

Gastroenterology elsewhere

Søgaard KK, Horváth-Puhó E, Grønbaek H, *et al.* **Risk of venous thromboembolism in patients with liver disease: a nationwide population-based case–control study.** *Am J Gastroenterol* 2009;104:96–101.

Liver disease is known to cause an imbalance in the coagulation system, but existing studies on liver disease and risk of venous thromboembolism (VTE) are few and conflicting. This study nationwide Danish case–control study looks at the risk of VTE in patients hospitalized with liver diseases. Incident cases of VTE (n=99,444) from 1980 to 2005, and 496,872 population controls were included.

Conditional logistic regression was used to compute the relative risk of VTE in patients with liver disease compared to population controls. Patients with known risk factors like malignancy (diagnosed either before or up to 3 months after VTE), fractures, trauma, surgery, or pregnancy within 90 days before VTE were excluded to estimate the risk associated with unprovoked VTE. For analysis, there were 67,519 cases with unprovoked VTE (deep VTE n=36,959, pulmonary embolism n=30,560) and 308,614 controls. Slightly more cases were women than men and one-third of both cases and controls were older than 75 years.

Patients with liver disease had an increased relative risk of VTE – 1.74 (95 % CI, 1.54 – 1.95) for cirrhosis and 1.87 (95 % CI, 1.73 – 2.03) for non-cirrhotic liver disease. The risk was higher for deep venous thrombosis compared with pulmonary embolism. For unprovoked VTE, relative risks were higher – 2.06 (95 % CI, 1.79 – 2.38) for cirrhosis and 2.10 (95 % CI, 1.91 – 2.31) for non-cirrhotic liver disease. There was a decreasing risk of VTE over time both for cirrhosis and non-cirrhotic liver disease; this may be because of the standard use of antithrombotic prophylaxis.

Thus, liver diseases are strong risk factors for VTE, and other unidentified risk factors for venous thrombosis supersede any decrease in coagulation associated with liver disease.

Regueiro M, Schraut W, Baidoo L, *et al.* **Infliximab prevents Crohn's disease recurrence after ileal resection.** *Gastroenterology* 2009;136:441–50.

Almost 75% of patients with Crohn's disease require an intestinal resection for complications related to stricturing or penetrating disease. Surgery for Crohn's disease is not curative and almost 70%–90% of patients have endoscopic evidence of recurrent disease one year after surgery. Several studies have evaluated the efficacy of medications for prevention of postoperative recurrence, with most therapies showing little benefit. Infliximab, which is effective for the induction and maintenance of moderate to severely active

Crohn's disease, has been shown to be beneficial in preventing postoperative recurrence in open-label studies.

This single center, randomized, placebo-controlled study investigated the efficacy of infliximab to prevent endoscopic, clinical, and histologic Crohn's disease recurrence one year after intestinal resection. Twenty-four patients with Crohn's disease who had undergone ileocolonic resection were randomly assigned to receive intravenous infliximab (5 mg/kg at 0, 2, and 6 weeks, followed by every 8 weeks for 54 weeks; n=11) administered within 4 weeks of surgery and continued for 1 year, or placebo (n=13). Patients on corticosteroids and antibiotics discontinued these medications within 12 weeks of surgery. Patients on concomitant immunomodulators and mesalamine were included if the medication dose was stable 12 weeks before surgery and remained constant throughout the duration of study.

There were more active smokers (45.5% vs 7.7%; $P=0.06$), and a trend for less concomitant immunomodulators use (36.4 vs 53.8%; $P=0.44$) or mesalamine use (9.1% vs 30.8%; $P=0.33$) in the infliximab group. The baseline ESR and CRP concentrations were higher in the infliximab group.

Endoscopic recurrence was seen at one year in one patient in the infliximab group (9.1%) as compared to 11 patients receiving placebo (84.6%). There was a higher proportion of patients in clinical remission (80.0% vs 53.8%; $p=ns$), and the histologic recurrence rate at 1 year was lower in the infliximab group (27.3% vs 84.6%) as compared with placebo. The occurrence of adverse events was similar between the two groups.

In conclusion, postoperative infliximab is effective in preventing endoscopic and histologic recurrence of Crohn's disease.

