LETTER

Assessment of faecal microbial transfer in irritable bowel syndrome with severe bloating

We read with interest the work by Halmos *et al*[1] in which they describe the effects of dietary FODMAP (Fermentable Oligo-, Di- and Mono- saccharides And Polyols) restriction in patients with IBS on the intestinal microbiota. They showed that low FODMAP intake was associated with reduced total bacterial and lower relative abundance of butyrate-producing *Clostridium* cluster XIVa, changes that are generally considered unfavourable.[2] Therefore, they discourage long-term dietary FODMAP restriction, a suggestion also supported by the recent work of McIntosh and colleagues who noticed unfavourable changes in both microbiota and metabolome of patients with IBS who were on a low FODMAP diet.[3] Although low FODMAP intake reduces GI symptoms in almost 75% of patients with IBS, the effects of this diet on the intestinal microbiota might be disadvantageous in the long run.

Combining these observations with the important role for the intestinal microbiota in IBS pathogenesis,[4] we report here faecal microbiota transplantation (FMT) as an alternative to FODMAP restriction in patients with IBS. We applied FMT in 12 refractory IBS patients (Rome III

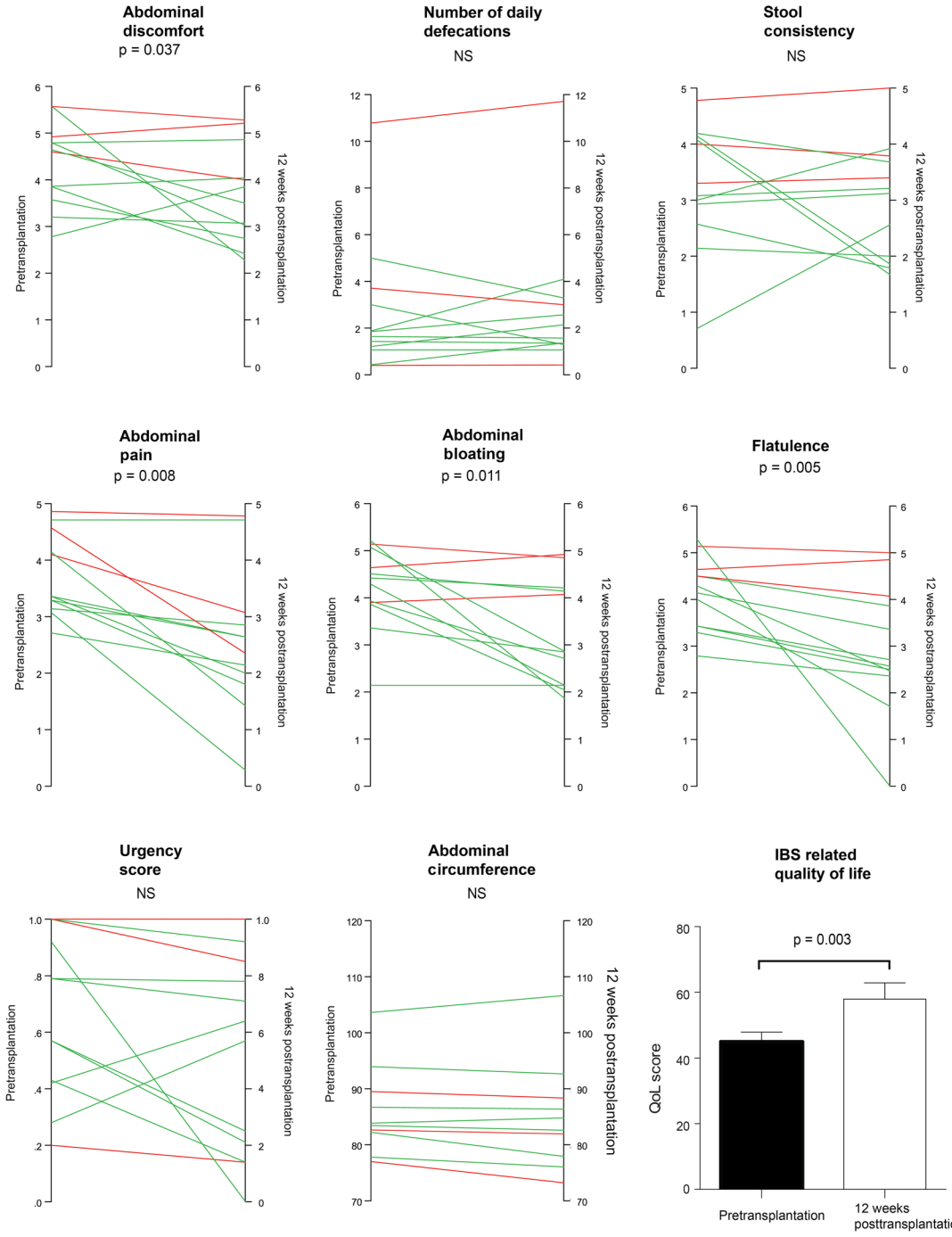

Figure 1 Changes in specific IBS-related symptoms at week 12 post-FMT. Lines in green represent responders to the FMT, lines in red represent non-responders. Wilcoxon's signed ranks test. FMT, faecal microbiota transplantation.

