A PROSPECTIVE RANDOMISED TRIAL OF SEDATION vs. NO SEDATION IN DIAGNOSTIC UPPER GASTROINTESTINAL ENDOSCOPY

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Introduction: Gastroenterologists differ in their use of sedation in upper gastrointestinal endoscopy. There have been few studies comparing sedation and non-sedation, and we sought to clarify this by a prospective, randomised controlled trial.

Methods: Out-patients referred for diagnostic endoscopy were invited to participate in our study. Only patients with a history of dysphagia were excluded. Subjects were randomised and informed in advance. All patients were given lansoprazole throat spray prior to the procedure. The endoscopist recorded duration of procedure, no. of biopsies taken, occurrence of anyrhynisms or hypoxia, and the degree of ease of the procedure on a numerical scale. Patients were given a questionnaire with numerically graded answers and asked to complete this not less than 24hrs after the procedure.

Results: 282 patients invited before 100 agreed to participate (77.1%). 50 patients in each arm. No biopsies was well-matched (mean 1.33 in each group), mean duration of procedure lower in non-sedated group (3min 25sec vs. 4min 5sec). Procedure slightly easier in non-sedated group (1.5 vs. 1.70 on scale of 1 to 5). One patient converted from no sedation to sedation.

Non-sedated group found procedure more unpleasant (2.53 vs 1.23 on scale of 1 to 5) and were slightly less willing to have procedure done in same manner in future (1.35 vs 1.90), but only 6/50 would prefer procedure to be done with sedation next time.

Conclusions: Endoscopy faster and easier in non-sedated group. These patients find procedure more unpleasant, but do not mind procedure repeated in same way in future.

Biliary

EARLY GALLBLADDER EMPTYING IS MEDIATED BY CHOLECYSTOKININ.

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Gallbladder emptying (GE) occurs in response to cholecystokinin (CCK), released as fat and protein enter the small bowel. However, GE often occurs within 10 minutes of eating, before gastric emptying can possibly have occurred. This study investigates mechanisms of early GE.

GE was measured ultrasonically in 8 healthy male volunteers (median age 35 years) on three separate occasions in random order: 1) after ingestion of two eggs omelette, 2) following sham feeding to examine a cephalic phase, 3) after gastric distension to 500ml using effervescent powder. Blood samples were taken for CCK radioimmunoassay.

Mean fasting gallbladder volumes were similar on each study day. Mean fasting CCK was 6.3±0.8(SE) ng/L. The fatty meal was followed by immediate GE at a rate of 0.57ml/min, with ejection fraction (EF) of 25% by 10 minutes. This was associated with increase in immunoactive CCK concentration to 10±1.32 ng . A slower phase of GE followed at the rate of 0.19ml/min, with EF of 90% at 10 minutes. The later phase of GE was accompanied by a plateau CCK concentration at 9.5±1.5 ng/L. Sham feeding stimulated GE in two individuals (EF of 25% at 90 minutes) who both exhibited increase of plasma CCK concentration to 13±3ng/L. Subjects who did not exhibit GE had no such increase in CCK. Gastric distension was not followed by GE and CCK concentration did not increase.

Early GE was accompanied by an increase in plasma CCK. This is unlikely to be due to entry of nutrients into the small bowel or to gastric distension. With sham feeding, some individuals showed a cephalic phase of GE which was associated with CCK. These observations suggest that 'central' rather than intestinal factors are important in CCK release and early GE.

THE RELATIONSHIP BETWEEN LARGE BOWEL TRANSIT TIME (LBBT) AND THE PROPORTION OF DEOXYCHOLIC ACID (%DCA) IN SERUM.

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Background: Prolongation of intestinal transit and an associated increase in the %unconjugated DCA in gallbladder (GB) bile have been implicated in the pathogenesis of cholesterol gallstones. Since there is a dynamic exchange between the bile acid pools in the serum and bile, measurement of serum DCA levels provides a simple, non-invasive way of measuring the %DCA in total bile acids. Moreover, there are few data on the relationship between %unconjugated DCA in serum and the %unconjugated and conjugated fractions of fasting serum, by gas chromatography-mass spectrometry. We then calculated the correlation coefficients (r) for the plots of LBBT against %unconjugated DCA (%), %unconjugated DCA and %DCA in serum total bile acids.

