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Welcome to this review of Australian Gastroenterology Week (AGW), the annual meeting of the Gastroenterological Society of Australia.

AGW is one of the significant scientific meetings in the Asia-Pacific region and features the latest advances in clinical management, cutting-edge translational and basic science, and original research in endoscopy, gastroenterology and hepatology. Since the inaugural meeting, AGW has grown in attendance from 25 to over 2,000 medical practitioners, surgeons, researchers, and allied health professionals from across the Asia Pacific region.

This review has been created to allow those unable to attend, but with a keen professional interest, to access a summary of some of the presentations. Selection and review of the research has been carried out independently by Professor Ian Lawrance, who attended the meeting.

The meeting has been published as a Special Issue online supplement to the *Journal of Gastroenterology and Hepatology* (September 2015) and abstracts can be accessed on the journal’s website: [http://onlinelibrary.wiley.com/doi/10.1111/jgh.2015.30.issue-s3/issuetoc](http://onlinelibrary.wiley.com/doi/10.1111/jgh.2015.30.issue-s3/issuetoc)

I hope you enjoy this review and I look forward to your feedback.

Kind Regards,

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A specified oral vitamin D supplementation regimen is effective for increasing serum 25(OH) vitamin D and is associated with a reduction in disease activity scores

**Authors:** Garg M et al.

**Summary:** In this study, 10 patients with isolated colitis, 5 each with Crohn’s disease (CD) and ulcerative colitis (UC), with mild–moderately active disease (i.e. faecal calprotectin [FC] >100 μg/g and serum 25(OH) vitamin D <75 nmol/L) were prescribed 12 weeks of oral vitamin D supplementation. At 12 weeks, of the 9 patients who completed the study protocol, 3 of 4 patients with CD and 2 of 5 with UC attained a 25(OH)D level of 100–125 nmol/L: the remaining patients achieved levels of 89–95 nmol/L. The mean rise in serum 25(OH)D from weeks 0–12 was 51 nmol/L (p<0.001) across all participants, and was similar between the CD and UC cohorts. The mean total dose of vitamin D taken amongst the 9 patients who completed the 12-week study period was 492,000 IU. Evaluations of change in clinical activity revealed a fall in Harvey-Bradshaw index (HBI) scores in the CD cohort (from a median of 2 at baseline to 1 at week 12; p=0.019) and in Simple Clinical Colitis Activity Index (SCCAI) scores in the UC cohort (from a median of 3 to 0; p=0.051). There were no changes in FC across all patients (median change +25 μg/g; p=0.975) or subgroups with CD or UC, in C-reactive protein (CRP), white cell and platelet count, or albumin. No cases of hypercalcaemia or hyperphosphataemia were reported. Mean 24-hour urinary calcium excretion remained stable throughout the 12 weeks for the entire cohort, although there was 1 case of new hypercalciuria. Supplementation was not associated with any serious adverse events and no patient required surgery or hospitalisation for worsening inflammatory bowel disease (IBD).

**Comment:** Vitamin D (Vit D) is known to have immunomodulatory effects and is decreased in the presence of inflammation, inversely correlating with the intestinal inflammation. This work therefore aimed to investigate if oral Vit D supplementation, to increase the serum 25(OH)D level to 100–125 nmol/L, would have a clinical impact on disease activity. In this small study, 5 CD and 5 UC patients with mild disease (FC >100 μg/g) and a Vit D level of <75 nmol/L, received Vit D supplements for 12 weeks. The supplementation increased the Vit D levels into the desired range but no change in objective measures of inflammation was achieved. This, however, may be due to several factors, including the fact that the patients did not have much inflammation and were not significantly Vit D deficient, which correlates with the mild inflammation detected by the FC levels. Further work needs to be undertaken, as Vit D may be involved in the processes surrounding the inflammation.

**J Gastroenterol Hepatol. 2015;30(Suppl. 3):126.**
Vitamin D excess is associated with worse outcomes in dextran sodium sulphate colitis

Authors: Ghaly S et al.

