Coin Ingestion in Children

Removal of coins from the upper gastrointestinal tract of children, specifically the esophagus, is a common procedure for pediatric gastroenterologists. There is some debate as to when these objects should be removed, and the purpose of this study was to perform a randomized, prospective study of patients less than 21 years of age who presented to the emergency department with a coin lodged into the esophagus confirmed by standard radiograph. After consent was obtained, patients were randomized into 2 groups. One group received immediate endoscopic coin removal while the other group was admitted to the hospital for observation including cardiac monitoring, pulse oximetry, intravenous fluids while the patient was kept non per os (NPO), and a repeat radiograph obtained in approximately 16 hours. The percentage of coins removed from each group was compared as were hospital length of stay and adverse events. Sixty patients were enrolled into the study with 30 patients per study arm. The two groups were similar in regards to age and gender although more patients in the observation group had coins in the upper esophagus.

Outcome measurements demonstrated that 77% of the observation group and 70% of the immediate endoscopy group required endoscopic coin removal. The length of stay for the observation group was statistically longer (approximately 8.7 hours). Neither group had complications related to coin impaction, and an equal number of patients in each group had spontaneous passage of coins (approximately 25%). All coins that passed spontaneously had done so within 19 hours. Spontaneous passage was more likely to occur in older patients, in male patients, and in cases where the coins were located in the distal esophagus. Since spontaneous passage of an esophageal coin was not an uncommon feature in this study, the authors have recommended that an 8 to 16 hour observation period can occur in those children with esophageal coins who are asymptomatic, have a recent history of ingestion, and have no underlying esophageal or tracheal abnormality. This study suggests that clinical observation may obviate the need for anesthesia and endoscopy for all pediatric coin ingestions. (Waltzman ML, Baskin M, Wypij D, (continued on page 98)
Capsule Endoscopy vs. Enteroclysis in Crohn’s Disease

Thirty-one patients with endoscopically and histologically proven Crohn’s disease underwent enteroclysis as their initial evaluation, followed by wireless capsule endoscopy (WCE). The radiologist was blinded to the results of standard index endoscopy, which included retrograde ileoscopy. Gastroenterologists were blinded to the results of enteroclysis at the time of interpretation of the wireless capsule endoscopy (WCE).

Abnormal findings were documented in 8 of 31 patients by using enteroclysis in 22 of 31 patients by using WCE. In sixteen patients with known involvement of the terminal ileum, the diagnostic yield of WCE versus enteroclysis was significantly superior (89 percent versus 37 percent). In fifteen patients without lesions in the terminal ileum, abnormal findings in the proximal small bowel were detected in 7 (46 percent) patients by WCE and only in 2 patients by enteroclysis. The capsule detected all but two lesions diagnosed by enteroclysis. WCE detected additional lesions that were not detected by enteroclysis in 45 percent of cases.

It was concluded that WCE is superior to enteroclysis in estimating the presence of small-bowel CD. WCE may be a new gold standard for diagnosing ileal involvement in patients with CD without strictures and fistulae. (Marmo R, Rotondano G, Piscopo R, et al. “Capsule Endoscopy vs. Enteroclysis in Detection of Small-Bowel Involvement in Crohn’s Disease: A Prospective Trial.” Clinical Gastroenterology and Hepatology, 2005; Vol 3, 772-776.)

CRP and IBD

One hundred and four Crohn’s disease (CD) patients and 43 ulcerative colitis and indeterminate colitis patients (UC) were identified between January, 2002 and August, 2003, who had a CRP, colonoscopy and either small bowel follow-through (SPFT) or a CT enterography (CTE) performed within 14 days. Clinical activity was assessed retrospectively through review of the medical record. In CD patients, moderate to severe clinical activity, active disease at colonoscopy and histologically severe inflammation were all significantly associated: with CRP elevation. Abnormal small bowel radiographic imaging was not significantly associated with CRP elevation. In UC patients, CRP elevation was significantly associated with severe clinical activity, elevation in sedimentation rate, anemia, hypoalbuminemia, active disease ileocolonoscopy, but not with histologic inflammation.