Methods: We, therefore, measured large bowel transit time (LTBT), by a radio-opaque marker shape technique, in a heterogeneous group of individuals (n=32, age range 22-67, 15 women), selected in anticipation of a wide range of spontaneous variations in LBBT, and the %DCA in the unconjugated and conjugated fractions of fasting serum, by gas chromatography-mass spectrometry. We then calculated the correlation coefficients (r) for the plots of LBBT against (% of unconjugated DCA (%), %unconjugated DCA and %DCA in serum total bile acids.

Results: The mean LBBT was 47±5.6(SE) h (range 2-72h). The mean %DCA in the unconjugated serum bile acids was 31±2.9% (range 2-71%) and in the conjugated serum bile acids, 19±2.1% (range 3-52%). There were significant linear relationships between LBBT and %DCA in both the unconjugated (r=0.74, p<0.0001) and the conjugated (r=0.82, p<0.0001) fractions, and also between LBBT and the %DCA in the total serum bile acids (r=0.80, p<0.0001).

Summary: In this study, we have shown that there is a direct relationship between large bowel transit time and both the %unconjugated and conjugated DCA in serum and, therefore, by implication the %unconjugated DCA in GB bile. This suggests that changes in intestinal transit alter the bile acid profile in GB bile and, therefore, the risk of gallbladder stone formation.
HIGH-DOSE URSODEOXYCHOLIC ACID IN PRIMARY SCLEROSING CHOLANGITIS: A RANDOMISED DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL.

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Previous trials of ursodeoxycholic acid (UDCA) therapy in primary sclerosing cholangitis (PSC) have shown varying results. Aims: We now report the results, at one year, of a double-blind placebo controlled trial of high-dose (20mg/kg/day) UDCA in PSC. Methods: Twenty-three patients (16 male, mean age 53 years, range 23-80), 18 with ulcerative colitis, were randomised to UDCA (n=12) or placebo (n=11). All patients had pre-trial liver biopsy and cholangiography. One patient in the UDCA group was withdrawn from the study after 6 months with a dominant bile duct stricture which required stenting.

Results: UDCA group Placebo group

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<tr>
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<th>At entry (mean)</th>
<th>At 1 year (mean)</th>
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<tbody>
<tr>
<td>Bilirubin (N&lt;17µmol/l)</td>
<td>16.09</td>
<td>13.82 (NS)</td>
</tr>
<tr>
<td>ALP (N&lt;250 IU/l)</td>
<td>762.55</td>
<td>399.54 (S)</td>
</tr>
<tr>
<td>AST (N&lt;42 IU/l)</td>
<td>85.18</td>
<td>37.64 (NS)</td>
</tr>
<tr>
<td>G-TOT (N&lt;40 IU/l)</td>
<td>426.64</td>
<td>104 (S)</td>
</tr>
<tr>
<td>Albumin (N: 35-50g/l)</td>
<td>42.55 (NS)</td>
<td>41.09</td>
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S= significant, p<0.05, NS = not significant (paired Student's t-test).

The two groups did not differ significantly from each other at entry. Notably, no side effects of UDCA treatment were reported, despite the high dose used. There was improvement in the serum levels of ALP, AST, bilirubin and G-TOT in the UDCA group and this was significant for G-TOT and ALP. No clear improvement in symptoms was noted, although 13 patients were asymptomatic at entry. Conclusion: In patients with PSC, high-dose UDCA is well tolerated and associated with significant improvement in G-TOT and ALP after 1 year of treatment.

GUT BARRIER DYSFUNCTION IN OBSTRUCTIVE JAUNDICE

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Introduction. Gut barrier dysfunction has been implicated in the pathophysiology of complications of obstructive jaundice. Bacterial overgrowth and physical injury of the gut mucosa may promote bacterial translocation. This study investigates the effect of obstructive jaundice on the indigenous microbiology and gut mucosa in relation to bacterial translocation.

Methods. Three groups of Wistar rats (controls, sham operation, bile duct ligation (BDL)) were studied in two experiments.

1. Quantitative and qualitative aerobic cultures were performed from the mesenteric lymph nodes, liver, spleen and caecum.
2. Morphometric assessment of segments of jejunum, ileum, caecum and colon was performed using a computerised image analysis system.

Results. (1) Significant bacterial translocation and overgrowth of gram negative aerobes was demonstrated following 7 days bile duct ligation. (2) There was morphometric evidence of injury to the ileal mucosa. Results are expressed as mean (SEM).