Summary: This study investigated the effect of very high vitamin D diets on the course of dextran sodium sulphate (DSS)-induced colitis in 6-week-old C57Bl/6 female mice raised on diets deficient (D-), 0 IU vitamin D₂, 2% calcium), sufficient (D+; 2280 IU D₃/kg, 1% calcium) or very high (D++; 10000 IU D₃/kg, 0.5% calcium) in vitamin D₃ for 4 weeks. Mice were treated with 3% DSS in their drinking water for 6 days; corresponding controls continued untreated water ad libitum. After 4 weeks, colitis was worse in the D++ group than in the D- group, as shown by a higher mean murine endoscopic index of colitis (MEICS) score at day 6 (D++ vs D-: p<0.001). Compared to the D- group, the D+ mice did not have worse colitis (mean MEICS at day 6; 4.1 vs 3.9, respectively; p=0.65). Both the D+ and D++ groups had greater percentage weight loss at day 7 than the D- group (reported as mean values): D+ vs D- (9.0% vs 4.5%; p<0.001) and D++ vs D- (7.6% vs 4.5%; p<0.001), indicating worse colitis. By day 7, serum 25(OH)D₃ concentrations dropped by 63% from baseline to a mean of 38 nmol/L in the D++ group and by 30% to a mean of 32.9 nmol/L in the D+ group. The magnitude of the drop corresponded with colitis severity. In the high vitamin D group, 25(OH)D₃ concentrations had not recovered to baseline measurements by day 35.

Comment: The role of vitamin D (Vit D) in colitis is unknown but it is known that Vit D decreases in patients with active CD. The rationale behind this decrease, however, has yet to be explored. This work used an animal model of colitis and with the animals fed concurrent UVB treatment. In colitis 25(OH) Vit D and 1,25(OH)₂ Vit D dropped, but Vit D binding protein increased. The colitis up-regulated Cyp24A1 levels which metabolised Vit D but the 25(OH) Vit D decrease in colitis could not be explained by this. Of note was that the colitis in animals with high circulating 25(OH) Vit D was significantly worse than in the other groups, with a greater weight loss, suggesting that caution should be exercised with Vit D replacement.

The predictive value of early serum infliximab, CRP and faecal calprotectin levels post-first infliximab rescue dose for acute severe colitis: ‘day 1 to 3 is key’

Authors: Beswick L et al.

Summary: This paper presents interim results from 13 patients with acute severe ulcerative colitis (as defined by Truelove-Witts criteria refractory to intravenous [IV] hydrocortisone) taking part in a study examining the predictive value of early measurement of serum infliximab levels and inflammatory biomarkers post-infliximab dosing in relation to clinical outcomes. Study participants received rescue therapy comprising 1 or 2 infliximab doses (IV 5 mg/kg). Clinical remission was defined as a partial Mayo score of zero. The primary endpoint was set if CRP <3 mg/L and also clinical remission was achieved at/prior week 6. Post-first infliximab dose, early higher CRP and FC levels predicted poorer week 6 outcomes, while decreasing infliximab levels from day 1 through day 3 appeared to be associated with better outcomes. In ROC analysis, the area under curve (AUC) of consecutive day 1 to 3 levels for serum infliximab (cut-off ≤158 μg/mL), CRP (≤33 mg/L) and FC (≤4910 μg/mL) each predicted the primary endpoint with sensitivity and specificity values of 83% and 71% (AUC 0.81; 95% CI, 0.57 to 1.0), 83% and 57% (AUC 0.81; 95% CI, 0.57 to 1.0), 83% and 100% (AUC 0.88; 95% CI, 0.66 to 1.0), respectively.