Porter CK, Tribble DR, Aliaga PA, Halvorson HA, Riddle MS. **Infectious gastroenteritis and risk of developing inflammatory bowel disease.** *Gastroenterology* 2008;135:781–6

Infectious gastroenteritis (IGE) is usually a self-limited illness; in some cases, the causative organism has been linked to several secondary or chronic health conditions, like irritable bowel syndrome and inflammatory bowel disease (IBD)

The authors retrospectively reviewed the demographic and clinical profile of military personnel from the US military forces between 1999 and 2006, with regards to diagnosis of IBD and episodes of IGE. During this period, 3019 subjects were newly diagnosed as IBD (Crohn's disease [CD]= 1037, ulcerative colitis [UC]= 1720); estimated IBD

incidence was 29.2 cases/100,000 person-years. A subset of 266 cases was analyzed to calculate a 6-month diagnostic delay window used for exposure classification and all diarrhea episodes within last 6 months of diagnosis of IBD were excluded. Ninety-three percent of the remaining cases were matched with 4 controls, with fewer controls identified for the other 7%. On initial univariate analysis, being single (OR 0.90; $p=0.002$), having a high school education or less (OR 1.05; $p=0.16$), being of Caucasian race (OR, 1.23; $p=0.0001$), and a previous diagnosis of IBS more than 6 months before IBD diagnosis (cases) or censoring (con-

trols) (OR 4.85; $p=0.0001$) were independently ($p < 0.20$) with IBD. Previous IGE episodes were most commonly viral (52%), with 150 having at least 2 IGE episodes. After controlling for potential confounders, a previous diagnosis of IGE was associated with an increased odds of IBD (OR, 1.40 [CD= 1.54, UC = 1.36]; 95% CI 1.19 –1.66). Risk of IBD in persons with a prior diagnosis of IBS was approximately 5 times that of persons without a prior IBS diagnosis. Among subjects without a prior IBS diagnosis, previous IGE remained significantly associated with both CD and UC.

Compiled by Prachi Patil, Akash Shukla, Mumbai

Gastroenterology India

Sharma P, Sharma BC, Purib V, Sarin SK. **An open-label randomized controlled trial of lactulose and probiotics in the treatment of minimal hepatic encephalopathy.** *Eur J Gastroenterol Hepatol* 2008;20:506–11.

Minimal hepatic encephalopathy (MHE) leads to difficulties in safely performing routine activities of life in patients with cirrhosis of the liver. Gut-derived nitrogenous substances, specifically, ammonia plays a major role in the pathogenesis of MHE.

190 cirrhotic patients without overt encephalopathy (age - 41.6 [12.7] years, men: 149; Child's A 71 patients, B 72, C grade 47) were screened for MHE. Psychometric tests (number connection tests [NCT A, NCT B], if literate and figure connection tests [FCT A, FCT B], if illiterate), P300 auditory event-related potential (P300ERP) and venous ammonia concentration estimation were done at enrollment and 1 month after treatment. MHE was defined by abnormal psychometric study and/or abnormal P300ERP. Patients diagnosed as MHE ($n=105$ [55.3%]; Child A 36 [51%]; B 39 [57%]; C 30 [60%]) were randomized in three groups of 35 patients each: group A (30–60 mL of lactulose/day), group B (1 capsule thrice daily of probiotic, containing *Strep. faecalis* 60 million, *Cl. butyricum* 4 million, *B. mesentericus* 2 million, lactic acid bacillus 100 million) and group C (lactulose plus probiotics). Significant improvement was seen in abnormal psychometry tests, P300ERP (group A: baseline 376.8 [22.3] vs. post treatment 344.3 [30.6] ms; group B: 385.4 [28.5] vs. 355.5 [27.9] ms, group C: 387.7 [27.5] vs. 347.7 [31.5] ms) and venous ammonia levels (group A: 102.3 vs. 69.3 $\mu\text{mol/l}$, group B: 108.2 \pm 37.5 vs. 75.7 \pm 33.0 $\mu\text{mol/l}$, group C: 96.3 \pm 27.7 vs. 68.7 \pm 28.4 $\mu\text{mol/l}$) after treatment. Normalization of abnormal psychometry and P300ERP was seen in 17/31 patients (54.8%), 16/31 patients (51.6%) and 17/30 patients (56.6%) of patients in groups A, B and C, respectively. Significant improvement was seen in Child class in all the three groups after 1 month of treatment.

The authors conclude that 55% of the patients with cirrhosis have MHE. Treatment with lactulose, probiotics and a combination of lactulose plus probiotics are equally effective and leads to improvement in MHE in about half the patients.

Saraswat VA, Saksena S, Nath K, *et al.* **Evaluation of mannitol effect in patients with acute hepatic failure and acute-on-chronic liver failure using conventional MRI, diffusion tensor imaging and in-vivo proton MR spectroscopy.** *World J Gastroenterol* 2008;14: 4168-78.

Mannitol decreases cerebral edema and raised intracranial pressure (ICP) level in patients with acute liver failure (ALF). This first pilot study evaluates the effect of mannitol on brain water content using MR imaging techniques - proton magnetic resonance spectroscopy (PMRS) and diffusion tensor imaging (DTI) in controls and in 5 patients each with ALF and acute-on-chronic liver failure (ACLF).

