Indian J Gastroenterol (Jan–Feb 2011) 30(1):52–54
DOI 10.1007/s12664-011-0086-8

Gastroenterology elsewhere

Boeckxstaens GE, Beaumont H, Mertens V, et al. **Effects of lesogaberan on reflux and lower esophageal sphincter function in patients with gastroesophageal reflux disease.** Gastroenterology. 2010;139:409–17.

Transient lower esophageal sphincter relaxations (TLESRs) are thought to be a major mechanism behind reflux episodes and are mediated by a vago-vagal reflex pathway. The γ-amino butyric acid type B (GABAB) receptors act on the vagal signaling pathway. The peripherally acting GABAB-receptor agonist lesogaberan (AZD3355) has been shown to reduce the number of TLESRs and reflux episodes, and increase the lower esophageal sphincter (LES) pressure in healthy subjects.

This randomized, double-blind, placebo-controlled, cross-over study, assessed the effects of oral lesogaberan on LES function and reflux when added to proton pump inhibitor (PPI) treatment in patients with GERD who had reflux symptoms despite continuous PPI treatment. Twenty-seven subjects (16 men) with at least 6 months' history of reflux symptoms were randomized. At the screening visit, patients underwent physical examination, laboratory tests, manometry and completed the reflux disease questionnaire and the gastrointestinal symptom rating scale. Patients received lesogaberan (65 mg) or placebo twice on day 1 and once on day 2, in addition to existing PPI treatment. After a washout period of 5–28 days, patients crossed over to the opposite treatment arm. Ambulatory impedance-pH monitoring was done for 24 h after the first dose. Stationary manometry and impedance-pH monitoring was done for 4 h after the last dose on day 2.

Lesogaberan reduced the geometric mean number of TLESRs by 25% (GMR, 0.75; 95% CI, 0.60–0.93) and increased LES pressure by 28% (GMR, 1.28; 95% CI, 1.05–1.57) compared with placebo in the 3 postprandial hours (1–4 h after the third dose). It reduced the total number of reflux episodes in the 3 postprandial hours by 47% and the total number of reflux episodes over 24 h by 35%.

The authors conclude that in patients with reflux symptoms despite PPI treatment, lesogaberan decreases the number of TLESRs and reflux episodes, and increased LES pressure compared with placebo.

Liu J, Yang HI, Lee MH, et al. REVEAL-HBV Study Group. **Incidence and determinants of spontaneous hepatitis B surface antigen seroclearance: a community-based follow-up study.** Gastroenterology. 2010;139:474–82.

Seropositivity for HBsAg is an important risk factor for cirrhosis and hepatocellular carcinoma (HCC). Spontaneous clearance of HBsAg, though rare, usually confers a good prognosis in the absence of pre-existing HCC or cirrhosis. There are no large, long-term, community based studies of HBV carriers to examine the factors leading to HBsAg seroclearance.

This prospective study aimed to elucidate the natural history and determinants of HBsAg seroclearance in adult HBsAg carriers. 89,293 residents of 7 townships in Taiwan were invited to participate in the REVEAL-HBV study; 23,820 (26.7%) individuals consented. 3,087 participants with no previous history of treatment for hepatitis B virus (HBV), who were seropositive for HBsAg, anti-HCV seronegative and free of cirrhosis, were included. HBsAg, HBeAg, serum HBV-DNA, ALT levels, anti-HCV were performed. Follow up visits and blood tests were done every 6–12 months. Participants whose baseline DNA levels were >10,000 copies had their HBV-DNA levels tested at every follow up visit. The first instance in which a participant tested negative for HBsAg was determined to be the date of seroclearance. The person-years of follow up evaluation for each participant were calculated.

During 24,829 person-years of follow up, 562 cases of cleared HBsAg (calculated annual seroclearance rate of 2.26%). The cumulative probability of HBsAg seroclearance increased with lower baseline serum HBV-DNA levels (69.3% with levels <300 copies/mL vs. 10.3%

with levels >1,000,000 copies/mL, $p < 0.001$) and increasing age (86.6% in age ≥60 y vs. 41.7% in 30–60 y, $p < 0.001$). A spontaneous decrease by ≥3 log in follow up HBV-DNA level was associated with seroclearance (adjusted OR 4.17, 95% CI 2.55–6.82). Cumulative incidence of HBsAg seroclearance at 60 and 100 months after serum HBV-DNA became undetectable was 25.8% and 51.3%, respectively; 95.8% had undetectable HBV-DNA levels before seroclearance.

This study reveals that viral load is an important predictor of the natural seroclearance of HBsAg. This will have significant clinical implications for future research and the treatment of chronic HBV.

Testoni PA, Mariani A, Giussani A, et al. SEIFRED Group. **Risk factors for post-ERCP pancreatitis in high- and low-volume centers and among expert and non-expert operators: a prospective multicenter study.** Am J Gastroenterol. 2010;105:1753–61.