It was concluded that CRP elevation in IBD patients is associated with clinical disease activity, endoscopic inflammation, severely active histologic inflammation in Crohn’s disease patients and several other biomarkers of inflammation, but not with radiographic activity. (Solem CA, Loftus EV, Tremaine WJ, et al. Correlation of C-Reactive Protein With Clinical, Endoscopic, Histologic and Radiographic Activity in Inflammatory Bowel Disease.” Inflammatory Bowel Disease, 2005; Vol 1, 747-712.)

ALT Normal Ranges in Obese Women

The upper limit of normal for ALT activity has been recommended to be lowered to 30 units per liter or less in men and 19 units per liter or less in women. These changes have been suggested to be diagnostically useful in subjects with nonalcoholic fatty liver disease (NAFLD) to investigate the prevalence and spectrum of NAFLD with regard to the new ALT guidelines in 233 women with class II/III obesity.

A comparison was carried out, comparing the prior reference range with an upper limit of normal to 30 or greater would be classified as having normal ALT levels, compared with 169 patients (72.5 percent), by the new and old standards, respectively. In patients with normal ALT activity, the prevalence of fatty liver (FL) 39.5 percent versus 40.2 percent, portal fibrosis and steatosis (IPF) 37.2 percent versus 33.7 percent and nonalcoholic steatohepatitis (NASH) 23.3 percent versus 26 percent, were similar. In comparison, newly defined patients with elevated ALT levels greater than 19 units per liter demonstrated an increased prevalence of FL (36 percent) and IPF (11.6 percent), but a 23.8 percent decrease in the prevalence of NASH as compared with the old standard. The sensitivity and specificity for NASH were 42 percent and 80 percent (ALT (continued on page 96)
greater than 30 units per liter), compared with 74 percent and 42 percent (ALT greater than 19).

It was concluded that a significant increase in the prevalence of FL and IPF is detected in subjects with elevated ALT level, with the application of a new standard. However, the diagnostic utility for ALT to identify NASH or IPF remains poor and significant health care expenditures may be incurred if this standard is adopted. (Kund ES, Blazenby AJ, Clements RH, Abrams GA. “Spectrum of NAFLD and Diagnostic Implications of the Proposed New Normal Range for Serum ALT in Obese Women.” *Hepatology*, 2005; Vol. 42, 650-656.)

**Drug-induced Liver Injury—Extensive Analysis**

A cooperative network was created in 1994 in Spain to identify all suspicions of drug-induced liver injury (DILI), following a prospective, structured report form. The liver damage was characterized according to hepatocellular, cholestatic, and mixed laboratory criteria and to histologic criteria, when available. Further evaluation of causality assessment was centrally performed.

From April, 1994 to August, 2004, 461 out of 570 cases involving 505 drugs were deemed to be related to DILI. The anti-infection group of drugs was the most frequently incriminated. Amoxicillin-Clavulanate accounted for 12.8 percent of the whole series. The hepatocellular pattern of damage was the most common (58 percent), which was inversely correlated with age and had the worst outcome.

The incidence of liver transplantation and death in this Group was 11.7 percent, if the patients had jaundice at presentation, 3.8 percent in non-jaundiced patients. Factors associated with development of fulminant hepatic failure were female sex, hepatocellular damage and higher baseline plasma bilirubin value.

It was concluded that patients with drug-induced hepatocellular jaundice had an 11.7 percent chance of progressing to death on transplantation. Amoxicillin-Clavulanate stands out as the most common drug related to DILI. (Andrade RJ, Lucena I, Fernandez C, et al, on behalf of the Spanish Group for the Study of Drug-induced Liver Disease.” *Gastroenterology*, 2005; Vol. 129, 512-521.)

