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Introduction Ulcerative colitis (UC) is an inflammatory disease of the colonic mucosa driven by a Th2-like response in which IL-13 leads to toxic effects to the mucosa and activation of the IL-13/STAT6 pathways. Inhibition of STAT6 activation has been shown to reduce the inflammatory response in UC. MicroRNAs are small non-coding RNAs inhibiting gene expression by pairing to the 3' UnTranslated Region (3'UTR) of their target mRNAs facilitating their translational repression/degradation. MiR-31 and miR-155 have been shown to be up-regulated in active UC and are involved in the regulation of innate and adaptive immune responses. Both microRNAs have been identified to target IL13Rα1.

Methods Paired biopsies from inflamed and non-inflamed areas of the sigmoid colon were taken in 11 UC patients. MicroRNA expression and mRNA expression of IL-13 dependant genes were assessed by qPCR. In vitro experiments on a human colonic cell line (HT-29 cells) and a macrophage/monocytic cell line (THP-1 cells) were stimulated with IL-13. SOCS1 and IL13Rα1 mRNA expression were measured by qPCR in the presence or absence of transfection with pre-miR-31, pre-miR-155 or a combination of both. Data were analysed using the Wilcoxon matched pairs test.

Results Our data shows a significant up-regulation of miR-31 and miR-155, as well as significant increase of IL-13 dependant mRNA expression of CCL18, SOCS1, Serpine and MMP-9 and a decrease of IL13Rα1 mRNA expression by 30% in the active segments of UC as compared to inactive disease. In vitro experiments on HT-29 cells and on THP-1 cells showed a marked reduction of mRNA expression of SOCS1 and IL13Rα1 in both cell types after treatment with pre-miR-31 and pre-miR-155 and their combination at a quarter of the original dose of each single pre-miR was equally efficacious.

Conclusion Our data reveals a clear up-regulation of miR-31 and miR-155 in inflamed UC as compared to neighbouring inactive tissue in the same patient. IL-13 dependant mRNA expression is also significantly increased in the same samples. The fact that IL13Rα1 mRNA expression is down-regulated in active disease in the presence of high levels of miR-31 and miR-155 may indicate a protective role for these microRNAs attempting to reduce IL13Rα1 expression and therefore the STAT6 pathway activation by IL-13 through IL13Rα1. Reduction of IL13Rα1 mRNA expression in our in vitro models transfected with pre-miRs confirms this finding. Interestingly the combination of the two microRNAs at lower doses achieving the same effect may indicate a possible synergy of action. MicroRNAs targeting IL13Rα1 in UC could have a potential therapeutic effect by down-regulation of the IL-13/STAT6 pathway and combination of microRNAs may have a synergistic effect.

Competing interests None declared.

OC-163 IDENTIFICATION OF INFLAMMATORY BOWEL DISEASE (IBD) USING FIELD ASYMMETRIC ION MOBILITY SPECTROMETRY (FAIMS)

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Introduction Resident colonic bacteria, principally anaerobes and firmicutes, ferment undigested fibre. The resultant volatile organic compounds (VOCs) formed are dissolved in the faeces but also absorbed and excreted in the urine. We have previously shown that electronic nose (E-nose) analysis of urine VOCs distinguishes between Crohn's disease (CD), ulcerative colitis (UC) and healthy volunteers (HV): the underlying principle is pattern recognition of disease-specific "chemical fingerprint". High-Field Asymmetric Waveform Ion Mobility Spectrometry (FAIMS) offers a possible alternative. The underlying principle is separation of VOC chemical components based on their different ion mobilties in high electric fields. We performed a pilot study in the above groups, the patients in remission (Rem) or with active disease (AD), to assess if this technology could achieve separation between the groups. The results were validated against E-nose analysis.

Methods 59 subjects were studied; HV n=14, UC (Rem) n=18, UC (AD) n=4; CD (Rem) n=19, CD (AD) n=4. Urine samples (7 ml) in universal containers (25 ml) were heated to 40±0.1 C. The headspace (the air above the sample) was then analysed using FAIMS. The data were analysed by Fisher Discriminant Analysis.

Results The technique distinguished between the three groups. Additionally, patients with active disease could be distinguished from those in remission. These results were concordant with E-nose analysis.

Conclusion This pilot shows that urine VOCs, analysed by the different approaches of E-nose and FAIMS, the latter a novel application, can distinguish the healthy from those with UC and CD when disease is active or in remission. The two technologies together offer a non-invasive approach to diagnosis and follow-up in inflammatory bowel disease.

Competing interests None declared.

