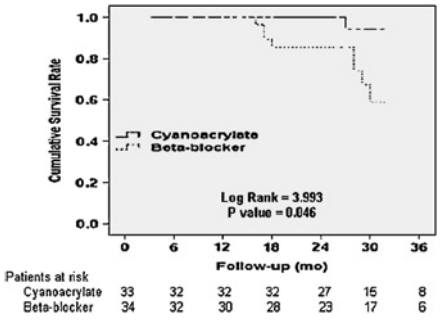
doi:10.1136/gut.2010.216283

Emad El-Omar, Severine Vermeire and Alexander Gerbes, *Editor and Deputy Editors*

Prevention of rebleeding from gastric varices: cyanoacrylate injection is superior to beta-blockers

Many studies have investigated the prophylaxis of rebleeding from oesophageal varices in patients with liver cirrhosis. In contrast, little information is available regarding secondary prophylaxis of gastric variceal bleeding. This clinically important trial Mishra *et al* compared the efficacy of beta-blocker therapy with cyanoacrylate injection for the prevention of gastric variceal rebleeding in 67 patients. The probability of gastric variceal rebleeding rate in the cyanoacrylate group was significantly lower than in the beta blocker group (15% vs 55%) during a median follow-up of 26 months. More importantly, mortality rate was significantly reduced upon endoscopic treatment. Gastric variceal rebleeding independently correlated with mortality. ***See page 729***.



Cyanoacrylate improves survival upon gastric variceal bleeding.

Azathioprine versus mesalazine for prevention of postoperative clinical recurrence in crohn's disease patients: randomised double-blind multicentre trial

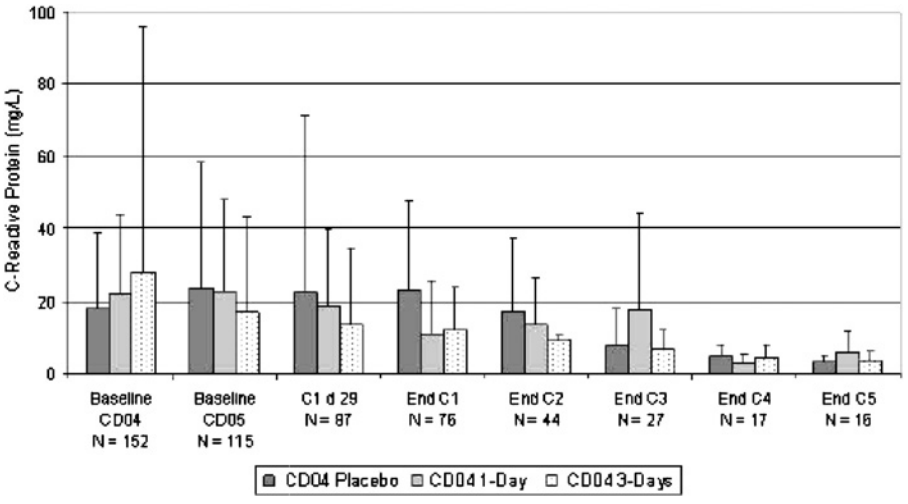
Surgical resection for Crohn's disease (CD) has shown not to be curative as many patients develop recurrence of their disease in the neoterminal ileum. Despite this observation, the therapeutic options for prevention of postoperative recurrence are limited. Although the best evidence exists for azathioprine, studies are not overwhelmingly convincing. In this one-year, double-blind randomized multicentre study, the authors compared azathioprine and mesalazine for prevention of post-surgical CD recurrence. A total of 78 adults with ileocaecal resection for CD and endoscopic recurrence but symptom free were randomized to azathioprine 2.0–2.5 mg/kd/day or mesalazine 4 g/day for 1 year. The primary endpoint was therapeutic failure, defined as CDAI score ≥200 and an increase of ≥60 points. The primary endpoint occurred in 22.0% (9/41) of azathioprine patients and 10.8% (4/37) of mesalazine patients (p=0.19). Clinical recurrence was significantly less frequent with azathioprine versus mesalazine (0% vs 10.8%, p=0.031), whereas study drug discontinuation due to adverse events only occurred in azathioprine-treated patients (22.0% vs 0%, p=0.002). The authors conclude that superiority for azathioprine versus mesalazine could not be demonstrated for therapeutic failure. ***See page 752***.

Change in endoscopy findings from baseline to final examination

Intention-to-treat	Azathioprine	Mesalazine	p Value
Rutgeerts' score: decrease ≥1 point	19 (63.3%) (n=30)	11 (34.4%) (n=32)	0.023*
Rutgeerts' score: median change (range)	−1.5 (−4.0, −2.0)	0 (−3.0, 2.0)	0.007†
N (%) of patients with Rutgeerts' score at final visit:			
(i_0) No lesions	7 (17.1%)	5 (13.5%)	
(i_1) ≤5 aphthous lesions	5 (12.2%)	4 (10.8%)	
(i_{2a}) >5 aphthous lesions	5 (12.2%)	3 (8.1%)	
(i_{2b}) Lesions confined to the ileocolonic anastomosis	4 (9.8%)	1 (2.7%)	
(i_3) Diffuse aphthous ileitis with diffusely inflamed mucosa	3 (7.3%)	4 (10.8%)	
(i_4) Diffuse inflammation with large ulcers	6 (14.6%)	15 (40.5%)	
Missing	11 (26.8%)	5 (13.5%)	
CDEIS score: mean change±SD	−2.68±4.38 (n=29)	−0.55±3.66 (n=33)	0.045†

Intravenous semapimod for moderate-to-severe Crohn's disease

Semapimod, a small molecule known to inhibit pro-inflammatory cytokine activity has been shown to be clinically and endoscopicaly beneficial, when given intravenously, in an open-label pilot study in patients with moderate-to-severe CD.



