PWE-243 REASSESSMENT OF CROHN'S DISEASE TREATED WITH 12 MONTHS OF ANTI-TNF THERAPY: A TERTIARY CENTRE EXPERIENCE

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[1,2]R Dart,* [3]N Griffin, [1]K Taylor, [1]J Duncan, [1]M Sastrillo, [1]S Anderson, [1,2]J Sanderson, [1,2]P M Irving. [1]*Department of Gastroenterology, St Thomas' Hospital, London, UK;* [2]*Diabetes and Nutritional Sciences Division, King's College London, London, UK;* [3]*Department of Radiology, St Thomas' Hospital, London, UK*

Introduction Anti-TNF therapy (ATT) is increasingly used in Crohn's disease (CD) in the UK. However, because of its expense, NICE guidance recommends that after a year of treatment, responders should be reassessed and withdrawal of treatment considered if they are in remission. We report our experience in a tertiary referral centre of reassessment after 1 year of ATT and of factors leading to continuation or withdrawal of treatment.

Methods We performed a 12-month retrospective review of patients with CD who had received ATT for >12 months by 31 December 2011. Reassessment was defined as having undergone one or more of the following investigations aimed at assessing disease activity: endoscopy, examination under anaesthesia, MRI or faecal calprotectin (FC). Results of investigations and outcome were recorded.

Results 91 patients (infliximab n=55, adalimumab n=36) were included of whom 80% (73/91) had their disease reassessed. Five patients were withdrawn from treatment (of whom one has already relapsed) and five are pending trial of withdrawal; two patients met criteria for withdrawal but required continuation for extra-luminal disease such as arthropathy. 84 (92%) continued therapy. 48 patients had endoscopic reassessment; mucosal healing (MH) was demonstrated in 25% (n=12), non-ulcerating inflammation in 40% (n=19) and ulceration in 35% (n=17). Of 12 with MH 3 withdrew from therapy and 3 are pending withdrawal. Of six patients who continue, two require ongoing ATT for arthropathy, three had radiologic evidence of activity, and one is undergoing further assessment. 24 patients had both endoscopy and MRI and 19 patients underwent MRI alone. Of the latter group, scans were normal in 21% (n=4), showed improvement but not resolution in 32% (n=6) and active disease in 47% (n=9). Of four normal scans, one patient was withdrawn, and 3 continue due to raised FC (n=1) or raised CRP (n=2). Disease was assessed by EUA in five patients, demonstrating active disease in four and quiescent disease in one who is pending trial of withdrawal. One patient continues on treatment on the basis of raised FC alone. One patient had mild mucosal inflammation on endoscopy and an unchanged MRI scan prior to withdrawal but relapsed within 4 months.

Conclusion Reassessment after at least 12 months of ATT showed ongoing disease activity in the vast majority (84%). Withdrawal was considered appropriate in only 13%. In patients with distal ileal and/or colonic disease, endoscopy is currently our mainstay of reassessment while for those with small bowel disease interval change on MRI is used. The role of CRP and FC remain to be defined.

Competing interests None declared.

PWE-244 DOES THROMBOPROPHYLAXIS IN ULCERATIVE COLITIS WORK?: DATA FROM THE UK IBD AUDIT

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[1]R W Lynch,* [2]M Roughton, [2]C Down, [1]I D Arnott. [1]*GI Unit, Western General Hospital, Edinburgh, UK;* [2]*CEEU, Royal College of Physicians, London, UK*

Introduction Venous thromboembolism (VTE) has been long recognised as a complication of inflammatory bowel disease (IBD) with prevalence being reported at between 1.25 and 6.7% and a threefold increased risk being reported when compared to matched cohorts. It has led to recommendations that all patients admitted with acute flares of ulcerative colitis should be given prophylactic subcutaneous heparin although data of efficacy in an IBD population are lacking. We aim to assess the incidence, prophylaxis and possible aetiology of VTE in ulcerative colitis.

Methods We audited 3049 patients with UC. Median age was 42; there were 1421 females and 1628 males. 495 admissions were for elective surgery and there were 2504 emergency admissions of which 882 were considered to have severe disease. 202 Sites audited a median of 18 UC patients per site that were admitted with IBD between 1 September 2009 and 31 August 2010. Data collected contained specific questions on the administration of subcutaneous heparin and whether the patient had a thrombotic event during their admission. We also assessed whether type of admission, age, co-morbidities, disease severity, surgical operations, gender, steroid therapy and treatment response were related to VTE.