OC-164 TREATMENT NAIVE ACTIVE ULCERATIVE COLITIS HAS A DISTINCTIVE MICRORNA PROFILE

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Introduction MicroRNAs (miRNAs) are becoming increasingly recognised as key players in a multitude of inflammatory pathways through their ability to regulate gene expression. Numerous miRNAs have been shown to have an abnormal expression in Ulcerative Colitis (UC), although published results are inconsistent possibly due to the grouping of different phenotypes and concomitant medication. Understanding the miRNA profile in homogeneous groupings is a major advance to understanding the mechanisms that underpin the aetiology of UC. The aim is to identify a distinctive miRNA signature for active sigmoid UC in patients who are treatment naïve.

Methods Sigmoid biopsies were taken from patients with Baron Grade 3 active UC (n=21), patients with previous sigmoid UC who have no inflammation (n=15) and healthy controls (n=20). All patients were matched for age, sex, ethnicity and no medication for ≥6 months. Deregulated miRNA candidates were first identified in active UC (n=6) and compared against controls (n=6) using Taqman® Array MicroRNA card A. Array cards were performed in pairs (active vs control). The differential expression of 377 miRNAs were calculated for each pair. The 20 miRNAs with the greatest increase and 20 with the greatest decrease in expression for each pair were then compared with the other array card pairs. MiRNAs that had a consistently increased or decreased expression in all array card pairs were validated using RT-qPCR. Differential expressions was calculated using the fold change compared with healthy controls. Statistical analysis was performed using Mann–Whitney test

Results Seven miRNAs were consistently deregulated across all miRNA array pairs. RT-qPCR confirmed a significantly increased fold change in three miRNAs; miR-31 (10.97, $p<0.001$), miR-223 (3.45, $p<0.001$) and miR-146b-5p (2.26, $p=0.002$). Four miRNAs were shown to have a statistically significant decreased expression by RT-qPCR. Only miR-31 and -223 were deregulated with statistical significance in inactive UC (fold increase of 2.83, $p<0.001$ and 2.47, $p<0.001$ respectively).

Conclusion (1) A distinct subset of miRNAs is deregulated in the mucosa of actively inflamed sigmoid UC in patients who are on no treatment. (2) miR-31 and -223 are constitutionally expressed in sigmoid UC and could offer a potential diagnostic tool for patients who have no active inflammation at the time of endoscopy. (3) Manipulating miRNA expression offers promise as a potential new therapeutic pathway in active disease. (4) When investigating miRNA profiles and function it is essential to use an accurately phenotyped and homogeneous patient group. (5) We are the first to show a miRNA profile for sigmoid UC in treatment naive patients.

Competing interests None declared.

OC-165 NO INCREASE IN SURGICAL COMPLICATION IN PATIENTS TREATED WITH RESCUE THERAPY FOR ACUTE SEVERE ULCERATIVE COLITIS: DATA FROM THE UK IBD AUDIT

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Introduction High dose steroids followed by colectomy if required remains the mainstay of treatment for active ulcerative colitis (UC). Recently we have seen the introduction of second-line medical therapies with the hope of avoiding the need for surgery when medical therapy fails. Using a cohort of 2981 and 3049 ulcerative colitis patients from the 2nd and 3rd rounds of the UK IBD audit we aim to assess whether the use of second-line medical therapies has an impact on the need for surgery and complication of surgery when needed.

Methods We audited 3049 patients with ulcerative colitis. Median age was 42; there were 1421 females and 1628 males. There were 495 elective admission for surgery and 2504 acute admissions of which 882 were considered to have severe disease. Of the 2504 acute admissions; 157 underwent surgery during their admission. 202 Sites audited a median of 18 UC patients per site that were admitted with IBD between 1 September 2009 and 31 August 2010. The results of this were compared against the results from the 2008 UK IBD audit which collected data on 2981 UC patients of which there were 863 with severe disease. Of the severe patients 163 patients underwent surgery. 209 sites audited a median of 17 UC patients per site that were admitted with IBD between 1 September 2007 and 31 August 2008.

