Gastroenterology and Hepatology From Bed to Bench.

Short Cut

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Kaviani MJ, Pirastehfar M, Azari A, Saberifiroozi M. (Gastroenterohepatology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran). ***Etiology and outcome of patients with upper gastrointestinal bleeding: a study from the south of Iran.*** *Saudi J Gastroenterol 2010; 16: 253-59.*

This prospective study enrolled 572 patients. These included patients admitted through the emergency department and inpatients that developed upper gastrointestinal bleeding with either melaena or haemetemesis. Only patients more 16 years were enrolled with a mean age of 54.97 years with 66% male.

The most common finding was gastric ulcer, followed by duodenal ulcer and then gastro-oesophageal varices. The mortality rate was 6-7%. This is in line with mortality rate in the Western countries. The most important risk factor mortality was age more than 60 years, orthostatic hypotension and steroid consumption. The first two are well-accepted risk factors according to the Rockall score.

In summary this study shows light into the epidemiology upper GI bleeding in Iranian population and findings are comparable and consistent with western literature.

Kadri SR, Lao-Sirieix P, O'Donovan M, Debiram I, Das M, Blazeby JM, et al. (MRC Cancer Cell Unit, Hutchison-MRC Research Centre, Cambridge CB2 2XZ). ***Acceptability and accuracy of a non-endoscopic screening test for Barrett's oesophagus in primary care: cohort study.*** *BMJ 2010; 341: c4372.*

The objective of the study was to determine the accuracy and acceptability to patients of non-endoscopic screening test for Barrett's oesophagus, using an ingestible oesophagus sampling device (Cytosponge) coupled with immunohistochemistry for trefoil factor 3.

This is a prospective cohort study in 12 UK general practices, with gastroscopies carried out in one hospital endoscopic unit. The study population included 504 of 2696 eligible patients aged 50-70 years with previous prescription for an acid suppressant (H2 receptor antagonist or proton pump inhibitor) for more than three months in the past 5 years.

The main outcome measures were sensitivity and specificity estimates for detecting Barrett's oesophagus compared with endoscopy as the ideal method, and patient anxiety and acceptability.

The incidence of oesophageal adenocarcinoma is increasing worldwide. Barrett's oesophagus is believed to be a significant risk factor for this cancer. Various studies have shown that the conversion from Barrett's to oesophageal adenocarcinoma is approximately 0.5% per annum and this happens up to 15 years after diagnosis. Oesophageal cancer has a mortality of 80% at 5 years.

However a screening programme for Barrett's has not been deemed appropriate due to relatively high mortality from oesophagectomy (5%) and the limited ability to perform screening gastroscopy (the current mode of diagnosis).

However there are newer less invasive treatments are becoming established namely radio frequency ablation and endoscopic mucosal dissection.

Therefore screening for Barrett's may merit consideration in the future.

The authors used a non– endoscopic device to diagnose Barrett's. This involved the patient swallowing a gelatin capsule at the end of string. The gelatin capsule dissolves in the stomach releasing an expandable mesh. Then the mesh is recovered by pulling the string out of the patient's mouth and send for histological analysis. Immunohistochemistry is used for detection of cells with intestinal metaplasia using a previously validated marker for trefoil factor 3. Patients with a positive result were then assessed with an endoscopy for definitive diagnosis of Barrett's.

Patients were selected from 12 UK general practices if they have been on acid suppressants for at least 3 months in the last 5 years. Exclusion criteria included previous diagnosis of Barrett's, gastroscopy in the last year and unsuitability for gastroscopy for any reason.

504 of 2696 eligible patients (187%) agreed to participate. Of these 99% swallowed the sponge. This is comparable with willingness for gastroscopy of 16% in patients with dyspepsia in the community shown from previous studies.

The sensitivity and specificity of Barrett's dignosis from the sponge method was 73.3% and 93.8% respectively for Barrett's of >1cm. The prevalence of Barrett's was 3%. There were no complications and the acceptability was high. The authors therefore suggest the Cytosponge test may be acceptable as screening tool but requires further assessment.

Gane EJ, Rouzier R, Stedman C, Wiercinska-Drapalo A, Horban A, Chang L, et al. (Auckland Clinical Studies, New Zealand). ***Antiviral activity, safety, and pharmacokinetics of danoprevir/ ritonavir plus PEG-IFN α-2a/RBV in hepatitis C patients****. J Hepatol 2011 Feb 24.*

The standard treatment of chronic hepatitis C infection is based on pegylated interferon alpha which is administered subcutaneously and Ribavirin which is taken orally. However the effectiveness of this combination is influenced by the genotype of the virus, resistance to the drugs and to a large extent by the side effect of these two drugs. More than 50% of genotype 1 fails to achieve a sustained virological response.

