PTU-102 DEVELOPMENT OF A FOOD RELATED QUALITY OF LIFE QUESTIONNAIRE FOR PEOPLE WITH IBD

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10.1136/gutjnl-2014-307263.176

Introduction The role of diet as a therapy for Inflammatory Bowel Disease (IBD) is well established and has improved treatment and prognosis for patients. However, little is understood about how IBD impacts on food-related quality of life. A qualitative study indicated a wide range of food related issues across a broad spectrum of IBD experiences which include, amongst others; identifying and avoiding trigger foods, uncertainty about eating and drinking, problems eating out and frustration around eating. This study aimed to develop a food-related quality of life (FRQoL) questionnaire for people with IBD.

Methods Semi-structured interviews with 28 IBD patients were coded and 150 FRQoL questionnaire items were generated. One hundred IBD patients ranked each item on i) if it had been relevant to them in the past two weeks and; 2) how important it was to them (regardless of whether it had been relevant). Items were removed based on ceiling/floor effects and high inter-item correlations. The 41 highest ranking items were retained with a 5 point Likert (disagree-agree) response scale. Subsequently, 287 IBD patients, 100 asthma patients (chronic disease control) and 117 healthy volunteers completed the FRQoL questionnaire alongside clinical measures, MUST nutritional screening, food satisfaction and generic and disease-specific quality of life questionnaires. Psychometric testing of the FRQoL questionnaire has been carried out including principle components analysis, construct and discriminant validity and test-retest reliability.

Results Initial principle components analysis identified seven components explaining 68.35% of variance with high internal reliability (Cronbach's alpha = 0.96). The FRQoL sumscore (higher scores indicate worse quality of life) correlated with younger age ($r = -0.12$), higher MUST score ($r = 0.17$) and lower BMI ($r = -0.13$). Worse FRQoL was associated with female gender ($p < 0.001$), a diagnosis of Crohn's Disease ($p < 0.05$), surgery ($p < 0.05$) and high MUST score ($p < 0.05$).

Conclusion An FRQoL questionnaire has been developed to identify issues around food, eating and nutrition for people with IBD at all stages of the disease process. Preliminary psychometric testing indicates that the questionnaire sumscore is related to clinical characteristics indicative of poor FRQoL. Further testing will determine the validity and reliability of the questionnaire for clinical use to identify IBD patients who may require further support with eating and drinking.

Disclosure of Interest None Declared.

PTU-103 INTRA-LUMINAL INTERLEUKIN (IL)-27 IS A POTENTIAL FUTURE THERAPEUTIC FOR INFLAMMATORY BOWEL DISEASE

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10.1136/gutjnl-2014-307263.177

Introduction Oral *Lactococcus lactis* engineered to express the immunoregulatory cytokine IL-27 (LL-IL27) is therapeutically

active in chronic murine enterocolitis. Here, efficacy in acute colitis was examined.

Methods 2 mg 2,4,6-trinitrobenzene sulfonic acid (TNBS) was delivered intra-rectally in 45% ethanol or 45% ethanol alone into 6–8 week old male SJL mice. *L. lactis* control (LLC) or LL-IL-27 was delivered by oral gavage on 4 occasions, 24 h apart, commencing at colitis induction. Therapeutic effect was assessed clinically and histologically. Potential mechanisms of action were investigated.

