High faecal pH and low total microbial load associate with normalisation of faecal calprotectin in children with Crohn’s disease treated with exclusive enteral nutrition; results from iPENS, a multicentre, prospective study

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BACKGROUND AND AIMS
• Normalisation of faecal calprotectin (FCAL) varies among patients with Crohn’s disease (CD) treated with Exclusive enteral nutrition (EEN).
• To better understand disease characteristics related to EEN efficacy and its mechanism of action, we compared clinical and microbial parameters between patients whose FCAL normalised against those whose did not at EEN completion.

METHODS
84 children and young adults with CD clinically responding to EEN provided a single stool sample

FCAL<250mg/kg
VS.
FCAL≥250mg/kg

Short and branched chain fatty acids
Total microbial load (qPCR)
Sample parameters (pH, Bristol stool score, %H2O)
Weight, height and BMI Z-scores
CRP, ESR, albumin
Use of immunosuppressants
Disease location and duration

Random forest analysis was used to identify best predictors of EEN response among clinical, faecal and anthropometry parameters

RESULTS
FCAL; Median (IQR) FCAL levels at EEN completion: 643 (146, 2033) mg/kg; 42% of patients with FCAL <250mg/kg

In patients with FCAL<250mg/kg at EEN completion
• higher faecal pH (faecal ph; FCAL<250mg/kg; 8.3 (8.1, 8.6) vs FCAL>250mg/kg; 7.95 (7.6, 8.3), p=0.001)
• lower total microbial load (log10 16S rRNA copies/g; FCAL<250mg/kg;10.7 (10.4, 10.9) vs FCAL>250mg/kg; 11.0 (10.5, 11.2), p=0.02)
• non-significantly higher BMI z-scores (FCAL<250mg/kg; 0.02 (-0.24, 0.73) vs FCAL>250mg/kg; -0.21 (-0.87, 0.36), p=0.052

A RF model including all parameters was significantly associated with an accuracy of 71%, a sensitivity of 69% and a specificity of 71% (p<0.001). Faecal pH, BMI z-scores and total microbial load were the most influential parameters (Fig 1A, 1B).

Figure 1A: Random forest (RF) classification between FCAL responders and non-responders using clinical, anthropometry and microbial data. 1B: Area under the curve of the best RF model. 1C: Barplots of categorical variables included in RF model.

AUC = 0.739

Use of immunosuppressants at EEN completion, disease duration and location did not differ according to FCAL grouping (Fig 1C)

CONCLUSION
This study suggests that efficacy of EEN in reducing gut inflammation might be, at least in part, mediated via reducing gut bacterial biomass and modulating luminal pH and the downstream effects this may have on inflammatory members of the microbial community.

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