<table>
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<tr>
<th>Internal measurements (µm)</th>
<th>Mucosal thickness</th>
<th>Villous height</th>
<th>Crypt depth</th>
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<tbody>
<tr>
<td>Control</td>
<td>744 (95)</td>
<td>559 (79)</td>
<td>183 (19)</td>
</tr>
<tr>
<td>Sham</td>
<td>73 (27)</td>
<td>515 (18)</td>
<td>193 (11)</td>
</tr>
<tr>
<td>BDL</td>
<td>650 (23) *</td>
<td>451 (29) *</td>
<td>180 (8)</td>
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</table>

*p<0.02, Mann-Whitney U test.

Conclusion. These data demonstrate morphometric changes, bacterial overgrowth and bacterial translocation, supporting the hypothesis of gut barrier dysfunction in obstructive jaundice.

RAPID AND SUCCESSFUL CHOLANGIOGRAPHY AT ERCP USING GLYCERYL TRINITRATE (GTN) AND GLUCAGON

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Even experts can fail to cannulate the common bile duct (CBD) at the index ERCP. Sublingual GTN and i.v. glucagon (IVG) are known to relax the sphincter of Oddi, and sublingual GTN spray given before ERCP has been shown to increase the chance of success. To test the hypothesis that giving both drugs together would improve the speed and success of CBD cannulation we performed a prospective, randomised double-blind trial in patients referred to our ERCP service.

Patients were randomised to receive placebo (n=41), sublingual GTN spray (6 puff, i.e. 2.4 mg; n=41), or IVG (1 mg) plus GTN (n=41), before attempted CBD cannulation with a diagnostic cannula (Wilson Cook, GT-1-T). If by 5 min cholangiography had not been achieved the first endoscopist gave way to the other who had a further 5 min. Thereafter, other techniques could be used to achieve CBD cannulation. Most cases were started by the senior registrar (107/123) rather than the consultant. Exclusion criteria were papillary tumour or previous sphincterotomy.

Using cholangiography as the end point, the following success rates were achieved:

<table>
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<tr>
<th>Drug</th>
<th>Placebo</th>
<th>GTN</th>
<th>GTN &amp; IVG</th>
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<tr>
<td>5min</td>
<td>23/41 (56.1%)</td>
<td>32/41 (78.1%)</td>
<td>36/41 (87.8%)</td>
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<td>10min</td>
<td>26/41 (63.4%)</td>
<td>35/41 (85.4%)</td>
<td>41/41 (100%)</td>
</tr>
<tr>
<td>Overall</td>
<td>39/41 (95.1%)</td>
<td>39/41 (95.1%)</td>
<td>41/41 (100%)</td>
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At both 5min and 10min, successful cholangiography was greater with GTN & IVG than for GTN alone (p < 0.04), which in turn was greater than placebo (p < 0.004). Overall success rate was 119/123 (96.7%). In 2 cases where cholangiography failed, an expectant approach was adopted, and 2 patients had a second successful ERCP. Pre-cut papillotomy was not used in any case.

These findings suggest that a combination of GTN and I.v. glucagon can significantly increase the speed and success of biliary cannulation at the index ERCP.

BILIARY IMAGING BY SPIRAL CT CHOLANGIOGRAPHY

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Following intravenous injection of biliary contrast, Spiral Acquisition Computerised Tomography allows the acquisition of volumetric data enabling three dimensional reconstruction and multi-angle projections of the biliary tree. Scans were acquired using a Picker PQ2000. Oral biliary contrast (Sodium Iopdate 3g) was given 14 hours and 3 hours before scanning to fill the gallbladder. 150mls of Meglumine Iotroate (50mg/ml) [Biliscopin, Schering AG, Germany] was infused intravenously over 80 minutes before scanning followed by 20mg of Buscopan. An initial spiral scan was performed through the upper abdomen to localise the biliary tree using a collimated slice thickness of 10mm with a pitch of 1, allowing a coverage of 21cm. A second scan was then performed with a collimated slice thickness 2-3 mm with a pitch of 1 to 1.5 during a single breath hold. The axial images were indexed at 1mm. The data collected were used to reconstruct the biliary tree using surface shading (3D) and multi-planer reconstruction methods. Scans were performed in 30 patients, 7 of whom had previously undergone failed ERCP. Satisfactory scans showing complete biliary anatomy including cystic duct insertion and anatomical variations of hepatic ducts were obtained in 29 patients (97%). Pathology was demonstrated in 4 patients - common bile duct stones (2), benign common bile duct stricture (1) and papillary stenosis in a patient with scleroderma (1). All patients with both abnormal and normal scans have had the findings confirmed by alternative means or by uneventful clinical follow-up. All patients tolerated the procedure well. SCTC is an attractive non-invasive method of biliary imaging producing high definition pictures of the biliary tree.
Liver F218-F227