Edward Gane and colleagues have produced some promising results from their clinical trial where they used two new drugs which can be administered orally. Subjects in the trial were randomised to receive a combination of RG7128, an HCV polymerase inhibitor and Danoprevir , a protease inhibitor. After 13 days of treatment the combination of RG 7128 and Danoprevir suppressed the viral load in a substantive number of the patients - with a few even having undetectable viral load. There were few significant side effects with treatment.

Even though it is an early phase trial it has opened the doors to the possibility of developing an interferon free orally administered therapy against hepatitis C.

Rothwell PM, Wilson M, Elwin CE, Norrving B, Algra A, Warlow CP, et al. (Stroke Prevention Research Unit, Department of Clinical Neurology, University of Oxford, Oxford, UK). ***Long-term effect of aspirin on colorectal cancer incidence and mortality: 20-year follow-up of five randomised trials.*** *Lancet 2010; 376: 1741-50.*

The study by Prof Rothwell and colleagues provides robust evidence on the effectiveness of low dose aspirin [75mg daily] in reducing the incidence and mortality from colo-rectal cancer. The 60-70% reduction in death was due to a reduction in the incidence of cancer of the proximal colon with no effect on cancer of the distal colon. The study also showed that very low dose aspirin [30mg/day] is not effective in preventing colorectal cancer.

The 1.5% absolute risk reduction in proximal colon cancer with aspirin has practical implications as precancerous lesions in the proximal colon are not

seen on sigmoidoscopy and often missed during colonoscopy [1%]. The addition of low dose aspirin as part of a cancer prevention strategy is therefore not that far from reality.

Hussain SP, Amstad P, Raja K, Ambs S, Nagashima M, Bennett WP, et al. (Laboratory of Human Carcinogenesis, National Cancer Institute, NIH, Bethesda, Maryland 20892, USA). ***Increased p53 mutation load in noncancerous colon tissue from ulcerative colitis: a cancer-prone chronic inflammatory disease.*** *Cancer Research* 2000; 60: 3333-37.

Vaji S, Salehi Z, Aminian K. (Department of Biology, Faculty of Sciences, University of Guilan, Rasht, Iran). ***Association of p53 codon 72 genetic polymorphism with the risk of ulcerative colitis in northern Iran.*** Int J Colorectal Dis 2011; 26: 235–38.

The potential significance of the *p53* tumour suppressor gene in the transformation of ulcerative colitis (UC) to colorectal cancer (CRC) has been recognised for a number of years. Chronic inflammation is known to be linked to an increased risk of cancer and previous research has suggested mechanisms by which inflammation progresses to malignant change in ulcerative colitis.

In particular researchers found a high frequency of mutated *p53* alleles in inflamed lesional areas of the colon in UC patients which was consistent with the hypothesis that reactive species could induce such mutations. Now researchers at the University of Guilan have added to the understanding of the genetic associations of UC and the possible role of the *p53* gene in the development of UC. Comparing genomic DNA from colonic biopsy tissue in patients with UC and blood samples of controls they found a significant increase in the frequency of a polymorphism of codon 72 on the *p53* gene.

Furuta Y, Kawai M, Yahara K, Takahashi N, Handa N, Tsuru T, et al.(Department of Medical Genome Sciences, Graduate School of Frontier Sciences, University of Tokyo, Minato-ku, Tokyo 108-8639, Japan). ***Birth and death of genes linked to chromosomal inversion****. Proc Natl Acad Sci U S A. 2011;108: 1501-506.*

Researchers in Japan have used the Helicobacter pylori genome to discover a unique mechanism of DNA replication. They compared the genome sequences of ten *H. Pylori* strains (five "Western strains" and five "Eastern strains") with notable differences in outer membrane protein (OMP) genes between the two groups. The OMPs they looked at play important roles in host interaction and pathogenicity. Sequence analysis of the different strains paying attention to the genes encoding OMPs allowed the researchers to hypothesize how the *H. Pylori* genomes have developed. In particular they proposed a process of DNA duplication which they termed DNA duplication associated with inversion (DDAI). This research adds to the understanding of genome evolution and may be relevant to other organisms.

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