Welcome to issue 69 of Gastroenterology Research Review.

This issue begins with research reporting on the risk of perianal disease in patients with UC, finding that the incidence is greater than in the general population, with distinct clinical features and poor outcomes. An RCT has found that MaZiRenWan, a Chinese herbal medicine, was well tolerated and effective for increasing spontaneous bowel movements (similar to senna) in patients with functional constipation when compared with placebo. Other researchers have reported the characteristics of patients treated with anti-TNF therapy for IBD who experienced TB (tuberculosis) reactivation despite isoniazid prophylaxis. The final research paper selected for this issue compared endoscopic SEMS (self-expandable metallic stent) placement with gastrojejunostomy for palliative treatment in patients with malignant gastric outlet obstruction.

We always appreciate your input, so please send us any comments and feedback you have.

Kind Regards,
Dr Ian Kronborg
ian.kronborg@researchreview.com.au

Inflammatory bowel disease and mycobacteria: how much can we trust isoniazid prophylaxis during antitumor necrosis factor therapy?

Authors: Akyuz F et al.

Summary: These researchers reviewed the medical records of 60 patients with latent TB infection who received 9 months of isoniazid prophylaxis concomitantly with anti-TNF treatment for IBD. Four of these patients experienced TB reactivation in spite of isoniazid prophylaxis, with active TB diagnosed after 18–84 months of anti-TNF treatment. Mycobacterium bovis was also detected in one of these four patients and M. genavense in another.

Comment: The risk of reactivation of TB by biologic therapy is the reason for screening prior to commencement of therapy. In high-risk areas, the positive rate at screening is up to 32%, and if positive, 9 months of isoniazid therapy is recommended. This study looked at the risk of reactivation of TB despite the use of isoniazid and found four of 60 patients did reactivate. Another recent study in Portugal showed one in 18 patients reactivated. The evidence is thus consistent; patients who are at risk despite isoniazid therapy need to be monitored carefully for reactivation of TB.


Abstract
Incidence and clinical impact of perianal disease in patients with ulcerative colitis

Authors: Song EM et al.

Summary: The incidence of perianal disease was investigated in Korean population- and hospital-based cohorts of patients with UC, comparing clinical characteristics and outcomes according to its presence. The incidence rate of perianal disease in the population-based cohort was 3.74 per 1000 person-years, with a standardised incidence ratio of 2.88 (95% CI 2.50–3.32). The respective 1-, 5-, 10- and 20-year cumulative probabilities of perianal disease following UC diagnosis in the hospital-based cohort were 1.0%, 2.3%, 4.0% and 6.3%. Patients with UC and perianal disease from both cohorts had greater corticosteroid use, extensive colitis at diagnosis and requirements for anti-TNF therapy and colectomy before and after matched analysis.

Comment: Perianal disease is a well-recognised complication of CD but less documented in UC, for example the UpToDate entry doesn’t mention it. This study is a nationwide-based study, but the source data are from a Korean National Health Insurance claims database, and the exact criteria for diagnosis of UC are not clear. However, despite this the data are convincing that there is significant perianal disease in conjunction with UC. The incidence increasing with both the duration of disease and the severity of disease. The presence of a subgroup of patients could be explained by saying there are CD cases misdiagnosed as UC, but the alternative explanation is that some patients with UC do have perianal disease. Clearly whatever the reason, these patients have a worse disease course than the average patient and probably need a more aggressive treatment programme to avoid colectomy.

Reference: J Gastroenterol Hepatol 2019;34:1011–7

Low-dose aspirin can reduce colorectal cancer mortality after surgery

Authors: Sung JJJ et al.

Summary: The effects of low-dose aspirin after surgery for CRC (colorectal cancer) on 10-year mortality were explored in 13,528 patients. Among patients taking aspirin before being diagnosed with CRC (n=3292), 80.7% continued it and 19.3% discontinued it after surgery. In this cohort, continuing aspirin was associated with significantly reduced CRC-related and all-cause mortality (respective HRs 0.69 [95% CI 0.59–0.81] and 0.61 [0.55–0.68]). Among patients who had not used aspirin prior to their CRC diagnosis (n=10,236), 10.3% started it and 89.7% did not start it postsurgery. Starting aspirin postsurgery was also associated with reduced CRC-related and all-cause mortality (respective HRs 0.88 [95% CI 0.80–0.98] and 0.87 [0.81–0.94]).

Comment: The role of aspirin in preventing CRC is examined in this study looking at the effect of aspirin after surgery for CRC. The study looked at four cohorts: patients taking aspirin prior to surgery who continued it, those taking it prior and stopping after surgery, those not taking it before and after surgery, with the last group being those who only started aspirin after surgery. The marked improvement in overall mortality was a little surprising after the recent large study by McNeil et al., which showed no improvement in overall survival in an RCT of aspirin use in the healthy elderly. This study clearly supports the use of aspirin in patients with the risk of CRC, but remember there are conflicting data, including a recent American study showing increased metastatic disease in the general population using aspirin.

