PWE-076 ABSENCE OF GUT MICROBIOTA REDUCES LIPOPOLYSACCHARIDE-INDUCED EPITHELIAL CELL SHEDDING IN THE SMALL INTESTINE

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Introduction Cell shedding, the process by which intestinal epithelial cells (IECs) are extruded from the small intestinal (SI) villus, is known to be elevated in patients with inflammatory bowel disease (IBD) and is correlated with disease relapse. Importantly, the epithelial barrier is in contact with intestinal bacterial communities (i.e. the microbiota) and studies have correlated disturbances in the microbiota with IBD. Thus, we hypothesised that cell shedding may be modulated by the microbiota.
Methods Specific pathogen free (SPF) and germ-free (GF) C57BL/6 mice, including GF mice reconstituted for 4 weeks with altered Schaedler flora (ASF), stable Defined Moderately Diverse Microbiota (sDMDMm2), or SPF faeces, were given 10mg/kg Lipopolysaccharide (LPS) intraperitioneally to induce SI cell shedding. Animals were euthanized 1.5 h post-LPS. Tumour Necrosis Factor-α (TNF-α) and cleaved caspase 3 (CC3) ELISA were performed on whole SI homogenates. Immunohistochemistry (IHC) for CC3 was performed on formalin fixed paraffin embedded SI tissue and CC3 +ve villus IECs quantified using WinCrypts and Score programs. Statistics were performed using ANOVA with Dunnett's post-test.
Results ELISA analysis showed significant decreases in CC3 in GF vs SPF mice following LPS administration (2.6-fold+/-0.3, $p < 0.01$). Decreased levels of TNF-α (GF, 189+/-56 pg/ml vs SPF, 548+/-66; $p < 0.01$), showed a potential mechanistic basis for this change. Reconstitution with ASF or sDMDMm2 failed to restore levels of shedding observed in LPS treated SPF mice. CC3 ELISA (ASF, 1.1-fold+/-0.3, ns; sDMDMm2, 1.0-fold+/-0.1, ns); TNF-α ELISA (ASF, 311+/-48 pg/ml, $p > 0.05$; sDMDMm2; 231+/-77 pg/ml, $p < 0.05$). IHC and count analysis confirmed that LPS treated GF, ASF or sDMDMm2 mice were unable to mount a normal cell shedding response vs LPS treated SPF mice: Mean% CC3 positive IECs along the length of the villus of 4.3%+/-1.2, 0.6%+/-0.3, 0.5%+/-0.2 vs 7.9%+/-1.1, respectively (all $p < 0.01$). Importantly, when LPS was delivered to GF mice reconstituted with SPF faeces, similar rates of shedding to LPS treated SPF mice were observed and TNF-α production was restored.
Conclusion GF mice are largely refractory to LPS induced cell shedding, when compared to SPF or fully reconstituted GF mice, via modulation of the pro-inflammatory cytokine TNF-α. These data strongly implicate the intestinal microbiota in cell shedding and may help to shape microbiota-based treatment of IBD patients.
Disclosure of Interest None Declared.

PWE-077 ACCESS TO A FAECAL CALPROTECTIN SERVICE PROVIDES CLINICIANS WITH THE CONFIDENCE TO DIAGNOSE AND TREAT CONCOMITANT FUNCTIONAL BOWEL SYMPTOMS IN KNOWN IBD PATIENTS

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Introduction An accurate clinical assessment of disease activity in inflammatory bowel disease (IBD) is essential to provide appropriate management strategies. The concurrent presence of functional symptoms in IBD patients is common and said to occur in 80% of proctitis patients, 60% of UC patients and 40% of Crohn's patients.[1] A high symptom index can strongly influence clinical assessment and expose patients to unnecessary investigations. Faecal calprotectin (FC) has a high negative predictive value of 96% for inflammation therefore allowing use in this cohort to differentiate functional and organic symptoms.[2]
Methods All FC data over a 2 year period was collected in IBD outpatients with a diagnostic uncertainty about symptoms being functional or organic in nature and whether further endoscopic examination was necessary. FC results were regarded as normal (<50 μg/g), borderline (50–100 μg/g) or positive (>100 μg/g) and correlated with endoscopic assessment and subsequent influence on management.
Results 262 FC measurements were performed in IBD patients where there was diagnostic uncertainty about symptoms being organic or functional in origin. In this cohort, unnecessary colonoscopy was spared in 83% (218/262), including 62/66 with normal FC, 26/27 borderlines and 130/169 positives.

Despite a normal FC, 4 patients underwent further assessment via colonoscopy for routine surveillance with no evidence of active disease. In addition, some patients were investigated with CT colonography as an alternative assessment method. 0/2 scans in the borderline group showed positive findings with 6 being performed in the positive FC group. Of these, 5 had active disease with 1 showing a psoas abscess requiring inpatient treatment.

As a result of a positive FC, a direct change in management was made in 114/169 (67%) without the need for further endoscopy. In the case of a negative FC result, 14/66 (21%) patients had an alteration in their treatment regimes to focus upon targeting functional bowel symptoms.
Conclusion Faecal calprotectin measurement spared 80% of the colonoscopies being considered to assess symptomatic IBD patients. Both positive and negative results had a strong influence on subsequent management. FC measurement provides clinicians the confidence to isolate and manage functional symptoms in their IBD cohort, whilst preventing unnecessary treatment escalation. In those with a positive FC result, appropriate treatment could be initiated whilst avoiding the increased risks of endoscopy in acutely inflamed patients.

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Disclosure of Interest None Declared.

PWE-078 MEAN CORPUSCULAR VOLUME BUT NOT LYMPHOCYTE COUNT IS A PREDICTOR OF THIOPURINE DOSE ADEQUACY AND TOXICITY

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Introduction The thiopurines, azathioprine (AZA) and mercaptopurine (MP), commonly used in the treatment of inflammatory