

P270 DUODENAL BULB BIOPSIES INCREASE THE DETECTION OF VILLOUS ATROPHY WHEN ASSESSING ADHERENCE IN COELIAC DISEASE

Sarah H Coleman*, Anupam Rej, Elisabeth MR Baggus, Lauren Marks, Michelle Lau, David S Sanders. *Academic Unit of Gastroenterology, Royal Hallamshire Hospital, Sheffield Teaching Hospital NHS Foundation Trust, Sheffield, UK*

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Introduction Duodenal bulb biopsies have been demonstrated to increase the diagnostic rate of newly diagnosed coeliac disease (CD) by 10%. The aim of this study was to assess the utility of duodenal bulb biopsies for the assessment of established CD.

Methods A prospective study of 375 established CD patients (mean age 51.0 years; 69.9% female) who underwent endoscopy for assessment of persisting symptoms or remission at Sheffield Teaching Hospitals was performed, between 2013–2019. Quadratic biopsies were taken from D2 in addition to duodenal bulb biopsies.

Results 63.2% (n=237) of patients had ongoing villous atrophy (VA). Table 1 outlines the histological appearance of D1 and D2 biopsies. Among those with VA (n=237), this was confined to D1 in 10.2% (n=14) and to D2 in 8.0% (n=11). There was no significant difference in number of patients with VA confined to D1 versus D2 (p=0.69). There was no difference in age (p=0.18) or gender (p=0.10) between patients with VA confined to D1 compared to the remaining cohort. As time from diagnosis increased, the proportion of individuals with complete duodenal mucosal healing (defined as Marsh 0 in both D1 and D2 biopsies) also increased. Two years after diagnosis 4.9% (n=11) of patients had complete healing, increasing to 10.7% (n=24) after 4 years, 17.3% (n=39) after 6 years, 20.9% (n=49) after 8 years and 24.0% (n=54) after 10 years. A further 11.1% (n=25) of patients achieved complete healing after more than 10 years since diagnosis.

Abstract P270 Table 1 Histological appearance of D1 and D2 biopsies

		D1 histology		
		Normal (Marsh 0)	Marsh 1/2	Marsh 3a-c
D2 histology	Normal (Marsh 0)	36.8% (n=138)	3.2% (n=12)	0.5% (n=2)
	Marsh 1/2	5.6% (n=21)	17.9% (n=67)	3.2% (n=12)
	Marsh 3a-c	1.3% (n=5)	1.6% (n=6)	29.9% (n=112)

Conclusions Duodenal bulb biopsies increased the detection of VA by 10% in established CD, highlighting the importance of bulbar biopsies in established CD for the first time in the literature. Complete mucosal healing can occur in established CD after a significant delay, suggesting development of immune tolerance in these individuals.

P271 BILE ACID MALABSORPTION DOES NOT CAUSE A LOW FAECAL ELASTASE

Benjamin Shandro*, Joshua Chen, Jennifer Ritehnia, Andrew Poullis. *St George's University Hospitals NHS Foundation Trust, London, UK*

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Introduction The coordination of biliary and pancreatic secretions is vital for normal digestion. However, it is unknown if bile acid malabsorption (BAM) is associated with pancreatic exocrine insufficiency (PEI). Faecal elastase-1 (FE1) is the only widely available test for PEI. Its limitations include a falsely low (positive) result in patients submitting dilute stool samples, as might occur in patients with BAM. We studied the association between BAM and PEI, and the impact of coexisting BAM on the management of patients with low FE1.

Methods We carried out a retrospective study at a London teaching hospital. All outpatients investigated with both FE1 and a SeHCAT scan between 2012 and 2018 were identified. Demographic and clinical information was retrieved from the electronic medical record. PEI was defined as FE1 <200 µg/g, and BAM as 7-day SeHCAT retention ≤15%. Where FE1 had been repeated, any normal result led to classification as not having PEI. Logistic regression was used to explore the dependence of PEI on BAM, and multivariable logistic regression was used to adjust for age, sex and ethnicity. Pearson's Chi² test was used to study the association between BAM and repeating FE1, imaging the pancreas, and the initiation and response to pancreatic enzyme replacement therapy (PERT). Complete case analysis was used where any data were missing.

