Indian J Gastroenterol (November–December 2011) 30(6):288–291
DOI 10.1007/s12664-011-0151-3

Gastroenterology Elsewhere

Boeckxstaens GE, Annese V, des Varannes SB, et al. **European Achalasia Trial Investigators. Pneumatic dilation versus laparoscopic Heller's myotomy for idiopathic achalasia**. N Engl J Med. 2011;364:1807–16.

The current treatment options for achalasia cardia (AC) are mainly endoscopic pneumatic dilation (EPD) or laparoscopic Heller's myotomy (LHM) with therapeutic success rates of 70% to 80% and 89% to 100%, respectively. LHM is considered to be superior to EPD and is increasingly considered to be the treatment of choice for AC. This multicenter randomized study compared EPD and LHM with Dor's fundoplication.
Two hundred and one patients with newly diagnosed AC and Eckardt symptom score >3 were randomized to EPD (n=95) or LHM with Dor's fundoplication (106). Exclusion criteria included unacceptable surgical risk and previous treatment for achalasia. The primary outcome was therapeutic success (reduction in Eckardt score to ≤3) at yearly follow up assessment. The secondary outcomes included need for retreatment, LES pressure, esophageal emptying, quality of life (QoL), and complication rates. Patients completed QoL questionnaires and underwent esophageal manometry and a timed barium esophagogram to quantify esophageal stasis at baseline, 1 month after treatment and yearly thereafter. Twenty-four hour pH-metry and endoscopy were performed 1 year after treatment and every 3 years thereafter. The first EPD was performed with a 30-mm balloon, followed 1–3 weeks later by dilation using a 35-mm balloon. All patients underwent at least two and maximum 3 dilations with re-dilatations allowed twice for symptom recurrence. In the LHM group, myotomy was followed by an anterior 180-degree Dor's fundoplication. The mean follow up time was 43 months (95% CI, 40–47).
On intention-to-treat analysis, there was no difference in therapeutic success between the two groups (EPD 90% and 86%, LHM 93% and 90% after 1 and 2 years of follow up, respectively). Four patients did not respond to the initial EPD, and 23 patients had recurrent symptoms requiring re-dilation. Fifteen patients in the LHM arm failed treatment. Symptoms and LES pressure were reduced, and esophageal emptying and QoL improved to a similar extent in the two groups. Esophageal perforation occurred in 4% patients in the EPD group. The perforation rate was higher (31%, p= 0.001) when a 35-mm balloon was used for the first dilation; 12% patients in the LHM group had a mucosal tear.
The authors conclude that LHM is not associated with superior rates of therapeutic success compared to EPD and suggest that graded dilation is a reasonable protocol for EPD.

Galmiche JP, Hatlebakk J, Attwood S, et al. **LOTUS Trial Collaborators. Laparoscopic antireflux surgery vs. esomeprazole treatment for chronic GERD: the LOTUS randomized clinical trial.** JAMA. 2011;305:1969–77.

Gastroesophageal reflux disease (GERD) is chronic disease that negatively affects patients' health-related quality of life (HR-QoL). The two commonly used treatment options are maintenance with proton pump inhibitors (PPI) and anti-reflux surgery. The LOTUS (Long-Term Usage of Esomeprazole vs. Surgery for Treatment of Chronic GERD) trial compared standardized laparoscopic anti-reflux surgery (LARS) with optimized maintenance esomeprazole (ES) therapy in patients with chronic GERD who initially responded to acid-suppression.
In this 5-year exploratory randomized, open label, multicenter trial, 554 patients were randomized to ES (n=266, dose: 20–40 mg/day) or LARS (n=288 of whom 248 underwent LARS). Three hundred and seventy-two patients (ES192; LARS 180) completed 5-year follow up. GERD was diagnosed by typical clinical history and esophagitis (classified by Los Angeles grade) at endoscopy, and/or pathological

24-hour pH-metry. A 3-month run-in period was required to verify the clinical response to ES 40 mg/day; patients who responded were randomized. Patients were followed up 6 months after randomization and 6 monthly thereafter. Follow up endoscopy with biopsies was planned at 1, 3, and 5 years. Patients underwent pH-metry at baseline, 6 months and 5 years. Symptom severity was classified as none, mild, moderate or severe. HR-QoL and patient-reported symptoms were assessed by administering QoL questionnaires to patients at randomization and annually thereafter. The primary end point was time to treatment failure (for LARS, defined as need for acid suppressive therapy; for ES, inadequate symptom control after dose adjustment).

In the intention-to-treat population, at 5 years, 85% (95% CI, 81–90) in the LARS group and 92% (95% CI, 89 to 96) in the ES group remained in remission (log-rank $p=0.048$). The results of the per-protocol analysis were similar. The difference between groups was not significant following best-case scenario modeling of the effects of study dropout. The prevalence and severity of symptoms at 5 years in the ES and LARS groups, respectively, were 16% and 8% for heartburn ($p=0.14$), 13% and 2% for acid regurgitation ($p<0.001$), 5% and 11% for dysphagia ($p<0.001$), 28% and 40% for bloating ($p<0.001$), and 40% and 57% for flatulence ($p<0.001$). The incidence of serious adverse events was similar (ES: 24.1%, LARS: 28.6%).