All patients received standard anti-coma measures. ICP recordings were not done and patients were not hyperventilated. After a baseline MRI scan of brain, an intravenous bolus of 20% mannitol solution (1 g/kg body weight) was given over 10 minutes and repeat MRI scanning was done in the same position about 30 minutes after completion of mannitol infusion. Arterial ammonia was measured before or within 6 h of imaging. The parameters compared before and after mannitol infusion were (1) relative metabolite alterations in the right parietal region using *in-vivo* PMRS, (2) brain water content using DTI metrics, and (3) changes in the brain parenchyma volume as well as cerebrospinal fluid (CSF) volume. The metabolite ratios of N-acetylaspartate (NAA), choline (Cho), glutamine (Gln), glutamine/glutamate (Glx), and myoinositol (mI) were calculated with respect to creatine (Cr). All patients had grade 3 or grade 4 hepatic encephalopathy. None of the patients showed improvement in terms of the grade of encephalopathy, clinical

signs of cerebral edema or MR findings after mannitol infusion. On PMRS, no difference was observed in the metabolites ratios of NAA/Cr, Cho/Cr, Gln/Cr, Glx/Cr, and ml/Cr between the pre- and post-mannitol study. In all subjects, none of the DTI metrics showed any significant difference nor was there any significant change in brain parenchyma volume as well as CSF volume after mannitol infusion.

The study concludes that mannitol does not have an early effect over 45 min in patients with ALF and ACLF.

De BK, Gangopadhyay S, Dutta D, Baksi SD, Pani A, Ghosh P. **Pentoxifylline versus prednisolone for severe alcoholic hepatitis: A randomized controlled trial.** *World J Gastroenterol* 2009;15:1613-9

Prednisolone or pentoxifylline (with anti-inflammatory [TNF- α inhibition] and antifibrogenic properties) are used in patients with acute alcoholic hepatitis (AAH) with Maddrey discriminant function (DF) \geq 32. The authors compared the efficacy of these two drugs in a randomized double-blind controlled manner in patients with severe AAH.

Sixty-eight patients with AAH (DF $>$ 32; 67 men) received either pentoxifylline (400 mg thrice daily orally, group I, n = 34, age - 47.5 years) or prednisolone (40 mg once daily for 4 weeks, n = 34, group II, age: 46.5 years) and subsequently in an open study (with a tapering dose of prednisolone in group 2) for a total of 3 months, and were followed up over 12 months. There was no difference

in baseline bilirubin (5.4 vs 6.6 mg/dL), creatinine (1.4 vs 1.2 mg/dL), INR (1.97 vs 2.04), Maddrey DF score (54.3 vs 57.8), Child's score (11.9 vs 12.2), and MELD score (23.1 vs 22.7) between the two groups. The 3-month mortality was higher among patients receiving prednisolone (12/34; 35.29%) as compared to those receiving pentoxifylline (5/34; 14.71%; p=0.04). None of the patients in group I developed hepatorenal syndrome (HRS) while six patients in group II died of HRS. No more patients succumbed to the disease after 3 months. On follow-up, recurrent encephalopathy was observed among five patients in group I in contrast to none in group II. Baseline Maddrey DF score and INR were higher among patients who died compared to those who survived (p = 0.038 and 0.049 respectively). The baseline MELD score, Glasgow Alcoholic Hepatitis Score and Child's score were not different among the patients who expired as compared to those who survived. The decrease in DF score and GAHS was comparable among patients receiving pentoxifylline or prednisolone. At the end of 4 weeks, MELD score was lower among those receiving pentoxifylline compared to those receiving prednisolone (15.5 vs 3.6 vs 17.8, p=0.04).

The study concludes that of the different liver function scores, only a higher Maddrey DF score is associated with increased mortality in patients with severe AAH. Pentoxifylline is superior to prednisolone for treatment of severe AAH, and has better safety profile and renoprotective effects.

Compiled by Sundeep Shah, Mumbai

News and notices

Medical Education Fellowships-2010

CMCL-FAIMER Regional Institute, Christian Medical College, Ludhiana

The CMCL-FAIMER regional Institute's Fellowship is a two-year fellowship program designed for Indian medical school faculties who have the potential to play a key role in improving medical education at their institutes. The program is uniquely designed to teach education methods and leadership skills, as well as to develop strong professional bonds with other medical educators. The fellowship is now running in its fifth year

Twenty fellowships are on offer for the year 2010. Requirements for selection include submission of a curriculum innovation project proposal and letter of support from applicant's institute. Limited funding is available to support fellows' travel, local expenses and course fee.

The application process is online at <https://faimeronline2.ecfmg.org/>

For details, please visit <http://cmcl.faimer.googlepages.com/home>

Important Dates

Applications open: July 1, 2009; Applications Close: October 15, 2009

First session at Ludhiana: January 12-18, 2010

For information: contact Dr. Tejinder Singh, Professor and Head of Pediatrics and Director of the Program, Christian Medical College, Ludhiana 141008 at cmcl.faimer@gmail.com