Comment: In patients with acute severe colitis (ASC) who have failed intravenous hydrocortisone, infliximab is frequently the first choice for rescue therapy to avoid colectomy. This work examined the infliximab pharmacokinetics, disease burden and timing of infliximab doses with its efficacy in this context. Using the Truelove-Witts criteria for treatment failure patients received either 1 or 2 infliximab doses (5 mg/kg IV) as rescue therapy. In this pilot study, patients with a higher CRP and FC level had a worse outcome at week 6 consistent with potentially more severe disease. However, patients who had a decrease in infliximab levels from day 1 through day 3 appeared to have a better outcome, potentially due to appropriate infliximab binding in these patients and thus disease control. This finding may be of potentially predictive value in ASC and further work is under way.

J Gastroenterol Hepatol. 2015;30(Suppl. 3):118.
Concurrent infliximab and cyclosporin treatment for severe colitis

Authors: Hendy P, Florin TH

Summary: Outcomes are reported for 3 female patients (aged 22–43 years) prescribed concurrently cyclosporin and infliximab for episodes of severe colitis. Two patients were intolerant of steroids due to psychiatric side effects. The other patient had steroid-refractory disease. All patients satisfied Truelove and Witts’ criteria for ASC. Two patients had UC (one left-sided and one with pancolitis confirmed on colonoscopy). The other patient had distal Crohn’s colitis. Treatment consisted of daily cyclosporin infusions of 2 mg/kg for 3–5 days then oral liposomal cyclosporin for 3 months. Early clinical response was poor, so the patients were prescribed infliximab 5 mg/kg induction doses while continuing cyclosporin. Two patients continued infliximab as maintenance therapy, with concomitant thiopurines. Despite a good initial response, the left-sided UC patient developed severe infectious complications with herpetiform gingivostomatitis secondary to parainfluenza III infection and disseminated bacterial folliculitis. All immunomodulatory therapy was ceased and the patient underwent colectomy for severe left-sided colitis 10 weeks after commencement of the combination treatment. The other two patients achieved clinical remission. A colonoscopy at 19 months showed complete healing of the fistula and colonic mucosal healing in the Crohn’s patient. A colonoscopy at 2 months showed macroscopic mucosal healing in the patient with pancolitis.

Comment: ASC occurs in 25% of UC patients at some stage in their disease and those who fail intravenous hydrocortisone require rescue therapy in order to avoid colectomy. Infliximab and cyclosporin are the two choices for rescue therapy but sequential use of cyclosporin and infliximab is considered a risk. This is a report of 3 IBD patients who received cyclosporin and infliximab concurrently for episodes of acute colitis. Patients received 2 mg/kg daily cyclosporin for 3–5 days followed by oral therapy for 3 months. Due to lack of clinical response, infliximab 5 mg/kg induction doses were prescribed while continuing therapy with cyclosporin. One patient developed a severe infective complication and went to colectomy while the other two achieved remission. This regime may thus be something to consider, but there are significant risks associated with it and should not be undertaken lightly.

J Gastroenterol Hepatol. 2015;30(Suppl. 3):130.

Immunomodulators provide no reduction in loss of response for inflammatory bowel disease patients starting anti-TNF-alpha therapy

Authors: Varma P et al.

Summary: This retrospective analysis included data from 94 patients with IBD (CD, n=91; UC, n=3) receiving tumour necrosis factor (TNF) inhibitor therapy in a single tertiary care centre; 53 patients were treated with infliximab and 41 with adalimumab. Thirteen patients received monotherapy and 81 were co-treated with immunomodulators. Loss of response (LOR) defined by an admission or surgery post-induction, escalation of anti-TNF dose or concurrent immunomodulators for clinical LOR, emergence of a new fistula or rising Crohn’s Disease Activity Index >150 (CDAI) occurred in 45 (45%) patients during follow-up (23 infliximab and 19 adalimumab-treated patients; p<ns). Causes for LOR included hospital admission (n=13; 31%), clinical LOR (n=21; 50%), surgery (n=6; 14%), or new fistula (n=2; 5%). The median time to loss of response was longer in the concomitant immunomodulator therapy group compared with the anti-TNF monotherapy group (1027 days vs 980 days; p=0.78). The types of immunomodulator co-therapy or anti-TNF agents used made no difference as to time to loss of response. No correlations were observed between baseline CDAI or body mass index and time to loss of response. Moreover, baseline haemoglobin, albumin and CRP did not differ between those who experienced loss of response and those who did not.

