-week-old male and female C57BL/6 mice were treated with broad-spectrum antibiotics (ampicillin and neomycin) in drinking water from 4-22 months (ADD), 19-22 months (AND), or no antibiotics (n=15/group, total n=45/sex). LCMKs (for the purpose of this study, MK9-12) were measured in liver, kidney, jejunum, and colon, and quantified by LC-MS and HPLC. LCMK levels were compared by sex and treatment groups by 2-factor ANOVA, followed by Tukey's HSD for multiple comparisons.

Results: Among the tissues analyzed, LCMKs were detected in liver and colon. Male mice treated with antibiotics in both ADD and AND had higher colon MK9-12 concentrations compare to untreated male controls (all P values $\leq$0.01). No sex differences were observed in colon LCMK levels. MK10 was the only LCMK identified in liver, and levels were lower in female mice that received antibiotics in both ADD and AND compared to untreated female controls (P=0.003). There was no effect of antibiotic dosing duration on LCMK concentrations in colon or liver in either male or female mice (all P values $\geq$0.14). Moreover, liver MK10 concentrations were higher in female versus male mice across all treatment groups (P< 0.001).

Conclusions: Manipulation of the intestinal microbiome through oral antibiotic treatment influenced LCMK content in liver and colon regardless of dosing duration. This study expands our understanding of the contribution of bacterially produced LCMKs to regulating tissue vitamin K concentrations. Future studies are needed to determine the mechanisms by which LCMKs are transported from the colon to peripheral tissues.

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P27-029-24 Emu Oil-Modulated Faecal Microbiota Transplantation Improves Disease Indicators in a Mouse Model of Crohn's-Like Colitis

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Objectives: Faecal microbiota transplantation (FMT) studies have revealed variable therapeutic efficacy in Crohn's disease (CD) management. Orally administered Emu Oil (EO) has demonstrated anti-inflammatory and reparative properties in models of intestinal disease. The current study aimed to determine whether EO-modulated FMT could reduce disease severity in a mouse model of trinitrobenzene sulfonic acid (TNBS)-induced Crohn's-like colitis.

Methods: Female ARC(s) mice were assigned to FMT donor (n=5/group) and recipient (n=10/group) groups. *Donor* mice were orally administered either Water (80µl), Olive Oil (OO) or EO (160µl) daily (days -7 to 0); fresh faeces were collected (days -1 to 3) and group pooled. *Recipient* mice intrarectally received TNBS (3mg; day 0) and donor faecal supernatant (120µl; day 3) and killed on day 6. Daily bodyweight (BW) and disease activity index (DAI), colonoscopically-assessed disease severity, organ weights, intestinal permeability (fluorescein isothiocyanate [FITC]-dextran), histologically-assessed colonic damage (disease severity, crypt depth), intestinal barrier function (mucin-secreting cells), acute inflammation (myeloperoxidase [MPO]) and faecal microbiome (16S rRNA amplicon sequencing) were assessed. p< 0.05 was considered significant.

Results: TNBS induced BW loss in all groups, which normalised to day 0 values on the day of kill. Daily DAI remained elevated throughout the trial in all groups; only EO FMT normalised DAI on day 6 compared with day 0 (p< 0.05). TNBS increased colonoscopically-assessed disease severity scores (p< 0.05), with no significant EO nor OO FMT effect. EO FMT resulted in decreased liver weights and greater small intestinal weights relative to BW, reduced histologically-assessed disease severity and increased colonic mucin counts compared with Water and OO FMT (p< 0.05). The most abundant genera across groups were *Muribaculaceae*, *Eisenbergiella* and *Bacteroides*; while alpha and beta diversity, taxonomic profiles, FITC-dextran, crypt depth and MPO activity remained unchanged (p >0.05).

Conclusions: Compared with Water and OO FMT, EO FMT improved clinically- and histologically-assessed indicators of colonic disease and barrier function. EO-modulated FMT may enhance current FMT treatment, improving CD management.

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