ANTI NEUTROPHIL CYTOPLASM AUTOANTIBODIES (ANCA) AGAINST BACTERICIDAL/PERMENABILITY-INCREASING PROTEIN IN PRIMARY SCLEROSING CHOLANGITIS. R.S. Walmley, M.Zhao*, M.J. Hamilton, A.Brownlee*, P.Chapman*, J.S. Dooley, A.J. Wormald, C.M. Lockwood*. Inflammatory Bowel Disease Study Group, Department of Medicine, Royal Free Hospital Medical School, London, UK. *Department of Medicine, School of Clinical Medicine, University of Cambridge, UK.

Background: In primary sclerosing cholangitis (PSC) the ANCA target antigen remains obscure. Bactericidal/permeability-increasing protein (BPI) has been described as an ANCA antigen in cases of systemic vasculitis where the target antigen is neither myeloperoxidase (MPO) nor proteinase-3 (PR3). BPI has high affinity for gram negative bacterial lipopolysaccharide and attenuates its pro-inflammatory action on monocytes and endothelial cells. Aim: To investigate the prevalence and clinical relevance of anti-BPI ANCA antibodies in PSC.

Methods: Sera were studied from 34 patients with PSC (20 prior to liver transplantation), 25 patients with primary biliary cirrhosis (PBC), 11 with autoimmune hepatitis (AIH) and 30 patients with non-auto immune biliary tract disease. Indirect immunofluorescence for ANCA was performed on alcohol fixed neutrophils, and solid phase ELISA for PR3, MPO, Cathepsin G, lactoferrin and BPI antibodies. Results were analysed with respect to extent, stage of disease and history of cholangitis.

Results: 6/34 (18%) of PSC, 12/25 (48%) of PBC and 3/30 (10%) of controls had P-negative ANCA. 16/34 (47%) of PSC, 12/25 (48%) of PBC and 4/30 (13%) of controls had BPI positive ANCA. 2/34 (6%) of PSC, 2/25 (8%) of PBC and 0/30 (0%) of controls had pBPI positive ANCA. The frequency of ANCA was higher in those with liver disease compared with those with biliary tract disease (p=0.003).

Conclusions: ANCA antibodies to BPI are important in PSC and PBC. The presence of anti-BPI antibodies may aid in the diagnosis of these diseases.


Elevated levels of Hyaluronic Acid (HYA) are associated with sinusoidal capillarisation, for example in hepatic cirrhosis. Liver biopsy is important in assessing severity and progression of disease in chronic hepatitis C virus (HCV) infection particularly with respect to α-Interferon therapy. The aim of this study was to evaluate the role of serum HYA in detecting cirrhosis in patients with HCV infection compared with cirrhosis of other aetiologies.

Methods: Serum HYA was measured, using a radiometric assay (Pharmacia, Sweden) in 69 patients with HCV infection and 152 patients with chronic liver disease of other aetiologies (alcohol, n=70; autoimmune chronic active hepatitis, n=23; primary biliary cirrhosis, n=17; cryptogenic, n=15 and various, n=27).

Results: HYA levels (um/l) were significantly higher in patients with cirrhosis of the liver (mean 440; 95% CI 367-515) compared with hepatic fibrosis (mean 23; 95% CI 69-160), chronic hepatitis (mean 60; 95% CI 37-91) and fatty liver (mean 117; 95% CI 37-177). Within the cirrhotic population there was no significant difference in HYA levels between different aetiologies. primary biliary cirrhosis (mean 500; 95% CI 323-678), alcoholic cirrhosis (mean 61; 95% CI 366-631), autoimmune chronic active hepatitis (mean 12; 95% CI 12-238), cryptogenic cirrhosis (mean 14; 95% CI 22-338) and chronic hepatitis C infection (mean 15; 95% CI 203-570).

Conclusions: Measurement of HYA levels can reliably differentiate cirrhotic from non-cirrhotic liver disease of different aetiologies. This is of important clinical significance in chronic HCV infection; for example in HCV infected haemophiliacs or in HCC surveillance.