A PRELIMINARY STUDY OF THE EFFECTS OF OBETICHALIC ACID, A FARNESOID X RECEPTOR AGONIST, IN PATIENTS WITH CHRONIC DIARRHEA SECONDARY TO CROHN’S ILEAL DISEASE

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Introduction Chronic diarrhoea occurs frequently as a result of excess faecal bile acid (BA) loss. Secondary bile acid diarrhoea (SBAD) is common in Crohn’s disease with ileal inflammation and/or resection. The normal ileum produces Fibroblast Growth Factor 19 (FGF19) in response to BA absorption and farnesoid X receptor (FXR) activation. FGF19 acts as a hormonal regulator of hepatic BA synthesis. We showed previously in 10 patients with primary bile acid diarrhoea, diagnosed by 7d SeHCAT retention <100%, that the semi-synthetic BA and potent FXR agonist obeticholic acid (OCA) significantly increased low FGF19 levels producing significant clinical improvement. We aimed to see if these findings could be extended to patients with SBAD due to Crohn’s and in idiopathic diarrhoea controls.

Methods Out of 32 patients recruited to this pilot trial, 8 SBAD patients (6F:2M, median age 45, ileal resection 0–48 cm, median 22.5 cm, and/or SeHCAT <11%), and 7 controls (2F:5M, SeHCAT 16–35%, median 25%) received OCA 25 mg daily for 2w after a 2w run-in period. BA sequestrants were discontinued. Symptoms were recorded and a stool index calculated from frequency, stool form and lopamidol use. On the first and last days of OCA therapy, blood samples were assayed for FGF19, total BA levels and the BA precursor, 7αOH-4-cholest-3-one (C4) in fasting and for 6h after OCA and meals.

Results In the SBAD group, 7 out of 8 patients showed positive but variable changes in stool form and stool index (both p = 0.07, Wilcoxon). Pain frequency (p = 0.05) and severity (p = 0.07) improved. Ileal resection length was related to the change in stool number (r = 0.78, p = 0.01, Spearman), index (r = 0.61, p = 0.05) and urgency (r = 0.63, p = 0.03) so that those with the smallest resections had the greatest improvements. Increases in FGF19 fasting and post-prandial levels were relatively small except in 2 patients, but were associated with improvements in urgency (r = 0.93, p < 0.01). The reductions in post-prandial BA response (p = 0.01), fasting and peak BA values were significantly greater in those with shorter resections. C4 was related inversely to FGF19 and positively to the resection length. By contrast in the diarrhoea controls, there were no significant changes in clinical symptoms or FGF19. However BA responses were lower (p = 0.03) and significant relationships between FGF19 and BA responses were found.

Conclusion This pilot study has shown that OCA produces clinical benefit in many patients with chronic diarrhoea including those with SBAD, particularly with short resections, but not in idiopathic controls. Further trials are warranted.

Disclosure of Interest None Declared.

PTH-108 SEHCAT: NICE OR NOT NICE?

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Introduction Bile acid malabsorption (BAM) is increasingly recognised as the underlying diagnosis in many patients with D-IBS and Crohn’s disease, and SeHCAT testing has greatly increased. The 2012 NICE consultation document 1 acknowledges lack of evidence of cost effectiveness and advocates trial of treatment with bile acid sequestrants (BAS) rather than SeHCAT for Crohn’s patients, but often these are poorly tolerated and the response equivocal. We review our experience of SeHCAT testing and review it with respect to NICE.

Methods Retrospective review of 121 consecutive patients who had SeHCAT performed between April 2009 and December 2012. Patient demographics, associated diseases (Crohn’s disease, right hemicolectomy, radiotherapy, HIV, microscopic colitis, coeliac disease, vagotomy and pyloroplasty, Graves disease, intestinal

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<th>PTH-108 Table 1</th>
<th>Sensitivity</th>
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