Comment: Studies examining the use of anti-TNF therapy alone, or in combination with an immunomodulator, suggest that infliximab used in combination is more efficacious, but adalimumab does not appear to receive this benefit, and combination therapy may be harmful. This study aimed to determine if monotherapy was associated with earlier loss of response in IBD than combination therapy. This retrospective audit included 94 patients (42 adalimumab) and 81 received combination therapy (13 monotherapy). The study found that there was no difference between the type of anti-TNF, immunomodulator co-therapy, and time to loss of response, suggesting a lack of efficacy of combination therapy. This, however, will require further investigation, as only 13 patients did not receive combination therapy, suggesting underpowering and the efficacy of infliximab in combination has already been examined in a prospective, randomised controlled study and demonstrated significant benefit.

J Gastroenterol Hepatol. 2015;30(Suppl. 3):140-1.

Five years of faecal calprotectin: can it deliver on convenience, cost reduction and clinical decision making in IBD?

Authors: Motaganahalli S et al.

Summary: These researchers retrospectively analysed data from 358 FC tests performed on 244 patients with IBD (75% had CD, 25% had UC) during a 5-year period. The median follow-up post-FC testing was 2 years. At the time of FC testing, 25% of patients were on anti-TNF and 57% on immunomodulator therapies. FC was negative (≤100 μg/mL) in 38% of patients, positive (≥100 μg/mL) in 62%, and moderate/high (≥250 μg/mL) in 42%. FC testing resulted in treatment (de-) escalation in 42% at next clinic visit. Post-FC testing, only 16% of patients proceeded to colonoscopy within 3 months. By end of follow-up, 61% had avoided colonoscopy and only 5% had cross-sectional imaging post-FC. An independent clinician assessment determined that, in absence of FC, 67% of cases would have warranted colonoscopy at time of FC testing. FC testing therefore potentially enabled a cost reduction of 71% from total $AU32,2416 (colonoscopy only) to $AU94,683 (FC +/- colonoscopy). Patients with FC ≥250 were scoped earlier than those with FC <100 μg/mL (median 0.49 vs 1.0 years; p=0.03). Post-FC, patients with FC ≥250 μg/mL had a shorter time to documented IBD flare/surgery compared with those with FC <100 μg/mL (p<0.01). Of 69 patients with ≥2 serially performed FC tests, those with FC normalisation (compared to those with no change or worse FC) had more likely been escalated to anti-TNF and/or immunomodulator therapy but were less likely to be on steroids (p<0.05), with no other significant differences in IBD characteristics.

Comment: FC is a complex of the mammalian proteins and is as much as 60% of the soluble protein content of neutrophil cytosol. It becomes available in the intestinal lumen via leukocyte shedding, active secretion, cell disturbance, and cell death. It is resistant to enzymatic degradation, and can be easily measured in stool. Calprotectin has been shown to be able to differentiate between IBS and IBD symptoms. It is, however, not federally funded and thus may cost the patient. This study examined their use of faecal calprotectin over 5 years where 358 samples were examined on 244 confirmed IBD. FC was negative in 38%, positive in 62% and highly positive (≥250 μg/mL) in 42%. FC testing resulted in treatment change in 42% and 61% avoided a colonoscopy. FC had a significant impact on the prediction of a flare, triaging colonoscopy and monitoring response to therapy and should be used within the management of IBD.


Australian Gastroenterology Week (AGW)

Concurrent infliximab and cyclosporin treatment for severe colitis

Five years of faecal calprotectin: can it deliver on convenience, cost reduction and clinical decision making in IBD?
Outcomes post–liver transplant for primary sclerosing cholangitis: colitis activity and malignancy

Authors: Greenup A-J, et al.

