Intestinal dysbiosis occurs in iron deficiency as well as active IBD

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Introduction: We have previously shown that decreases or increases in dietary iron exacerbate murine models of inflammatory bowel disease (IBD). Active IBD is associated with a dysbiosis typified by a reduction in *Bacteroidetes* and an increase in *Firmicutes*. We have investigated the human intestinal microbiome in relation to luminal iron, by studying patients with iron deficiency anaemia (IDA) and inactive/active IBD. We report results of changes at the phylum level.

Methods: Bacterial gDNA was extracted from faeces of patients with IDA (10), Crohn's disease (CD 6 active, 24 inactive), ulcerative colitis (UC 7 active, 13 inactive) and healthy controls (24). Faecal iron and calprotectin were assayed by ELISA. Microbiota composition was determined from the sequence of V4 region of *16S* rDNA on the Illumina MiSeq platform. Statistical inferences were made using Welch's t-test with post-hoc analysis (*Bioinformatics* 2010; 26:715-21). Shannon Diversity Index (SDI) and Principal Component Analysis (PCA) were employed to compare population and phylum-level changes among study groups.

The results: Faecal iron concentrations were least in IDA (ANOVA, $p=0.001$) and significantly lower in IDA than each other group (post hoc $p<0.05$ for all comparisons). Calprotectin concentrations were increased in association with IBD disease activity.
Faecal phyla changes were seen in IDA as well as in IBD: *Proteobacteria* were markedly reduced in IDA (1.4%) compared to active IBD (15.5%); IBD and IDA were associated with increased proportions of *Firmicutes* ($P=0.01$ and $P=0.05$ respectively).

Conclusion: Dysbiosis occurred in IDA as well as in active IBD. *Proteobacteria* are clearly iron-responsive: the increase in luminal iron associated with active IBD appears to promote their growth and might contribute to the excess of this phylum during relapse. The changes in *Bacteroidetes* appear independent of luminal iron, unlike *Firmicutes*. The influence of iron deficiency and supplementation upon the colonic microbiome warrants further investigation.

Keywords: Microbiota, iron, IBD