Reference: J Gastroenterol Hepatol 2019;34:1027–34
Efficacy of MaZiRenWan, a Chinese herbal medicine, in patients with functional constipation in a randomized controlled trial

Authors: Zhong LLD et al.

Summary: Patients with functional constipation (n=291) were randomised in a 1:1:1 ratio to receive the Chinese herbal medicine MaZiRenWan 7.5g twice daily, senna 15 mg/day or placebo for 8 weeks with an additional 8 weeks of follow-up. A greater proportion of MaZiRenWan recipients achieved a complete response by week 8 when compared with placebo but not senna recipients (68% vs. 33.0% and 57.7%, respectively (p values <0.005 and 0.14), with similar findings at 16 weeks (47.4% vs. 17.5% and 20.6%). MaZiRenWan recipients also had significant improvements in colonic transit, severity of constipation, straining, incomplete evacuation and global constipation symptoms compared with placebo and senna recipients (p<0.05 for all).

Comment: The use of traditional or alternative medicines is very common, but there are little data about their effectiveness. This well-designed, blinded RCT gives some data in a head-to-head comparison to senna for constipation. After 8 weeks both active treatment groups had similar response rates but the MaZiRenWan group had more improvement in some secondary endpoints including colonic transit, severity of constipation, straining and overall symptoms. Thus, MaZiRenWan is at least as effective as senna and can be considered as an alternative therapy for functional constipation.

Reference: Clin Gastroenterol Hepatol 2019;17:1303–10
Abstract

Efficacy of live attenuated herpes zoster vaccine in patients with inflammatory bowel diseases

Authors: Khan N et al.

Summary: These researchers reported herpes zoster infection incidences for a retrospective cohort of US veterans aged ≥60 years with IBD (n=39,983) comparing those who received herpes zoster vaccine (n=7170) with those who did not during follow-up of ~16 years. Compared with nonvaccinated veterans, those who received herpes zoster vaccine had a significantly lower crude incidence rate of herpes zoster infection over the follow-up period (4.09 vs. 6.97 per 1000 person-years; adjusted HR 0.54 [95% CI 0.44–0.68]).

Comment: The use of traditional or alternative medicines is very common, but there are little data about their effectiveness. This well-designed, blinded RCT gives some data in a head-to-head comparison to senna for constipation. After 8 weeks both active treatment groups had similar response rates but the MaZiRenWan group had more improvement in some secondary endpoints including colonic transit, severity of constipation, straining and overall symptoms. Thus, MaZiRenWan is at least as effective as senna and can be considered as an alternative therapy for functional constipation.

Abstract

Higher odds of irritable bowel syndrome among hospitalized patients using cannabis

Authors: Adejumo AC et al.

Summary: These researchers explored the relationship between cannabis use disorder and IBS in adults from the 2014 US Nationwide Inpatient Survey (evaluate n=4,709,043) with cannabis use disorder, IBS or established risk factors for IBS. 0.33% had a primary admission for IBS and 1.32% had cannabis use disorder. The presence of cannabis use disorder was associated with an increased likelihood of having IBS (adjusted OR 2.03 [95% CI 1.53–2.71]), but the association was significant for males (3.48 [1.98–6.12]), not females (1.48 [0.88–2.50]), and for Hispanics (5.28 [1.77–15.76]) and Caucasians (1.80 [1.02–3.18]) but not Blacks (1.80 [0.65–5.03]). Propensity-matching revealed that cannabis use disorder increased the likelihood of IBS by 80%.

Comment: The use of CBDs is common in the community and it is increasingly being used as a therapeutic option. The endogenous cannabinoid system modulates many pathological processes in IBS and thus may well be affected by CBD use. This study looks at the relationship of CBD use and IBS in a population-based study in the US; usage of other illicit drugs but not alcohol and nicotine led to exclusion from the dataset. The criteria for diagnosis of IBS were strict and probably excluded up to 90% of possible cases, but meant the risk of misclassification was low. If there was CBD use, there was an 80% increase in the risk of IBS, but interestingly not in Blacks or females. The subgroup variation raises the possibility CBD may protect in some populations but worsen others. The results, while important, really ask more questions than they answer, but where there is smoke (CBD) there seems to be IBS.

Reference: Eur J Gastroenterol Hepatol 2019;31:756–65
Abstract

Efficacy of injection of freshly collected autologous adipose tissue into perianal fistulas in patients with Crohn's disease

Authors: Dige A et al.