Results Of the 3049 patients admitted with ulcerative colitis, 2668 (87.5%) patients were given prophylactic heparin. 66 (2.2%) patients experienced thrombotic events during their admission. The rate of VTE among heparinised patients, 2.2% (59/2668), did not differ significantly when compared to a rate of 1.8% (7/381) within the population who didn't receive prophylaxis (p<0.8). VTE was associated with the need for surgery: 39.4% (26/66) of patients with VTE underwent surgery compared with surgery in 26.2% (781/2983) without VTE (p<0.02). Of these 26 surgical patients within the VTE population, four of these patients' VTE were post-operative. When patients undergoing elective surgery are excluded VTE is associated with co-morbidity: 46.0% (23/50) of the VTE population compared to 32.4% (810/2504) in the non-VTE population (p<0.03). There was no association of VTE with disease severity (severe disease in 42.0% (21/50) with DVT vs 34.4% (861/2504) without VTE, p<0.3) or the use of steroids (steroids used in 96.0% (48/50) with VTE vs 89.6%% (2244/2504) without VTE, p<0.08).

Conclusion Although there was no difference in the frequency of VTE in patients given or not given heparin the numbers of VTE within this group are small. This analysis does however demonstrate that patients with co-morbidity and those undergoing surgery are at higher risk of VTE. Additional measures to prevent VTE should be considered in these patients such as a combination of heparin and compression stockings. All IBD patients admitted to hospital should continue to receive prophylactic subcutaneous heparin.

Competing interests None declared.

PWE-245 ANTI-TNFα ANTIBODY THERAPY AND PARENTERAL CORTICOSTEROIDS DEMONSTRATE DISTINCT EFFECTS IN THE TREATMENT OF EXPERIMENTAL *TRICHURIS MURIS*-INDUCED CHRONIC COLITIS

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[1]S E Levison,* [2]M C Little, [2]R K Grencis, [1]J T McLaughlin, [1]J L Pennock. [1]*Translational Medicine;* [2]*Manchester Immunology Group, University of Manchester, Manchester, UK*

Introduction Anti-tumour necrosis factor (TNF) α antibody treatment and corticosteroid therapy represent central strategies in the management of Crohn's disease. Yet, over 30% of patients fail to respond. Understanding the mechanism of effect for each therapy is complicated by disease heterogeneity, and the complexities of effector and regulatory immune cell responses. We characterised the biological and immunological effects of infliximab and hydrocortisone therapy in a genetically identical murine model of experimental colitis.

Methods Mice (AKR) susceptible to chronic *Trichuris muris*-induced colitis were infected with 300 *T muris* eggs. A single 5 mg/kg dose of Infliximab, or daily hydrocortisone treatment (2 mg/kg, QDS) were

administered intraperitoneally once chronic colitis had established (from day 35 post-infection, p.i.). Systemic, mesenteric lymph node (MLN) and colonic effects were analysed at day 45 p.i. MLN cell cytokine bead-array and colonic gene expression (RT-qPCR) analysis were performed. Colonic histopathology, tissue $Foxp3^+$ and macrophage recruitment were determined. Treated groups were compared to naïve and untreated-infected AKR (n=5 per group).

Results Neither treatment altered worm expulsion. Anti−TNFα Ab and corticosteroid therapy preserved colonic length, compared to untreated disease. Colonic inflammation was less severe with steroid treatment (p=0.005) and infliximab (p=0.07). An increase in MLN TH2 cytokines was suggested with both treatments. Reduced colonic TNFα, IL-1β, IFNγ and IL-12p40, and increased IL-13 expression were observed following Infliximab. Down-regulated TH1 cytokines, elevated TH2 cytokines (IL-4, IL-5, IL-13), and up-regulated colonic IL-10 expression were detected following corticosteroid treatment. Colonic $Foxp3^+$ cell numbers increased with disease but were unaltered by either treatment. A significant reduction in tissue $F4/80^+$ macrophages was observed with infliximab treatment alone.

Conclusion Anti−TNFα Ab and corticosteroid therapy suppress TH1-driven experimental colitis. Up-regulated transcription of TH2 and regulatory (IL-10, TGFb, Foxp3) pathway molecules was seen with corticosteroid treatment. This was not accompanied by an increased influx of $Foxp3^+$ T-cell, suggestive that corticosteroids may alter regulatory-cell function more significantly than recruitment, in the reduction of pathology and disease activity. Anti−TNFα Ab treatment reduced colonic pro-inflammatory macrophage recruitment. With differing modalities of immunosuppression demonstrated, this model may increase understanding of why either mode of therapy can induce benefit in man even if the other has failed.

Competing interests None declared.