**PEG Interferon and Ribavirin: Shorter Term Therapy in Genotype 2 or 3 Hepatitis C**

Patients chronically infected with HCV genotype 2 or 3 are commonly treated with pegylated Interferon-Alpha and Ribavirin for 24 weeks. This study evaluated the potential for shorter term therapy.

Thirty-nine patients with HCV-2, one patient with HCV-2/3 and 113 patients with HCV-3 were treated with PEG Interferon Alfa-2A (180 µg/week), plus Ribavirin 800 mg to 1200 mg/day). HCV RNA was quantitatively assessed after 4 weeks. Patients with a rapid virologic response (HCV RNA below 600 i.u./mL) were randomized for a total treatment duration of 16 or 24 weeks (group A and group B). All patients with HCV RNA 600 i.u. or greater at week four (group C) were treated for 24 weeks. End of treatment and sustained virologic response were assessed by qualitative RT-PCR. Only 11 of 153 patients (7 percent) were allocated to group C. End of treatment and sustained virologic response rates were 94 percent and 82 percent in group A, 85 percent and 80 percent in group B and 73 and 36 percent in group C, respectively.

In patients infected with genotype HCV-3 in a high viral load (greater than 800,000 i.u./mL), a significantly lower sustained virologic response rate was found than in patients with a viral load lower or equal to 800,000 i.u./mL (59% vs. 85%, respectively).

It was concluded that in HCV-2 and 3, with low viral load-infected patients who have a rapid virologic response, treatment for 16 weeks with PEG Interferon Alfa-2A and Ribavirin is sufficient. In patients infected by HCV-3, high viral load, longer treatment may be required. (Von Wagner M, Huber M, Berg T, et al. “PEG Interferon-Alfa 2A (40KD) and Ribavirin for 16 or 24 Weeks in Patients with Genotype 2 or 3 Chronic Hepatitis C. *Gastroenterology*, 2005; Vol. 129, 522-527.)

**Rifampicin and UDCA in Cholestatic Diseases**

Rifampicin (RIFA) and Ursodeoxycholic Acid (UDCA) improves symptoms and biochemical markers of liver injury in cholestatic liver diseases by largely unknown mechanisms. The molecular mechanism fraction of these drugs in humans was carried
out. Thirty otherwise healthy gallstones patients scheduled for cholecystectomy were randomized to RIFA (600mg/day for one week), or UDCA (1 gram/day for three weeks), or no medication before surgery. Bile acids were analyzed in serum, urine and bile. A wedge liver biopsy specimen was taken to study expression of hepatobiliary (ABC) transporters, as well as detoxification enzymes and regulatory transcription factors, RIFA-enhanced bile acid detoxification as well as bilirubin conjugation and excretion. These molecular effects were paralleled by decreased bilirubin and deoxycholic acid concentrations in serum and decreased lithocholic and deoxycholic acid concentrations in bile. UDCA, on the other hand, became the predominant bile acid after treatment and lowered the biliary cholesterol saturation index.

It was concluded that RIFA-enhanced bile acid detoxification, as well as bilirubin conjugation and export systems, whereas UDCA stimulates the expression of transporters for canalicular and basolateral bile acid export, as well as canalicular phospholipase flip-pase. These independent, but complementary effects may justify a combination of both agents for the treatment of advanced cholestatic liver disease and may support the combined use of both agents for the treatment of operable hepatocellular carcinoma (HCC) developed in 7 of 342 patients cured of HCV infection by Interferon monotherapy. No patient had used alcohol or had diabetes mellitus or obesity. Resected specimens were histologically evaluated. DNA extracted from HCC was examined by polymerase chain reaction to locate hepatitis B virus DNA. HBV integration sites in human genome were identified by cassette-ligation-mediated PCR. HBV DNA was not identified in serum samples from any of the 7 patients with HCC, but was found in the liver in four patients. HBV DNA was integrated in these patients with human genome of HCC. In two of these patients, covalently closed circular HBV (CCV) was also detected. Patients with HBV DNA integration were free of HCV for more than three years. In two of the three patients without HBV DNA integration, the surrounding liver showed cirrhosis. The liver of HCC with HBV DNA integration had not progressed to cirrhosis.

