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Letter to the Editor

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How to Increase the Butyrate-producing Capacity of the Gut Microbiome: Do IBD Patients Really Need Butyrate Replacement and Butyrogenic Therapy?

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We read with great interest the paper by Laserna-Mendieta *et al*. reporting the reduced butyrate synthesis capacity of the gut microbiome in Crohn's disease [CD] and ulcerative colitis [UC].[1]

Recently, we also performed a pilot comparative study of faecal microbiota among patients with mild-to-moderate active UC [n = 37] and healthy controls [HCs; n = 38], with an emphasis on the genetic capacity of the microbiome to synthesise butyrate, by quantifying butyryl-CoA:acetate CoA-transferase [BCoAT, *but*] gene, using the same primers and technique.[2] BCoAT gene content was significantly lower in the UC group as compared with HCs [p <0.05]. UC patients also had significantly lower *Faecalibacterium prausnitzii* counts than HCs, and *Bacteroides thetaiotaomicron* was detected less frequently in UC patients than in HCs. UC patients also were characterised by a higher *Bacteroides fragilis* group/*F. prausnitzii* ratio compared with HCs. No other taxa were altered between UC patients and HCs.

Later, 40 mild-to-moderate active left-sided UC patients were enrolled in an open study and randomised to receive either oral calcium butyrate plus inulin as a supplement to oral mesalazine [Group 1] or mesalazine alone [Group 2] for 28 days.[3] Oral butyrate plus inulin significantly enhanced the faecal butyrate-producing bacteria [BPB] pool, evaluated as BCoAT gene content [p <0.05], significantly reduced the elevated baseline *B. fragilis* group/*F. prausnitzii* ratio, and lowered serum pro-inflammatory biomarkers in Group 1, while being safe and well tolerated. In Group 1, 85% of UC patients demonstrated significant improvement in both rectal bleeding and stool frequency by Day 14, compared with only 55% in Group 2 [p <0.05].

Our results showed a significant reduction in the genetic capacity for butyrate synthesis by the gut microbiota in active UC patients as compared with controls.[2] The oral butyrate plus inulin as a supplement to standard treatment with mesalazine in active UC not only increased BCoAT gene content in faecal microbiota, but also improved symptoms, which meant that it was clinically relevant.[3] Previously, only one study reported that oral butyrate may improve the efficacy of oral mesalazine in active UC.[4]

Since butyrate is an important energy source for colonic epithelial cells, maintains the integrity of the intestinal barrier, and exerts anti-inflammatory effects,[5] we believe that it is useful both to redress the butyrate deficiency, and to restore the BPB pool, at least in patients with active disease. Dietary fibre also can be effective in inflammatory bowel disease [IBD], but it should most likely be used in an inactive disease because of possible side effects. Larger studies will be required to assess the efficacy of oral butyrate and usefulness of dietary fibre in IBD. The disease activity and BCoAT gene level should be considered.

Finally, the present data support the usefulness of BCoAT gene content determination as a valuable biomarker to assess gut microbiota function in the management of patients with IBD.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Author Contributions

All authors drafted and critically revised the manuscript, and approved the final version.

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