The authors conclude that most patients with GERD remain in remission at 5 years with contemporary anti-reflux therapy using either LARS or esomeprazole.

Les I, Doval E, García-Martínez R, et al. **Effects of branched-chain amino acids supplementation in patients with cirrhosis and a previous episode of hepatic encephalopathy: a randomized study.** Am J Gastroenterol. 2011; 106:1081–8.

The treatment of hepatic encephalopathy (HE) is based on suppression of precipitating factors, reduction of ammonia absorption, and nutritional measures. Although a low-protein diet is considered the mainstay of treatment and prevention of HE in cirrhosis, protein restriction can worsen the malnutrition. Patients with advanced cirrhosis have decreased concentration of branched-chain amino acids (BCAA). Although oral supplementation with BCAA improves cognitive function in chronic HE, the exact role of BCAA in HE is uncertain. This randomized, double-blind, multicenter study investigated the long-term effects of supplementing a protein-controlled diet with BCAA in patients with cirrhosis and a previous episode of HE.

One hundred and sixteen patients were included, and received a standard diet of 35 kcal/kg per day and 0.7 g of proteins/kg per day, and a supplement of 30 g of BCAA (BCAA group) or maltodextrin (MDX group) during 56 weeks. The supplements were administered twice daily mixed with fruit juice or yogurt. Treatment for preventing recurrence of HE and for infection or gastrointestinal bleeding was given as required. Compliance was considered when a patient achieved ≥80% of standard diet for ≥80% of days of the study. The primary end point was HE-free survival. Clinical and dietetic visits were scheduled at 8 weekly intervals. Analytic and anthropometric parameters, neuropsychological tests and health related quality of life questionnaire testing were performed at 8, 24, 40, and 56 weeks.

HE-free survival was not different between groups (BCAA: 47%, MDX: 34%, $p=0.274$). There was no difference in number of patients who developed HE (BCAA: 24, MDX: 32, $p=0.137$), chronic persistent HE (BCAA: 6, MDX: 5, $p=0.7$) or chronic recurrent HE (BCAA: 14, MDX: 16, $p=0.6$). Patients in the BCAA group exhibited a better outcome on two neuropsychological tests and an increase in the mid-arm muscle circumference. Recurrence was associated with low plasma albumin at baseline and a decrease in sodium and an increase in creatinine during follow up. Global cognitive function improved during follow up in patients who did not experience episodes of HE ($n=50$), while remaining stable (assessed after the episodes of HE) in those who developed HE ($n=44$). Thus, while diet supplementation with BCAA after an episode of HE does not prevent recurrence of HE, it improves minimal HE and muscle mass. Also, the characteristics of patients who showed recurrence of HE suggest that therapies for hyponatremia and circulatory dysfunction may be useful for this purpose.

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Gastroenterology India

Varma S, Menon MC, Garg A, et al. **Hepatitis C virus infection among patients with non-Hodgkin's lymphoma in northern India**. Hepatol Int. 2011;5:688–92.

Hepatitis C virus (HCV) has been postulated to be an etiological agent for lymphoid malignancies. A high prevalence of HCV infection in non-Hodgkin's lymphoma (NHL) patients has been shown to exist in many geographical areas of high HCV prevalence. This study determines, prospectively, whether an association exists between HCV and NHL and whether HCV RNA testing would pick up a greater number of such patients than serological test alone.

A total of 57 consecutive patients (male 37, age 47.8 years [range: 18–80]) newly diagnosed patients with B cell NHL and 171 age and sex-matched controls underwent third generation enzyme immunoassay to detect HCV antibodies. Of 57 NHL patients, 44 (77.2%) were of the diffuse large B cell type (high grade), 6 (10.5%) of the follicular type (intermediate grade) and 7 (12.3%) of the small lymphocytic type (low-grade). None of the patients in the B cell NHL group tested positive for anti-HCV; one patient who had received blood transfusion (1.75%) tested positive for HBsAg. Among the age- and sex-matched controls taken, one tested positive for HBsAg (0.58%) and two tested positive for anti-HCV antibody (1.16%). The prevalence of anti-HCV (OR 0; 95% CI [0–12.40]) and HBsAg (OR 1.51 [0.13–17.05]) was similar between controls and patients. One patient in the B cell NHL group tested positive for HCV RNA (genotype 1); he had tested negative for anti-HCV. Two control subjects, who tested positive for the anti-HCV antibody, tested positive for HCV RNA.

This study did not find an association between HCV infection and NHL. However, more prospective studies from different regions with larger sample size would be needed.