Results 258 patients were identified; mean age 51 years; 65.5% female; 61.6% white ethnicity. BAM was diagnosed in 111 patients (43%). PEI was diagnosed in 39 patients (15.1%), with no subjective difference between those with and without BAM (15.3 v. 15.0%). On univariable analysis, BAM was not associated with PEI (OR 1.03; 95% CI 0.52 to 2.04; p=0.94). After adjusting for age, sex and ethnicity, this lack of association held (OR 0.78; 95% CI 0.37 to 1.64; p=0.52).

43 patients (16.7%) had FE1 repeated, with 9 patients (20.9%) reclassified from PEI to normal as a result. There was no difference between patients with and without BAM in FE1 being repeated (15.3% v. 17.7%; p=0.61) or the repeat FE1 leading to reclassification of PEI status (23.5% v. 19.2%; p=0.74). In patients with PEI, there was no difference in the rate of pancreatic imaging between those with and without BAM (64.7% v. 63.6%; p=0.61), but pancreatic abnormalities were detected more frequently in patients with coexisting BAM (58.3% v. 20.0%; p=0.04). Findings included atrophic or fatty pancreas, and one pancreatic cancer. There was a non-significant trend towards fewer patients with PEI and BAM receiving PERT (58.8% v. 72.7%; p=0.36), but no difference in clinical response when treated (77.8% v. 76.9%; p=0.96).

Conclusions BAM is not associated with PEI. However, when a patient with BAM does have a low FE1, our findings suggest most are representative of PEI, rather than false positives.

P272 CHOOSING WISELY: DUODENAL BIOPSIES WITHOUT SEROLOGICAL EVIDENCE OF COELIAC DISEASE, WHY CAN'T WE DO BETTER?

Byron Theron, Deepanjali Banerjee, Iain Bain*. *Northern Devon District Hospital, Barnstaple, UK*

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Introduction The BSG guidelines recommend anti tissue transglutaminase antibody (tTG) testing as a first line test for

coeliac disease.¹ Duodenal biopsies (D2) should be performed only after a positive serological test or a negative test with a high clinical suspicion by gastroenterologist. Previous studies have demonstrated that random D2 biopsies are not cost effective.² We aimed to analyse whether current practice is now in keeping with guidelines.

Methods This was a retrospective review of the electronic records of 422 patients who had had duodenal (D2) biopsies in 1 year. Furthermore, we collated the annual number of duodenal biopsies from 2009 to 2018 to determine if the new guidelines had made an impact.

Results The indications for endoscopy were iron deficiency anaemia (IDA) (68%), low ferritin (3%), weight loss, loose stool and non-specific gastrointestinal symptoms (29%). Only 1 patient with a negative tTG had a positive biopsy.

Prior to D2 biopsy, 192(45%) patients had no previous TTG or D2 biopsy. Of these, 9 had a positive biopsy and were subsequently found to be tTG positive. 203 (48%) patients had biopsies despite a negative tTG. 31 (7%) had previous normal D2 biopsies (12 also negative TTG).

The excess cost incurred for processing biopsies after a negative TTG was £12,180. £9882 would have been saved by carrying a TTG test in subjects having a negative biopsy.

The number of biopsies over 10 years remained largely unchanged with a low of 412 in 2012 and a high of 522 in 2018 with a median of 437 biopsies per year.