Summary: Clinical outcome data were retrospectively analysed from 48 patients (mean age 58 years) undergoing liver transplantation for primary sclerosing cholangitis (PSC) at Royal Prince Alfred Hospital from January 1986 to December 2014. Mean follow-up was 11 years. Forty-seven patients underwent at least one colonoscopy, with a median interval of 1.74 years. Colitis was histologically active in 32 (68%) patients post-transplant, including 22 patients who had quiescent disease preceding transplant. Of 3 patients treated with anti-TNF agents, 2 achieved remission and the remaining patient required a colectomy. An additional 4 patients also underwent colectomy for refractory colitis. In the remaining 15 patients, colitis was quiescent post-transplant. Six further patients had a total or hemi colectomy for the indications of cancer (n=3), invisible dysplasia (n=1), endoscopically unetectable polyoid dysplasia (n=1) and caecal volvulus (n=1). An additional 4 patients had a history of invisible dysplasia and 4 endoscopically resectable polyoid dysplasia.

Comment: PSC increases the risk of colorectal cancer (CRC) in patients with IBD by 16-fold and CRC may be even higher in post-liver transplant cases. This group examined the IBD activity, and rates of colonic dysplasia and cancer in their cohort of IBD patients post–liver transplantation for PSC. Over a 29-year period, 48 patients (UC 28 and CD 20) were followed for a mean of 11 years. A colonoscopy was performed at least once on 47 patients. Colitis was active in 68% (32) of patients including 22 who had quiescent disease prior to transplant. Dysplasia/cancer was detected in 14 patients and colectomy was undertaken in 11, which was 3.1-fold greater than IBD patients without a transplant. This emphasises the important of colonoscopic vigilance in these patients, as both disease control and dysplasia may be a greater issue than pre-transplant.


Does a low FODMAP diet reduce symptoms associated with functional gastrointestinal disorders? A meta-analysis

Authors: Marsh A et al.

Summary: This meta-analysis included data from 6 randomised controlled trials (RCTs) and 16 non-randomised interventions, which evaluated the efficacy of a low FODMAP (Fermentable, Oligo-, Di-, Mono-saccharides And Polyols) diet in the treatment of functional gastrointestinal symptoms such as abdominal pain, bloating, constipation, diarrhea and flatulence in patients with irritable bowel syndrome (IBS) or IBD. A low FODMAP diet was associated with a significant reduction in IBS Symptom Severity Score (SSS) scores in both the RCTs (odds ratio [OR] 0.44; 95% CI, 0.25 to 0.76) and non-randomised interventions (OR 0.03; 95% CI, 0.01 to 0.20). There was also a significant improvement from baseline in the IBS Quality of Life score for RCTs (OR 1.84; 95% CI, 1.12 to 3.03) and for non-randomised interventions (OR 3.18; 95% CI, 1.60 to 6.31). Adhering to a low FODMAP diet significantly reduced symptom severity for abdominal pain (OR 1.81; 95% CI, 1.13 to 2.88), bloating (OR 1.75; 95% CI, 1.07 to 2.87) and overall symptoms (OR 1.81; 95% CI, 1.11 to 2.95) in the RCTs. Similar findings were observed in the non-randomised interventions.

Comment: IBS is a very common diagnosis in gastroenterology and effects between 7–15% of the general population. It is characterised by functional symptoms in the absence of inflammation or anatomical abnormalities. Diet is a potential trigger for symptoms in almost 60% of patients. It is also very common in patients with IBD even when the intestinal inflammation is fully controlled. The FODMAP diet is an understanding of how foods are digested and which foods can be difficult for humans to process. FODMAPS are associated with increased wind, diarrhea and constipation. Meta-analysis of RCTs and non-randomised IBS studies both show that symptoms significantly reduce on a FODMAP diet and that the patient quality of life increases. In both IBS and IBD sufferers the use of a dietician and explanation of the FODMAP diet can be of great benefit to symptom modification.


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