response, adverse effects or biochemical abnormalities. Careful patient selection and monitoring is warranted to identify uncommon, yet serious adverse events.

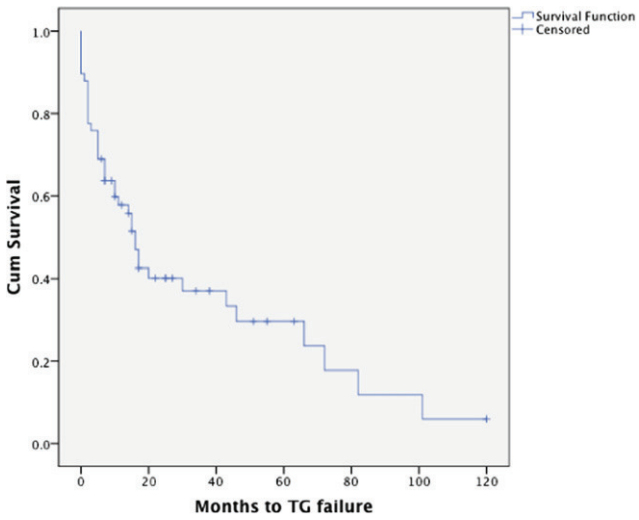

Figure 1 Time to TG Failure

Table 1 Failure at 12 months

	Number	Percent
Not failed	34	58.6
New course steroids	2	3.4
Start anti-TNF	1	1.7
Surgery	10	17.2
Drug withdrawn (adverse effects)	9	15.5
No response (switched to alternative IM)	2	3.4
Total	58	100.0

References

1. Sandborn WJ et al. Azathioprine or 6-mercaptopurine for induction of remission in Crohn's disease; Cochrane Review 2009
2. Patel V et al. Methotrexate for maintenance of remission in Crohn's disease; Cochrane Review 2009

Clinical utility of measuring adalimumab trough levels and antibodies to adalimumab in patients with inflammatory bowel diseases

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Introduction: Adalimumab (ADA) is an effective therapy for inducing and maintaining response in patients with inflammatory bowel disease (IBD). Nevertheless a considerable proportion of patients develop secondary loss of response. The measurement of drug levels (DL) and antibodies to ADA (ATA) may be useful in this situation. Where as good data exists defining therapeutic DL and antibodies to infliximab, little is known of absolute values that are associated with active disease and clinical remission in patients treated with ADA.

Aims: To describe initial clinical experience with a commercially available ELISA kit for the measurement of DL and ATA in a tertiary IBD centre.

Methods: Patients with IBD who underwent DL and ATA testing between February 2012 and March 2013 were reviewed. LISA-TRACKER Premium ELISA kits (Theradiag, Marne La Vallee, France) were used to determine free DL and ATA. Measurement range was 0.1 to 5 ug/mL for DL and 10 to 160 ng/mL for ATA (>10 ng/mL considered positive). Samples with DL above 5 ug/mL were diluted 1:3 or 1:4 to derive absolute values. Clinical details were obtained from the electronic patient record. Patients were classified as in remission or as active disease after review by two IBD physicians blinded to DL/ATA results. Anti-TNF resistant disease was defined as active disease with DL >5 ug/mL despite dose escalation to 40 mg weekly.

Results: 31 patients (19 male, median 33 years) had 32 samples collected; 27 with Crohn's disease, 3 IBD – unclassified and 1 ulcerative colitis. Median duration ADA treatment was 26 months (4–48). 12/32 (38%) patients had active disease. 20/32 (63%) samples had DL above upper limit of detection, of which 11 were diluted to derive absolute values. Hence 23 patients had absolute DL available for analysis. DL were significantly higher in patients in remission (median 8.3 ug/mL, IQR 4.9–17.9) compared to active disease (median 4.6 ug/mL, IQR 3.2–9.6,$p = 0.45$). This significance was further strengthened when patients with anti-TNF resistant disease ($n = 4$) were excluded (remission DL median 8.3 ug/mL, IQR 4.9–17.9 vs active disease DL median 3.5 ug/mL, IQR 1.4–4.8,$p < 0.001$), (Fig 1). ROC analysis identified an optimal AD DL > 4.9 ug/mL (sensitivity 83%, specificity 65%, AUC 0.75) to predict clinical remission (Fig 2). The association between this therapeutic DL (4.9 ug/mL) and clinical remission remained statistically significant ($p = 0.03$) when samples with undiluted DL > 5 ug/mL were also considered, (Fig 3). 1/32 (3%) samples were ATA positive; (undetectable DL); this patient had active disease.

Conclusions: As has been demonstrated with drug level testing for infliximab, initial experience suggests that measuring DL in adalimumab-treated patients may be clinically useful. The significance of antibodies is less clear given their low prevalence, however it is important to note bridging ELISA detects free ATA only, hence undetectable ATA may have contributed to the lower DL seen in non-responders in this study. A therapeutic level of approximately 5 µg/ml concurs with data from other centres using this assay.[1]