CRP changes over time for placebo-treated and Semapimod-treated patients.

In the randomized, double blind, placebo-controlled multicentre study (CD04), published in this issue of GUT, the authors determined the optimal dose of semapimod necessary to achieve a response in CD. Participants who completed CD04 could participate in the open-label extension study, CD05. The main outcome measures included Crohn's disease activity index (CDAI), Crohn's Disease Endoscopic Inflammation Score (CDEIS), and serum C-reactive protein (CRP) changes. 152 patients were randomized in CD04. Responses for one- and three-day regimens were similar to placebo for CDAI, CDEIS and CRP (all non significant). There were however more infusion reactions (phlebitis) noted in the semapimod treated patients as compared to the placebo group. The authors conclude that single and three-day dosing of Semapimod was ineffective for the treatment of moderate-to-severe CD. ***See page 760***.

White light vs autofluorescence video endoscopy for adenoma detection in high-risk subjects

High risk patients with Lynch syndrome (LS) or familial colorectal cancer (CRC) families require regular and accurate colonoscopic surveillance. Standard while light endoscopy (WLE) misses 2–26% of adenomatous polyps and flat and depressed adenomas are often invisible to WLE. Ramsoekh *et al* compared the sensitivity of autofluorescence endoscopy (AFE) and (WLE) for the detection of colorectal adenomas in such high risk patients. They conducted a prospective single-centre study with 75 asymptomatic patients originating from LS or familial CRC families. WLE examination was followed by AFE or AFE followed by WLE. Back-to-back colonoscopy was performed by two blinded endoscopists. All lesions were removed during the second endoscopic procedure. WLE identified adenomas in 28/41 patients and AFE in 37/41 patients, corresponding to a 32% increase and most of the lesions missed by WLE were small. AFE had a significantly higher sensitivity compared with WLE (92% vs 68%; $p< 0.001$) and the authors advocate this approach to surveillance for such high risk patients. ***See page 785***.

Adenoma detection rate and size per patient group

Patient group	Lynch syndrome	Familial colorectal cancer
Adenoma-positive patients (n)	14	27
Adenoma (n)		
WLE+AFE	17	40
WLE only	4	4
AFE only	9	21
Mean size (±SD)		
WLE+AFE	6.1 (±2.3) mm	4.8 (±1.7) mm
AFE only	3.0 (±1.3) mm	3.1 (±1.1) mm

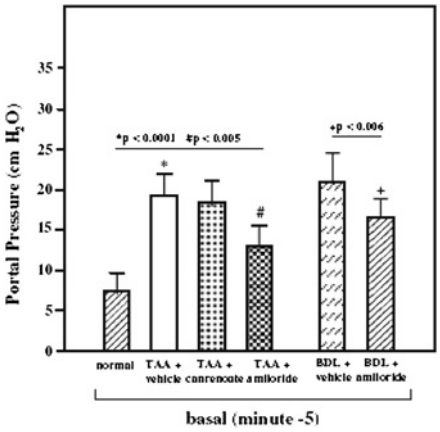
AFE, autofluorescence endoscopy; WLE, white light endoscopy.

Dietary folate, alcohol, and B vitamins and hypomethylation in colon cancer

Genome-wide DNA hypomethylation is believed to play an important role in genomic instability and carcinogenesis. Long interspersed nucleotide element-1 (LINE-1) hypomethylation is associated with poor prognosis of colon cancer. Folic acid and related B vitamins are essential for DNA methylation and adequate dietary intake of these nutrients has previously been related to a lower colon cancer risk while alcohol consumption increases colorectal this risk, possibly through its anti-folate effects. In this study, Schernhammer *et al* examined the association between dietary intake of folate, alcohol and B vitamins and LINE-1 hypomethylation in 609 incident colon cancers, utilising the database of two independent prospective cohort studies. They found that low folate and, to a lesser degree, vitamin B6 intake and excess alcohol consumption were associated with increased risk of colon cancers with LINE-1 hypomethylation. The elevation in risk was principally limited to participants with the lowest levels of folate and vitamin B6 intake. The findings support a possible aetiological link between deficiency in some one-carbon nutrients and genome-wide DNA hypomethylation during colorectal carcinogenesis. ***See page 794***.

Amiloride for prophylaxis of variceal bleeding?

Variceal bleeding is a life-threatening complication of portal hypertension in liver disease. An immediate increase in portal pressure is one of the major causes of variceal bleeding and activation of Kupffer cells plays an important role in this increase. This interesting paper investigates the role of the hepatic stellate cells, which are contractile cells in the liver. Amiloride, well known as diuretic drug, also inhibits the activity of hepatic stellate cells. The infusion of amiloride attenuated the Kupffer cell mediated portal pressure increase in perfused rat livers. The treatment with amiloride over 3 days reduced the basal and the maximal portal pressure in rats with experimental cirrhosis. Therefore, the treatment with amiloride might reduce the risk of variceal bleeding in patients with cirrhosis – a hypothesis which deserves testing in a clinical trial. ***See page 827***.



Amiloride but not canrenoate, reduces basal and maximal portal pressure in rat liver cirrhosis (TAA).