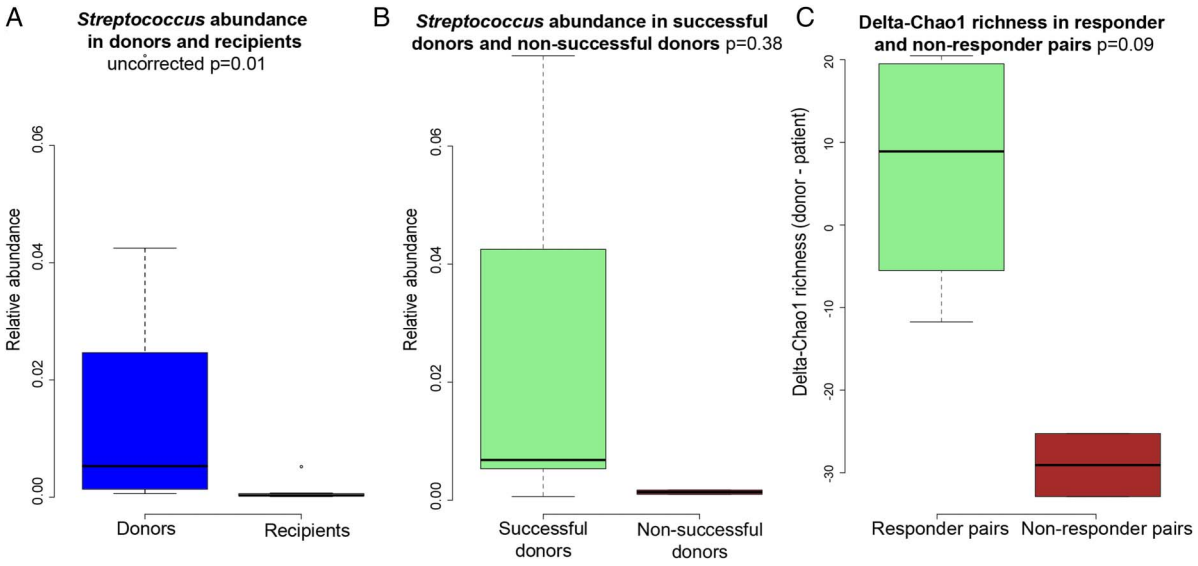

Figure 2 Baseline microbial differences between donors and patients and microbial differences according to the response to treatment. (A) The observed tendency for higher *Streptococcus* counts at baseline in donors compared with patients (uncorrected p=0.011). (B) The trend for higher baseline counts of *Streptococcus* in successful donors compared with non-successful donors. (C) The differences in delta richness (donor minus patient) values between patients with IBS responding to the FMT versus non-responders (Chao1 richness: p=0.095). FMT, faecal microbiota transplantation.

criteria) with intermittent diarrhoea and severe bloating, and mapped the associated microbiota changes after therapy [5 6] (see online supplementary file). In our cohort, the median disease duration was 14.5 years (5–40) and patients (8/12 female) had undergone at least three conventional treatment attempts prior to inclusion (see online supplementary table S1). Consecutive faecal samples were collected from the last seven patients for microbiome analyses.

In this study nine patients (75%) met the primary endpoint being: 'adequate relief of global IBS symptoms and abdominal bloating', 12 weeks after FMT. A significant reduction in general abdominal discomfort (−21%), abdominal pain (−26%), bloating (−35%) and flatulence (−37%) was reported. The overall quality of life also improved significantly (+12.9%) (see online supplementary tables S2 and S3, figure 1). Responders were followed up and 7/9 (78%) still reported significant relief of IBS symptoms after a period of 1 year, suggesting long-lasting effects of FMT.

Microbiota analysis showed no community differences between patients and donors and no difference in microbial dissimilarity between patient–donor responders and non-responder pairs at baseline. However, we observed a trend of higher *Streptococcus* counts in donors compared with patients (uncorrected p=0.011) and successful donors tended to have higher baseline counts of *Streptococcus* compared with non-successful donors (figure 2). Interestingly, we also observed a trend of higher enrichment potential in responders compared with non-responders (figure 2). In line with earlier observations in IBD, the median number of successfully transferred phylotypes was also higher in responders (n=6) versus non-responders (n=2.5) (not significant).[7]

With this open-label FMT study in patients with IBS, we found a similar response rate as for the low-FODMAP diet. Interestingly, positive effects on IBS-related symptoms seem to be linked to changes in the intestinal microbiota due to FMT. This study suggests FMT as a possible treatment option for IBS and supports correlations between abnormalities in the intestinal microbiota and IBS.

The main limitation of our study is its design as an open-label trial. Of note, however, placebo response rates in similar IBS patient cohorts are reported to be approximately 37.5%, which is considerably lower than the response rate of 75% that we report here.[8] Nonetheless, double-blind, placebo-controlled trials, addressing also microbial changes, are necessary to provide clear answers about the applicability of FMT in IBS and are currently on-going both in our centre (NCT02299973) and elsewhere (NCT02092402; NCT02154867).

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