It was concluded that integrated HBV DNA may play a role in hepatocarcinogenesis after the clearance of HCV by Interferon treatment. (Zamori A, Ishiguchi S, Shoimi S, et al. “Hepatitis B Virus DNA Integration in Hepatocellular Carcinoma After Interferon-Induced Disappearance of Hepatitis C Virus.” Amer J Gastroenterol, 2005; Vol. 100, 1748-1753.)

Capsule Endoscopy in Patients with Implantable Cardiac Defibrillators

In order to evaluate the safety of capsule endoscopy (CE) in patients with implantable cardiac defibrillators (ICD) and other electromedical devices, patients referred for the evaluation of occult gastrointestinal bleeding, and who also had an ICD were enrolled in the study after informed consent. Five consecutive patients were studied. All patients had transvenous ICDs located in the chest. Prior to the CE, patients had a baseline ECG and ICD interrogation. Thereafter, CE was performed in a hospital setting with telemetry and monitoring performed simultaneously.

When CE studies were reviewed, observations pertaining to technical difficulty and interference with video imaging was documented. No arrhythmia or other adverse cardiac events were noted during capsule transmission. No interference by the ICD on the CE video images was seen.

CE was performed safely in these five patients with ICD and was not associated with any adverse cardiac event. ICDs do not appear to interfere with video capsule imaging. (Leighton JA, Srivachsan K, Carey J, Sharma VK, High RI, et al. “Safety of Wireless Capsule Endoscopy in Patients With Implantable Cardiac Defibrillators.” Amer J Gastroenterol, 2005; Vol. 100, 1728-1731.)

Probiotics and Pediatric Irritable Bowel Syndrome

Probiotics, such as *Lactobacillus GG*, have recently been shown to be of possible clinical benefit in the treatment of irritable bowel syndrome (IBS). The authors of this study attempted to determine the efficacy of *Lactobacillus GG* in the treatment of pediatric IBS. Sixty-four children with a definitive diagnosis of IBS were enrolled into a controlled, double-blind, randomized trial and were assigned either *Lactobacillus GG* (one 10^10^ bacteria concentration capsule twice daily) or placebo for 6 weeks. Patients were followed on a weekly basis using the Gastrointestinal Symptom Rating Scale which is a 15-item questionnaire determining pain perception related to IBS.

Patients in the two groups were similar in age, gender, weight, symptom duration, and duration of follow up. The study demonstrated that 40% of patients in the placebo group improved with treatment in a statistical manner similar to other placebo trials for IBS. The *Lactobacillus GG*-treated group showed a 44% response rate which was not significantly different from the placebo group. Interestingly, patients who responded to either intervention had more severe abdominal pain at enrollment compared to nonresponders. No difference was noted between treatment groups in regards to gastrointestinal symptoms except that statistically more patients treated with placebo complained of abdominal distention compared to the *Lactobacillus GG* group (P = 0.022). No difference was noted between *Lactobacillus GG*-treated patients based on patient weight or response to treatment over time.

The authors conclude that *Lactobacillus GG* used at the dosage and treatment duration in this study was not superior to placebo for treatment of pediatric IBS with the possible exception of perceived abdominal distention. However, more studies are necessary to determine if beneficial, detrimental, or neutral effects exist when using probiotics for pediatric IBS. (Bausserman M and Michail S. “The Use of *Lactobacillus GG* in Irritable Bowel Syndrome in Children: A Double-Blind Randomized Control Trial.” The Journal of Pediatrics, 2005; Vol. 147, 197-201.)

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