Noor MT, Dixit P, Kochhar R, et al. **NSAIDs-related pyloroduodenal obstruction and its endoscopic management.** Diagn Ther Endosc. 2011;2011:967957.

Non-steroidal-anti-inflammatory drugs (NSAIDs) are commonly prescribed medications, and are often used for long period of time. Chronic NSAID consumption is a rare cause of gastric outlet obstruction (GOO). Endoscopic balloon dilatation (EBD) has become the cornerstone of management of benign GOO.

Ten consecutive patients (mean age 45.2 [16.9] y; 8 males) with symptomatic NSAID-induced GOO underwent upper gastrointestinal endoscopy, barium meal follow through, and contrast-enhanced computed tomography to note the site and length of gastric and duodenal stricture(s) and to rule out presence of jejunal and ileal involvement. The median duration of NSAID consumption was 8 years (IQR 3–20). Dilatation was done using wire-guided through the scope CRE balloon which was inflated to incremental diameters, for 60 s at each diameter. In patients with multiple strictures, the procedure was repeated at each narrowing. Dilatation was repeated at 2–3-week intervals until a 15 mm diameter balloon could be passed through the stricture. Patients were then followed up every 2 weeks and endoscopy was performed. During follow up endoscopic dilatation was performed till there was no residue in two consecutive endoscopies. All patients were given proton pump inhibitors until the end of dilatation. Successful dilatation was defined by the achievement of target diameter (15 mm), absence of symptoms, and no residue in two consecutive endoscopies. Median duration of symptoms was 9 months (IQR 1–120). All patients had vomiting, three had weight loss and one had abdominal pain. Stricture was present at pylorus in five patients, in duodenum in nine patients, and four patients had both the sites involved. The strictures were short 2–3 mm web-like circumferential narrowing, except in two patients with pyloric stenosis who had longer (~5 mm) segments of narrowing. The mean (SD) number of strictures was 2.0 (0.94). The mean (SD) number of dilatations to achieve target diameter of 15 mm was 2.0 (1.6). The mean number of dilatations required to maintain was 5.3 (2.7). Median weight gain was 5 kg (IQR 2–14), and the median duration of treatment was 4.5 months (IQR 2–15). Patients were followed up for a median of 12 months (IQR2–16). There was no recurrence during this period. There were no complications like bleeding, perforation, or any mortality. Nine patients were managed successfully; only one patient required surgery because of failure of endoscopic therapy.

The authors conclude that NSAID-induced pyloroduodenal strictures can be managed successfully in a majority of patients with EBD; however, the patient has to come for repeated dilatation. Surgery is a one-time procedure, and should be reserved for failed EBD.

Pratap N, Kalapala R, Darisetty S, et al. **Achalasia cardia subtyping by high-resolution manometry predicts the therapeutic outcome of pneumatic balloon dilatation**. J Neurogastroenterol Motil. 2011;17:48–53.

High-resolution manometry (HRM) provides detailed pressure topography of the esophagus and allows better identification of compartmentalized distal esophageal pressurization than conventional manometry. Based on HRM, achalasia cardia (AC) is classified into different subtypes. The subtypes of AC show variable response to endoscopic pneumatic dilatation (EPD).

Fifty-one patients (mean follow up 6 months) underwent HRM using a 16-channel water perfused catheter. Basal LES pressure was recorded for 3 min, followed by ten 5 mL wet swallows. The patients with impaired LES relaxation (integrated relaxation pressure ≥15 mmHg) were classified into three subtypes—type I (classic AC; distal esophageal pressure <30 mmHg in >8/10 wet swallows), type II (AC with esophageal compression; at least 2/10 wet swallows associated with a pan esophageal pressurization >30 mmHg) and type III (spastic AC; 2 or more spastic contractions with or without periods of compartmentalized pressurization). EPD was performed using a Rigiflex balloon with a 35 mm diameter inflated for 1 min. The need for further dilatation was determined by the persistence of symptoms 4 weeks after treatment. Twenty-four patients had types I and II AC each, and three patients had type III AC.

The mean age of patients with types II and III were similar, compared to type I with younger age (p=0.577). Dysphagia and regurgitation were more frequent in types I and II (p<0.001 and p=0.057, respectively) than type III. Patients with type III AC had a higher incidence of chest pain (p=0.041), and had spastic contraction in most of the swallows, and also had higher basal LES pressure and maximal esophageal pressurization when compared to types I and II (p<0.001). EPD was performed in 45 out of 51 patients. The response to EPD was best in type II (18/20, 90.0%) compared to type I (14/22, 63.0%) and type III (1/3, 33.3%). On multivariate logistic regression analysis, the types of AC was found to significantly correlate with response to EPD (p=0.042). Patients with type II AC had the best response to EPD: type II vs. I (p=0.045), and type II vs. III (p=0.016). Patients with type II AC responded better to EPD (OR, 5.14; 95% CI, 0.94–28.14) when compared to type I.

The authors conclude that patients with type II AC respond better to EPD.

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