Conclusion A significant proportion of duodenal biopsies are still done in patients with a negative TTG and/or previous normal D2 biopsy. Following BSG guidelines, would have saved over £20,000 in 1 year. We suggest an IT based solution where an alert is triggered to check tTG at the same time as a referral is made for endoscopy. Furthermore, D2 biopsy samples can be delayed until a tTG is checked if not done prior to endoscopy. Finally, a point of care tTG could be utilised in GP surgeries or endoscopy units to minimise any delay. These measures will be put forward to the CCG.

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Nutrition

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CHEMOGENETIC ANALYSIS OF HOW RECEPTORS FOR SHORT CHAIN FATTY ACIDS REGULATE THE GUT-BRAIN AXIS

Natasja Barki*, Daniele Bolognini, Laura Jenkins, Brian Hudson, Andrew Tobin, Graeme Milligan. *University of Glasgow, Glasgow, UK*

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Introduction Short chain fatty acids are produced mainly by the gut microbiota. They mediate a variety of biological effects by acting on a two of G protein-coupled receptors. These receptors are expressed by various cell types,

including in the gut. The exact contribution of free fatty acid 2 receptor (FFA2) in regulating gut physiology is unclear. Bolognini *et al*¹, recently employed a novel FFA2-Designer Receptor Exclusively Activated by Designer Drugs (DREADD) to study the physiological role of FFA2. Now we describe and further explore the physiological roles of FFA2 with a novel agonist, 4-methoxy-3-methyl-benzoic acid (MOMBA) for the FFA2-DREADD variant following transgenic expression in mice.

Methods Following an extensive screening of more than 1200 small molecules, MOMBA was identified as a potential agonist for the hFFAR2-DREADD receptor. (1) The selectivity of MOMBA was assessed with β -arrestin-2 recruitment assay in HEK293 cells expressing hFFA2-DREADD and hFFA2-eYFP. The effect of FFA2 activation on the release of enteroendocrine hormones (GLP-1 and PYY) was assessed on (2) isolated crypts and (3) intact colonic segments. Isolated crypts and intact colon segments were challenged with different test compound. Supernatants were subsequently collected and GLP-1 and PYY concentration was measured by ELISA. (4) Furthermore, role of FFA2 in sensory signalling was investigated by measuring intracellular calcium $[Ca^{2+}]_i$ in isolated nodose ganglion (NG) and dorsal root ganglion (DRG).

Results (1) MOMBA is selective for hFFA2-DREADD (2) MOMBA (1mM-0.001mM) induces a FFA2 specific concentration dependent increase in GLP-1 secretion in colonic crypts. (3) Intraluminal infusion of MOMBA also resulted in a FFA2 mediated increase in GLP-1 and PYY secretion from intact colon. Furthermore, (4) MOMBA induced a G_q mediated increase in $[Ca^{2+}]_i$ in cells isolated from DREADD mice. Conversely, C3 induced a G_i mediated increase in these cells.

Conclusion MOMBA specifically activates hFFA2-DREADD, hence providing a novel tool ligand to further study the physiological and pathophysiological roles of FFA2 within the gut, as well as other cell types that express this receptor.

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EFFECTS OF A BOWEL PREPARATION DIET ON THE GUT MICROBIOME

Gerum Gashaw Gebeyehu*, Alessandra Frau, Rachael Slater, Luke Flain, Chris Probert. *University of Liverpool, Liverpool, UK*

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Introduction Prior to colonoscopy, patients undergo a bowel preparation regimen to clear bowel contents and optimize view of the bowel wall. In the UK, the bowel preparation regimen may involve patients undertaking either a 3-day low-fibre/low-residue diet (LRD) or a 1 day clear liquid diet (CLD) before their procedure. The day before their procedure, all patients are required to take a laxative. A low-fibre diet has been associated with reduced gut microbiome richness and diversity. A low-fibre diet has also been associated with a *Bacteroides* enterotype and an enrichment of *Alistipes* and *Parabacteroides* genera. A transition from a high-fibre to a low-fibre diet has been shown to result in changes in the gut microbiome within 24 hours. We present the results of an