Summary: Twenty-one patients with CD received injections of freshly collected autologous adipose tissues into complex perianal fistulae in this prospective study. Twelve participants experienced complete fistula healing at 6 months after the last injection, three had cessation of fistula secretion and one had reduced fistula secretion. Nine of ten participants with trans-sphincter or intersphincter fistulae experienced complete fistula resolution, with the other showing a markedly reduced gracile fistula. Among participants who experienced complete fistula healing, nine required a single injection, two required two injections and one required three injections. Postprocedure proctalgia lasting a few days was the predominant adverse effect. Two participants developed small abscesses, one developed urinary retention and one experienced minor bleeding during liposuction. The procedure could be repeated up to three times. Some patients refused a second procedure, which suggests it wasn’t as minor as the paper suggests, but the reported complications were not severe. The results in these patients who had failed previous treatment resulted in 57% complete healing and improvement in another 19%. This needs to be replicated, but is very hopeful for this group of difficult-to-treat patients.

Comment: Fistulodisease occurs in up to 20% of patients with CD and is difficult. Treatment usually requires both medical and surgical approaches, and at best getting 50% healing rates. Recently it has been reported stem cells from adipose tissue have achieved healing rates of up to 83%, but obtaining the cells is difficult and expensive. The study looks at using the nonadipocyte fraction of recently collected adipose tissue; this fraction is enriched for stromal stem cells, which form 10–50% of the cells in this fraction. The collected tissue was injected around the fistula in a surgical procedure. The procedure could be repeated up to three times. Some patients refused a second procedure, which suggests it wasn’t as minor as the paper suggests, but the reported complications were not severe. The results in these patients who had failed previous treatment resulted in 57% complete healing and improvement in another 19%. This needs to be replicated, but is very hopeful for this group of difficult-to-treat patients.

Reference: Gastroenterology 2019;156:2208–16
Abstract
Assessment of small bowel mucosal healing by video capsule endoscopy for the prediction of short-term and long-term risk of Crohn’s disease flare

Authors: Ben-Horin S et al., on behalf of the Israeli IBD Research Nucleus (IRN)

Summary: Adults with small-bowel CD quiescent for 3–24 months with confirmed small bowel patency (n=61) underwent baseline MRE and patency capsule, clinical or biomarker assessment every 3 months and VCE (video capsule endoscopy) at baseline and every 6 months for 2 years or until clinical flare or disease worsening requiring treatment intensification. The proportion of participants who experienced a flare (≥70-point increase in Crohn’s Disease Activity Index score) over 24 months was 28%. Predictors of future flares were a baseline VCE Lewis score of ≥3.5 (AUC 0.79 [95% CI 0.66–0.88]) and baseline CRP level (0.73 [0.6–0.84]); faecal calprotectin level was not a significant predictor over 2 years (0.62 [0.49–0.74]), but was over 3 months (0.81 [0.76–0.85]). MRE global score was the only of four MRE-based indices that correlated with the 2-year risk of flare (AUC 0.71 [95% CI 0.58–0.82]). No clinico-demographic parameter predicted flares. A Lewis score increase of ≥3.83 points from baseline significantly predicted disease exacerbation within 6 months (AUC 0.79 [95% CI 0.65–0.89]). The VCEs had excellent safety and tolerability, with none being retained.

Comment: The prediction of flares in quiescent CD is a difficult clinical question. This study looked at the use of VCEs as part of an intensive monitoring strategy to predict the future course of quiescent CD. VCE was compared to MRE, CRP level and faecal calprotectin level. Faecal calprotectin level was best at predicting short-term risk. VCE predicted both short- and long-term risk. CRP level also predicted risk fairly well. Importantly, 29 of 90 patients screened were excluded because of non-patent small bowels. Looking at it overall, while VCE may add some improvement in predicting flares, the cost seems to outweigh the benefit over the standard MRE, CRP level and faecal calprotectin level.


Events within the first year of life, but not the neonatal period, affect risk for later development of inflammatory bowel diseases

Authors: Bernstein CN et al.

Summary: The IBD risk in individuals who experience critical events at birth and during the first year of life was evaluated in this population-based study involving 825 patients with IBD and 5999 matched controls. A maternal diagnosis of IBD was identified as the greatest risk factor for IBD (OR 4.53 [95% CI 3.08–6.67]). The only significant risk factor for IBD among neonatal events was being in the highest versus lowest socioeconomic quintile (OR 1.35 [95% CI 1.01–1.79]) and the only significant risk factors among first year of life events were being in the highest versus lowest socioeconomic quintile at birth (1.37 [1.06–1.77]) and infections (1.39 [1.09–1.79]; infection increased the risk of an IBD diagnosis before age 10 and 20 years (3.06 [1.07–8.78] and 1.63 [1.18–2.24], respectively). GI infections, GI disease and abdominal pain during the first year of life did not influence IBD risk.