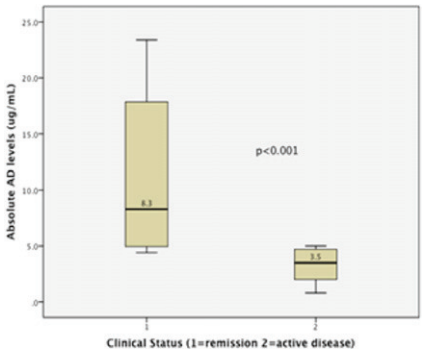

Figure 1 Absolute AD levels vs Clinical Status

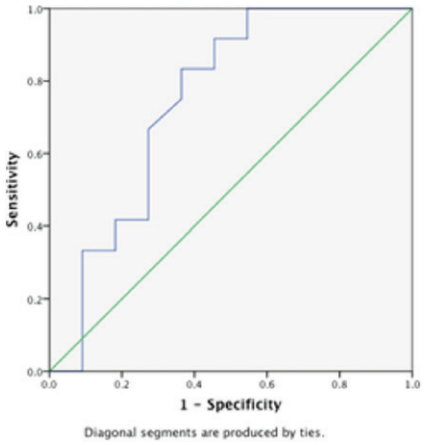

Figure 2 ROC for clinical remission

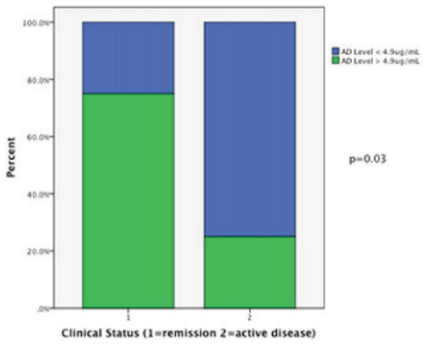

Figure 3 Clinical Status According Therapeutic Drug Level

Reference

1. Roblin X et al. Residual Adalimumab Levels Are Associated With Clinical Remission and Mucosal Healing in IBD.

Abstract DDW 2013

Prevalence and risk factors for functional b12 deficiency in patients with Crohn's disease

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Introduction: Risk factors for vitamin B12 deficiency in patients with Crohn's disease (CD) include ileal disease and previous ileal resections. Screening for B12 deficiency is traditionally through serum B12 which is relatively insensitive. Holotranscobalamin (holoTC) is a test that measures the metabolically active fraction of B12 available for cellular uptake and has been shown to perform better than traditional testing in identifying patients with functional B12 deficiency.

Aims: To determine the prevalence and risk factors for functional B12 deficiency in patients with CD using holoTC. We hypothesised that holoTC would identify B12 deficiency in patients with CD deemed to be B12 replete on traditional testing.

Methods: Consecutive patients with CD who underwent vitamin B12 measurement at a single tertiary centre between March 2012 and March 2013 were included. A control population of patients with ulcerative colitis (UC) was selected. A subgroup of randomly selected patients with CD underwent paired serum B12 and holoTC. Serum B12 < 107 pmol/L or holoTC < 25 pmol/L was defined as B12 deficient. Intermediate holoTC values between 25 pmol/L and 50 pmol/L underwent further assessment with methylmalonic acid (MMA), considered the gold standard in metabolic B12 deficiency. MMA > 280 nmol/L in patients < 65 years of age and > 360 nmol/L in patients > 65 years of age confirmed B12 deficiency. Risk factors for B12 deficiency were examined including Montreal classification, surgical history and the presence of ileal inflammation or stricture.

Results: 464 patients with Crohn's disease (221 males, median age 38, IQR 30–48years) were included. 102 (22%) were treated with B12 supplementation and excluded from further analysis. 120 UC controls were selected, 3(2.5%) were treated with B12. The prevalence of B12 deficiency was greater in CD n = 97, 27%; (95% CI 22–31%) compared with UC controls, n = 15, 13% (95% CI 7–19%) (p = 0.003). 92 patients with CD underwent paired serum B12 and holoTC testing. B12 deficiency was observed in 29 (31.5%); 13 (14.1%) with HoloTC alone and 16 (17.4%) after MMA analysis on intermediate results. Serum testing identified 5/92 (1.4%) patients with B12 deficiency; 3 were functionally deficient with HoloTC alone and 2 were replete when assessed by MMA. Risk factors for B12 deficiency on multivariate regression analysis were increasing length of ileal resection, OR 1.04, (95% CI 1.01 – 1.06, p = 0.006) and ileal inflammation, OR 2.82, (95% CI 1.45 – 5.49, p = 0.002). Neither disease location, behaviour, nor medication use was independently associated with the risk of B12 deficiency.

Conclusion: Vitamin B12 deficiency is common in patients with Crohn's disease and those with active ileal diease and a past history of ileal resection are at particular risk. HoloTC identifies vitamin B12 deficiency in a significant percentage of patients with CD otherwise considered replete on traditional testing. In addition serum B12 testing identifies patients who are not functionally deficient. Screening patients with Crohn's disease for B12 deficiency with holoTC is recommended.

Medications blocking the renin-angiotensin system may influence disease activity in patients with inflammatory bowel disease

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Background: There is accumulating evidence that the renin-angiotensin system (RAS) is active within the gastrointestinal tract, but its influence in intestinal inflammation, especially inflammatory bowel disease (IBD), is poorly understood.

Aim: To compare disease activity, concurrent medical therapy and requirement for surgery in patients with IBD treated concurrently with angiotensin converting enzyme inhibitors (ACEi) and/or angiotensin receptor blockers (ARBs), with patients not treated with either medication.

Methods: Consecutive patients attending the IBD Clinic at Box Hill Hospital were invited to list all medications currently being taken and duration of use. Demographic data and disease characteristics were collected, with disease activity indices analysed for the previous 2-year period. Disease activity was graded along a scale as follows: 0 – quiescent disease, 1 – up to 2 flares per year with quiescent disease in between, 2 – more than 2 flares per year or persistent disease activity for less than 50% of the time, 3 – persistently active disease for over 50% of the time, 4 – persistently active disease for over 50% of the time with flares. Requirement for immunomodulators (IM) and/or biologic therapy, surgery, and hospitalisations not requiring surgery were independently assessed. Patients taking ACEi and/or ARBs (RAS blockers) were compared with patients not taking these medications for these outcomes by chi square, multiple and logistic regression as appropriate, with adjustment for potential confounders including age.