PWE-246 INFLIXIMAB TREATMENT SIGNIFICANTLY REDUCES INFLAMMATORY MACROPHAGE NUMBERS WHILE PRESERVING REGULATORY MACROPHAGES IN A MOUSE MODEL OF CHRONIC CROHN'S COLITIS

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[1]S Levison,* [2]M C Little, [2]R K Grencis, [1]J T McLaughlin, [1]J L Pennock. *[1]Translational Medicine, University of Manchester, Manchester, UK; [2]Manchester Immunology Group, University of Manchester, Manchester, UK*

Introduction Inappropriate inflammatory responses to intestinal flora, augmented by host susceptibility genetics, contribute to the pathogenesis of Crohn's disease (CD). Transmural intestinal inflammation results from innate and adaptive immune cell infiltration, and pro-inflammatory cytokine accumulation. Activated macrophages represent a major source of TNFα production. The treatment of CD with anti-TNFα antibody (Ab) therapy has proved clinically beneficial, yet over 30% of patients fail to respond. We characterised the biological and immunological effects of Infliximab therapy in a model of experimental colitis.

Methods Genetically identical mice (AKR), susceptible to chronic *Trichuris muris*-induced colitis, were infected with 300 *T muris* eggs. A single 5 mg/kg dose of Infliximab was administered intra-peritoneally once chronic colitis had established (from day 35 post-infection, p.i.). Systemic, mesenteric lymph node (MLN) and colonic effects were analysed at day 45 p.i. MLN cell cytokine bead-array and colonic gene expression (RT-qPCR) analysis were performed. Colonic histopathology, tissue $Foxp3^+$, and macrophage recruitment and phenotype were determined. The treatment group was compared to untreated-infected, naive, and naïve AKR administered Infliximab (n=5 per group).

Results Treatment did not alter worm expulsion. Anti−TNFα Ab therapy preserved colonic length compared to untreated disease (p=0.049). Colonic inflammation was less severe with Infliximab treatment (p=0.07). Reduced TNFα, CCL2, and GMCSF proteins were measured in the MLN of Infliximab treated infected AKR. Reduced colonic expression of TNFα, IL-1β, IFNγ and IL-12p40, and increased IL-13 was observed following Infliximab treated disease. Colonic $Foxp3^+$ cell numbers increased with disease but were unaltered by treatment. Infected mice treated with Infliximab demonstrated a 50% reduction in colonic $F4/80^+$ macrophages (p=0.036). A relative increase of the proportion of colonic Arg^+ alternatively activated macrophages (AAMΦ) was observed with Infliximab treatment compared to untreated disease (29% vs 14%).

Conclusion Infliximab therapy suppresses TH1-driven experimental colitis. Anti−TNFα Ab treatment reduced pro-inflammatory macrophages recruitment, and for the first time in vivo has been shown to preserve colonic tissue regulatory AAMΦ. Whether a result of a fundamental alteration to macrophage recruitment, or the differentiation of a specific macrophage phenotype, requires further study. The presence of AAMΦ at index biopsy, or an increase in AAMΦ numbers following treatment initiation, may help to identify patient responders to Anti-TNFα Ab therapy.

Competing interests None declared.

PWE-247 ARE WE MEASURING VITAMIN D IN INFLAMMATORY BOWEL DISEASE (IBD) PATIENTS?

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S K Butt,* K Besherdas. *Department of Gastroenterology, Chase Farm Hospital, London, UK*

Introduction There is increasing interest in the role of vitamin D in IBD, outside of its traditional role in metabolic bone disease. Novel insights into additional roles for vitamin D are being established and these include anti-inflammatory and immune-modulating effects. Active vitamin D is known to exert its biological functions via the vitamin D receptor (VDR). Immune cells have been found to express VDR and possess the enzymes necessary to produce active vitamin D. This suggests vitamin D may have actions beyond endocrine activity. Furthermore, Vitamin D deficiency has been linked to higher rates of cancers including colorectal cancer. Previous studies have found that almost 50% of the IBD patients were vitamin D deficient at some point and 11% were severely deficient. Vitamin D deficiency has been demonstrated to be independently associated with higher disease activity scores in patients compared to those that had normal levels of vitamin D. Furthermore, vitamin D deficient Crohn's patients have a poorer quality of life when compared to patients who are not vitamin D deficient. Currently, ECCO guidelines do not mention measurement of vitamin D in patients with IBD but given its effects, we set out to identify whether we were checking for and correcting for vitamin D deficiency in our IBD patients.

Methods The aim of the study was to investigate whether we were measuring vitamin D levels at any encounter in out IBD patients. This study was conducted in a busy District General Hospital in North London. Information was gathered using the hospital powerchart system and the IBD database of patients.

Results A total of 225 patients were correctly identified as having IBD. Of these, 157 (70%) had Ulcerative colitis and 68 (30%) had Crohn's disease. 24 (15%) Ulcerative colitis patients and 8 (12%) Crohn's patients had their vitamin D checked on hospital records. The range of vitamin D levels were 14−84 with lower limit of normal being 50. 13/32 (41%) patients has low vitamin D levels Of these only two patients were also under the Rheumatology team for co-existing arthropathy/arthritis.