Comment: This retrospective study using an IDB database enabled an examination of risk factors for the development of IBD. The biggest risk factor in the neonatal period was maternal IBD, followed by being in the highest socioeconomic quintile. In the first year, highest socioeconomic quintile and infection carried the highest risk of IBD. The socioeconomic result may support the hygiene hypothesis, but the role of breastmilk also needs to be explored. The question whether it is the infection or the use of antibiotics is not answered. Antibiotics in the first year have been suggested to increase the risk of coeliac disease in other studies. GI illness in the first year did not increase the risk of IBD. The evidence suggests that the development of the microbiome in the first year is a key factor in later risk of IBD.

Reference: Gastroenterology 2019;156:2190–7

Follow-on RifAximin for the Prevention of recurrence following standard treatment of infection with Clostridium difficile (RAPID)

Authors: Major G et al., on behalf of RAPID Collaboration Group

Summary: Adults who had just experienced resolution of Clostridium difficile infection with metronidazole or vancomycin treatment were randomised to receive rifaximin 400mg three times a day for 2 weeks and then 200mg three times a day for 2 months (evaluable n=69) or placebo (evaluable n=61). Compared with placebo, rifaximin recipients had a nonsignificant trend for lower 12-week C. difficile infection recurrence (primary endpoint; 15.9% vs. 29.5%; risk ratio 0.54 [95% CI 0.28–1.05]). Adverse event and mortality rates were similar between the two groups.

Comment: The high rate of recurrence (15–30%) after C. difficile infection after primary treatment with antibiotics is thought to be related to a depleted microbiome, and this is reflected in newer treatments such as faecal transplant, more selective antibiotics and monoclonal antibodies to C. difficile toxins. Rifaximin has theoretical reasons to suppress C. difficile and allow regrowth of commensals. This study was an RCT to investigate the effectiveness of rifaximin to prevent recurrence of C. difficile infection. This was a difficult study to recruit, with 2157 being screened to find 300 suitable of whom one third were not suitable and 20% refused, meaning there were only 151 eligible and randomised patients prior to funding running out. There was a recurrence rate of 29.5% in the placebo arm compared with 15.9% in the treatment arm, giving a risk ratio of 0.54 (95% CI 0.28–1.05). There was no significant difference in side effects. The result is consistent with previous studies and suggests rifaximin is a useful agent for recurrent C. difficile infection.


Abstract

Independent commentary by Dr Ian Kronborg

After doing his medical training at Melbourne University Dr Ian Kronborg worked at the RMH and completed his gastroenterology fellowship. He then worked at The WEHI and went overseas to complete his training at the University of Southern California. He returned to Australia and worked at Western Health eventually becoming Head of Gastroenterology and Clinical Services Director for Medicine. He also established the Drug and Alcohol service and was lead clinician for IT in Western Health. He has published research in hepatology, IBD and addiction. Currently he continues an active research program and works in private practice.

Contact

geoff@researchreview.com.au

Phone 1300 132 322
Superiority of gastrojejunostomy over endoscopic stenting for palliation of malignant gastric outlet obstruction

Authors: Jang S et al.
Summary: Outcomes and factors associated with clinical success were reported for patients with malignant gastric outlet obstruction, comparing those who underwent endoscopic SEMS placement (n=183) with those who underwent gastrojejunostomy (n=127), in this retrospective, propensity score-matched research. There was no significant difference between the SEMS versus gastrojejunostomy group for clinical success rate (resumption of oral intake and relief of obstructive symptoms; 79.4% vs. 80.1% [p=0.83]), but gastrojejunostomy was associated with significantly longer mean patency duration (169.2 vs. 96.5 days) and survival (193.4 vs. 119.9 days). Independent risk factors for failure of enteral stenting and gastrojejunostomy were poor performance status, presence of ascites and low albumin level.

Comment: Malignant gastric outlet obstruction is a common but unpleasant complication in advanced upper GI malignancies. Gastrojejunostomy (open or laparoscopic) is the standard surgical approach. Recently SEMS has been used and trial results have been unclear. This retrospective study looked at SEMS (n=183) or gastrojejunostomy (n=127) at a single centre between 2011 and 2017. Clinical success was 80% in both groups, but patency and survival were significantly better in the surgical group. Outside of the procedure, nutritional status, ascites and preprocedure performance status were predictors of outcome. The problem is this is a retrospective study and bias in selection of the patients cannot be excluded. However, on the basis of these data, at this time, surgery is the intervention of choice in malignant gastric outlet obstruction.

Abstract:

PBS Information: Authority required for the treatment of adults with severe active rheumatoid arthritis and for adults with severe active psoriatic arthritis. Refer to the PBS schedule for full authority information. This product is not listed on the PBS for ulcerative colitis.

Before prescribing, please review full Product Information available from www.xeljanz.com.au


© 2019 RESEARCH REVIEW