Results There was no significant change in the operative rate among ASUC patients, 18.9% (163/863) in 2008 and 17.8% (157/882) in 2010 ($p<0.6$). Additionally there was no significant change in the mortality within the surgical populations 2.5% (4/163) in 2008 vs1.9% (3/157) in 2010 ($p<0.96$). There were significantly more patients proceeding to surgery following anti-TNFα therapy in 2010 10.82% (17/157) vs 3.7% (6/163) ($p<0.008$). Using the Travis criteria we also found that there were significantly less high risk surgical patients in 2010, 67.5% (106/157) compared to 83.4% (136/163) ($p<0.002$); this was also reflected in a significant reduction in the overall amount of high risk patients in the ASUC population. Post-operative complications are not statistically different between patients who did and did not receive rescue medical therapy 40.0% (26/65) vs 34.8% (32/92) ($p<0.8$). There was also no statistical difference in complications between rounds, 32.5% (53/163) in 2008 vs 36.9% (58/157) in 2010 ($p<0.4$).

Conclusion The surgical rate has remained the same over the two audit periods; however there has been a significant reduction in the proportion of high risk patients undergoing operations. This could in part be related to the increased use of second line medical therapies between the two audit rounds, with significantly more patients receiving anti-TNFα prior to surgery. The use of second line medical therapies did not increase the risk of surgery.

Competing interests None declared.

OC-166 PREDICTIVE FACTORS OF DISEASE RELAPSE FOLLOWING THIOPURINE WITHDRAWAL FOR SUSTAINED CLINICAL REMISSION OF IBD

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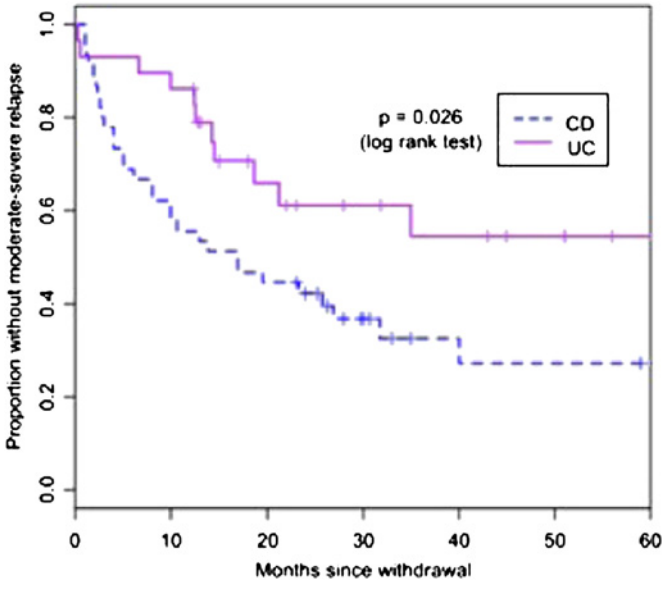
Introduction Thiopurine therapy is effective in maintaining clinical remission in IBD. However, long-term therapy is associated with an increased risk of lymphoma; therefore in clinical practice we aim to withdraw therapy after 4–5 years. Nevertheless, many patients will experience disease relapse within 12 months of drug withdrawal.[1]

Methods The aim of the present study was to retrospectively determine the relapse rate in ulcerative colitis (UC) and Crohn's disease (CD) following azathioprine (AZA) or mercaptopurine (MP) withdrawal and to determine factors predictive of relapse. Patients were identified by electronic case note review of an IBD research database in Edinburgh. Major inclusion criteria were AZA and/or MP therapy for a minimum of 3 years, AZA/MP withdrawn due to sustained clinical remission no steroid therapy for 6 months prior to drug withdrawal, and minimum 12 months follow-up. The primary outcome was disease relapse requiring AZA reinitiation, steroids or colectomy within 12 months of AZA/MP withdrawal, with secondary outcome assessed at 24 months. Clinical/laboratory predictors of relapse were sought. 1826 electronic records were reviewed (865 CD and 961 UC). 634 were treated with a thiopurine (348 CD and 286 UC). 74 met the strict study inclusion criteria (45 CD and 29 UC).

Results CD was associated with a significantly higher risk of relapse than UC on Kaplan–Meier analysis (Abstract OC-166 figure 1, $p=0.026$). The moderate-severe relapse rate for 12 months was 44% for CD and 14% for UC. For 24 months, relapse rates were 60% for CD and 48% for UC. Elevated platelet count ($p=0.03$) and elevated white cell count ($p=0.03$) were predictive of relapse for UC, while no predictive factors were identified for CD. Median (range) duration of thiopurine use was 6.2 (3.4–18.7) years for CD and 6.0 (3.1–18.0) years for UC. Median duration of follow-up was 32 months for CD and 45 months for UC. Retreatment with a thiopurine after relapse was successful in 7/7 cases for UC and 18/24 for CD.



Abstract OC-166 Figure 1 Survival curves for moderate to severe relapse following thiopurine withdrawal in Crohn's disease and ulcerative colitis