Results TNBS induced an acute severe distal colitis. LL-IL-27 led to a significant reduction in disease activity index compared to LLC (4.9 vs. 8.7/12 on day 2 ($p = 0.001$); 3.6 vs. 7.7/12 on day 3 ($p = 0.001$), improved macroscopic colitis score ($p < 0.05$), and reduction in serum CRP ($p = 0.003$, day 2). Histological colitis score was reduced ($p = 0.035$) with significant improvement in mucosal ulceration ($p = 0.008$). TNBS increased expression of distal colon *Il6*, *Il1β*, *Tnf*, and *Il10*, assessed by RT-PCR, with no differential effect seen with LL-IL-27. However, LL-IL-27 led to a significant reduction in IL-6 ($p = 0.002$), IL-1β ($p = 0.001$) and TNF ($p = 0.014$) protein assessed by ELISA. A significant reduction in colonic mucosal myeloperoxidase⁺ neutrophil infiltrate was seen in the LL-IL-27 group ($p = 0.004$), along with a significant decrease in the neutrophil chemoattractant CXCL2 ($p < 0.001$). LPS induced CXCL2 gene and protein expression in macrophages was not inhibited by recombinant IL-27 *in vitro*, suggesting an indirect mechanism *in vivo*. Peri-ulceration distal colonic mucosa was isolated by laser capture microdissection and RNA applied to mouse Genome 430 2.0 Affymetrix microarray. Principal component analysis grouped mice by treatment. 285 genes were differentially expressed ($>/<1.5$ fold change in expression plus $p < 0.05$) in the LL-IL27 group, including a striking down-regulation of mucosal humoral response genes, (for example, probe sets for IgA heavy chain (-20.6 fold), Igk chain var1 (-19.0 fold), Igλ chain CR2 (-4.8 fold)). This was not explained by a reduction in CD45R/B220⁺ B cell infiltrate ($p = 0.02$). Up-regulated genes include those involved with anti-microbial defense (*RegIIIb*, *Clec7A*, *ligp1*) and innate immune response (*cxcl10*, *cxcl9*).

Conclusion Intra-luminal IL-27 represents a potential therapy for human inflammatory bowel disease and acute colitis of differing aetiologies.

Disclosure of Interest M. McLean: None Declared, M. Hanson: None Declared, B. Gold: None Declared, Y. Golubeva: None Declared, M. Anver: None Declared, X. Wu: None Declared, D. Sun: None Declared, L. Steidler Employee of: ActoGenix, S. Durum: None Declared.

PTU-104 OUTCOMES OF INCREASED DOSE OF ALLOPURINOL IN IBD PATIENTS WHO DEVELOPED HEPATOTOXICITY ON LOW AZATHIOPRINE AND ALLOPURINOL CO-THERAPY TREATMENT

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10.1136/gutjnl-2014-307263.178

Introduction The thiopurines (azathioprine (AZA) and metcapotpurine (6MP)) are established first line therapies for inflammatory bowel disease (IBD). However, when these agents are used at their target dose side effects are common, gastrointestinal intolerance (10–20%) and hepatotoxicity ($>10\%$).¹ These side effects can often be bypassed by using low dose AZA and

Abstract PTU-104 Figure 1 Proposed model of thiopurine hepatotoxicity.

allopurinol (ALLO) co-therapy (LDAA). The current opinion is that hepatotoxicity is secondary to high red cell methylated metabolites (MMPR/MMP). However, many patients develop hepatotoxicity without high MMP levels.² We report a series of patients who regardless of low MMP developed hepatotoxicity whilst on allopurinol co-therapy, 3 of which were TPMT heterozygotes.

Aim to determine outcomes of increasing the dose of Allopurinol from 100 to 200 mg in patients with hepatotoxicity to LDAA.

Methods Patient records and our IBD database were searched for patients on LDAA who developed hepatotoxicity whilst on LDAA (100 mg of ALLO). Liver function tests (LFTs), liver screen, ultrasound results and clinical outcomes were determined.

Results From the 2500 patients with IBD locally, 600 were exposed to thiopurines and 300 were on LDAA. Nine patients had sustained hepatotoxicity, 3 were TPMT heterozygotes. Seven of these patients responded fully to increased dose of ALLO to 200mg. Two had a suboptimal response (1 had PSC as a potential cause). All patients had asymptomatic abnormalities of LFTs, negative chronic liver screen apart from 2 who had ultrasound proven fatty liver disease without abnormal LFTs prior to LDAA. We observed that all patients had improvements in their LFTs, whilst 7 had complete correction of abnormal AST, ALP and bilirubin. Median time for treatment was 24 months (range 12–48 months), with full response to therapy in all 7 patients.

