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Being cautious with clopidogrel ►

▲ Chan FKL, Ching JYL, Hung LCT, *et al*. Clopidogrel versus aspirin and esomeprazole to prevent recurrent ulcer bleeding. *N Engl J Med* 2005;**352**: 238–44.

Clopidogrel prevents vascular ischaemic events by inhibiting the platelet adenosine diphosphate receptor and causes fewer gastrointestinal bleeds compared with aspirin. It is indicated for patients that need an antiplatelet drug but are unable to take aspirin because of a previous gastrointestinal bleed. The efficacy of this approach compared with aspirin and acid suppression is unclear.

Chan *et al* evaluated this in a randomised double blind controlled trial of 320 patients who presented with a peptic ulcer bleed on aspirin. All were *Helicobacter pylori* negative or had the infection successfully treated and the ulcer was healed with acid suppression. A total of 161 patients were randomised to receive clopidogrel 75 mg daily and 159 aspirin 80 mg daily plus esomeprazole 20 mg twice daily. Patients were followed up for one year and recurrent peptic ulcer bleeding occurred in 13 of the clopidogrel group compared with one of the aspirin–esomeprazole group (absolute difference in rate 7.9% (95% confidence interval 3.4–12.4%)).

This is another well designed and important trial on the prevention of ulcer bleed from Hong Kong. It is unfortunate that an aspirin only arm was not included in the design to assess whether clopidogrel is safer than aspirin in this group of patients, but the authors felt this was unethical. These data however suggest that aspirin plus a proton pump inhibitor is a safer alternative to clopidogrel in high risk patients.

Use MRCP before ERCP ►

▲ Makary MA, Duncan MD, Harmon JW, *et al*. The role of magnetic resonance cholangiography in the management of patients with gallstone pancreatitis. *Ann Surg* 2005;**241**:119–24.

After recovery from acute gall stone pancreatitis, 20–30% will have persistent bile duct stones which can result in recurrent attacks of pancreatitis. This has led clinicians to recommend the use of routine endoscopic retrograde cholangiopancreatography (ERCP) to identify persistent duct stones and perform sphincterotomy and stone extraction if appropriate. ERCP is not however without complications and carries a major complication rate of approximately 1%, mainly due to acute pancreatitis, bleeding, perforation, and cholangitis.

In this study, patients with gall stone pancreatitis underwent magnetic resonance cholangiography (MRC) to identify duct stones to determine whether this might reduce the need for ERCP in this group of patients. Only 17 of 64 patients (27%) were found to have duct stones, the presence of which was confirmed by ERCP.

The need for ERCP can be reduced by using MRC to detect common bile duct stones preoperatively in patients with gall stone pancreatitis prior to laparoscopic cholecystectomy, potentially reducing complications related to diagnostic ERCP. The role of ERCP is changing and in patients who have recovered from acute gall stone pancreatitis it should be confined to patients with stones confirmed on non-invasive imaging.

It helps to be more human: Adalimimab in infliximab failed Crohn's ►

▲ Papadakis KA, Shaye OA, Vasiliauskas EA, *et al*. Safety and efficacy of Adalimumab (D2E7) in Crohn's disease patients with an attenuated response to Infliximab. *Am J Gastroenterol* 2005;**100**:75–9.

As the use of Infliximab spreads, more patients will lose responsiveness to the drug. In some this may be because of antibody development to the murine portion of infliximab (ATI), particularly in those not taking concomitant immunosuppression or who do not have regular maintenance infusions. (However up to 75% of those losing responsiveness may not have ATI.)

In a retrospective study from Los Angeles, Papadakis *et al* report the use of Adalimumab, a recombinant fully human IgG1 antibody to TNF, to treat 15 patients who have lost responsiveness to Infliximab. The starting dose was 80 mg subcutaneously, then 40 mg fortnightly. In six of these, the response was not maintained, and the dose was increased to as much as 80 mg weekly. Fifty four per cent had a complete and 31% a partial response. This is similar to results from Sandborn *et al*'s study (*Am J Gastroenterol* 2004;**99**:1984) who treated 24 patients either with acute or delayed infusion reaction, or who had lost response to infliximab (59% response, 29% remission over 12 weeks). Again, most required a dose increase to achieve response. No patient in either study had acute or delayed hypersensitivity reactions (although some had an injection site reaction). Although fully human, it is clear from rheumatoid arthritis studies that antibodies can develop to Adalimumab.

These response rates are not dissimilar to those obtained in Infliximab naïve patients but it appears that larger doses are needed, which will be costly. Similar response rates were observed in Natalizumab treated patients in the ENACT-1 study who received prior Infliximab. These are useful alternatives for Infliximab failures. I wonder whether we will see adequately powered head to head comparisons of these agents as primary biological therapy in Crohn's.

Fate of the ''presumed dead'' ►

▲ Radkowski M, Gallegos-Orozco JF, Jablonska J, *et al*. Persistent of hepatitis C virus in patients successfully treated for chronic hepatitis C. *Hepatology* 2004;**41**:106–14.

Standard combination therapy with interferon/ribavirin for chronic hepatitis C achieves ''sustained response'' with clearance of hepatitis C virus (HCV) RNA, normalisation of liver enzymes, and improvement in liver histology in approximately half of those treated. This has often been assumed as a ''cure''. Radkowski *et al* collected serum, peripheral blood mononuclear cells, and liver biopsies from 17 patients with ''sustained virological response'' over a mean period of 64 months after the end of treatment. In addition, lymphocyte and macrophage cultures were established. Using sensitive reverse transcriptase-polymerase chain reaction, the authors identified residual RNA in 15 (88%) subjects. HCV RNA was found in macrophages from 11 (65%), in lymphocytes from 7 (41%), in serum from 4 (24%), and in the liver from 3/11 (37%) tested. Residual viral loads were very low but it appears that HCV RNA persists in the tissues of the majority of sustained responders for up to nine years.

These results warn us against equating ''sustained virological response'' with a cure. Although recurrence of HCV infection (as defined as reappearance of RNA in serum) has been reported to be below 2% so far, the length of follow up of patients treated is still limited. Whether persistent HCV RNA could be associated with clinical exacerbations in immunosuppressed individuals similar to the phenomenon seen with hepatitis B virus infection is unclear at present.