Conclusion This is the first series which reports improvement of LFTs by increasing ALLO dose for patients on LDAA. This subgroup of patients were unlikely to have high MMPR as 3 of them were TPMT heterozygotes and all were on LDAA therapy, therefore a different mechanism, of hepatotoxicity is proposed (Figure 1). It is possible that reactive oxygen species generated from the oxidation of metcaptopurine are responsible, and this can be further improved by adjusting the dose of ALLO. Further studies are required.

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Disclosure of Interest None Declared.

PTU-105 EXPRESSION OF MICRORNAS MIR-31, MIR-146A AND MIR-155 IS SIGNIFICANTLY ELEVATED IN ANTI-TNF-ALPHA TREATMENT FAILURE IN COLONIC CD

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10.1136/gutjnl-2014-307263.179

Introduction Crohn's disease (CD) is a Th1/Th17 driven disease in which TNF- α and INF- γ play important roles. Anti-TNF- α drugs are used in moderate-severe CD to induce and maintain remission. Mucosal healing is an aim of therapy. MicroRNAs are noncoding RNAs which control translation of mRNA. MiR-31, miR-146a and miR-155 are involved in the regulation of immune responses and are deregulated in CD. Aim of this study is to evaluate the impact of medical treatment on microRNA expression in CD and to investigate microRNAs as biomarkers in CD.

Methods 37 patients with colonic CD undergoing colonoscopy were recruited. A partial Simple Endoscopic Score for CD (SES-CD) was assessed. Sigmoid biopsies were taken from 19 patients in remission (SES-CD=0) and 18 patients with active sigmoid CD (SES-CD $\geq$ 1). Remission (R) was defined as mucosal healing (SES-CD=0) and treatment failure (F) as an SES-CD $\geq$ 1 in the left colon. MicroRNA (miR-31, miR-146a and miR-155) and mRNA expression (TNF- α , INF- γ) were evaluated by qPCR. Sub-analysis compared treatment naïve patients (6 inactive/8 active) to patients on thiopurines (TP) (R= 5/F= 5) and anti-TNF- α therapy (R=6/F=7).

Results miR-31, miR-146a and miR-155 were significantly up-regulated as were TNF- α and INF- γ in active sigmoid CD compared to patients in remission. Patients on TP compared to treatment naïve patients showed significant down-regulation of TNF- α and INF- γ in remission, compared to treatment naïve patients with active CD. MicroRNA levels in TP failure were interestingly lower compared to patients in remission. In contrast, microRNA levels in the anti-TNF- α group in therapy failure were significantly elevated compared to active treatment naïve patients, behaving opposite to patients on TP. MicroRNA expression in remission showed levels similar to treatment naïve patients in remission. While TNF- α and INF- γ returned to base levels in remission on anti-TNF- α drugs, significantly lower compared to active treatment naïve CD, in therapy failure TNF- α remained elevated and INF- γ was significantly raised.

Conclusion Our data reveals a clear up-regulation of miR-31, miR-146 and miR-155 as well as of TNF- α and INF- γ in active colonic CD. TP and anti-TNF- α drugs significantly alter the expression of microRNAs miR-31, miR-146a and miR-155 compared to treatment naïve patients behaving in an opposing manner. MicroRNAs remain significantly elevated in patients with sigmoid CD failing to respond to anti-TNF- α treatment. MicroRNAs expression profiles may have a role as biomarkers in predicting treatment failure in CD.

Disclosure of Interest None Declared.

PTU-106 SUCCESSFUL PREGNANCIES WITH THIOPURINE-ALLOPURINOL CO-THERAPY FOR INFLAMMATORY BOWEL DISEASE

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10.1136/gutjnl-2014-307263.180

Introduction Combination of low dose thiopurine with allopurinol can improve the clinical efficacy and bypass some of the adverse reactions of thiopurine monotherapy. Thiopurines can be used safely during pregnancy but there is scarce data regarding allopurinol. We report twelve cases of safe use of thiopurine and allopurinol co-therapy to manage IBD during pregnancy.