Pancreatitis is one of the complications seen after ERCP. Prospective studies have identified a number of patient and procedure-related independent risk factors for post-ERCP pancreatitis. The relation of the endoscopist's expertise and the incidence of post-pancreatitis have not been evaluated.

This multicenter, prospective study was conducted at 21 centers in Italy over 6 months to identify risk factors for post-ERCP pancreatitis, and the impact of the endoscopist's experience and the center's case volume on this complication. Biochemical tests, amylase, and blood count were done before the procedure; blood count and amylase were repeated at predefined intervals. All patients were hospitalized for 24 h after the procedure, and for longer if complications occurred. Pharmacological prophylaxis of post-ERCP pancreatitis was avoided. Post-procedure pancreatic duct (PD) stenting was adopted in high-risk cases in some centers. Overall ERCP difficulty was graded from 1 (lowest difficulty) to 3 (highest difficulty). Operator's ERCP experience was low grade if total ERCPs done were <200 and/or the current number <40/year. Pancreatitis was defined, graded and investigated as per standard criteria and guidelines.

3,635 ERCP procedures were included. 2,838 (78%) were performed in the 11 high-volume centers (median 257 each) and 797 in the 10 low-volume centers (median 45 each). 3.4% ERCPs were diagnostic. 3,331 ERCPs were carried out by expert operators and 304 by less-skilled operators. There were significantly more difficult procedures in high-volume centers ($p < 0.0001$). Post-ERCP pancreatitis occurred in 137 (3.8%) patients and was mild in 120 (87.4%) and severe in 17 (12.6%). There was no difference in the rates of pancreatitis between high- and low-volume centers (3.9% vs. 3.1%) and expert and non-expert operators (3.8% vs. 5.5%, $p = 0.345$). In high-volume centers, there were 25% more patients with risk factors, and the pancreatitis rate was one-third higher among non-expert operators. On multivariate analysis, history of post-ERCP pancreatitis, biliary pain, >10 attempts to cannulate the papilla, PD cannulation and pre-cut technique, were associated with post-ERCP pancreatitis.

Technique-related risk factors are probably more important and numerous than patient-related ones in the risk of post-ERCP pancreatitis.

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Gastroenterology India

Mishra SR, Sharma BC, Kumar A, Sarin SK. **Endoscopic cyanoacrylate injection versus β-blocker for secondary prophylaxis of gastric variceal bleed: a randomised controlled trial.** Gut. 2010;59:729–35.

Gastric varices (GVs) have a high rebleeding rate (34–89%) and options to prevent rebleeding are not optimized. Eradication rates of GVs with cyanoacrylate (glue) injection range between 50 and 100%. β-blockers (BB) have been recommended empirically for GVs. No trials have compared BB treatment and glue injection for prevention of rebleeding from GVs.

Sixty-four patients with cirrhosis and GVs (GOV2 with eradicated esophageal varices or IGV1) were randomized to receive glue injection ($n = 32$) or propranolol ($n = 32$). Fifteen had active bleeding from GVs and were treated with an emergency single injection of glue; remaining 49 had a history of bleed within 15 days prior to enrolment. Glue was injected at multiple sites with a maximum of 2 mL per site. Second session if required, was done within a week. Propranolol was given to achieve a heart rate of 55/min or a maximal dose of 360 mg/day. All patients had complete obliteration of GVs in the glue group in a mean of 1.7 (0.4) sessions with mean volume of glue required 6.0 (1.7) mL. The mean daily dose of BB was 160 mg. The probability of GV rebleeding was lower in the glue group (9% vs. 44%; $p = 0.004$). All patients in the glue group had a decrease in size of GV (~25 [10–35] to ~5 [0–10] mm; $p < 0.01$). In the BB group, 44% had an increase in size of GVs (~25 [10–35] to ~30 [15–40] mm; $p < 0.01$). Median HVPG increased in the glue group (baseline-15 [10–23] mmHg vs. follow up-17 (11–24) mmHg; $p = 0.001$), and decreased in the BB group (14 [11–24] vs. 13 (8–25); $p = 0.003$). With respect to reduction in HVPG, 12 (42%) patients were responders in the BB group and none in the

glue group. Five responders bled during follow up. Two non-responders in the glue and 8 in the BB group bled. Mortality was lower in the glue group (3% vs. 25%; $p=0.016$). On multivariate analysis, the treatment method, portal hypertensive gastropathy and size of the GV >20 mm correlated with rebleeding.
This study shows that glue injection is more effective in the prevention of rebleeding from GVs. Propranolol is not effective in preventing rebleeding despite reduction in HVPG.

Negi S, Singh A, Chaudhary A. **Pain relief after Frey's procedure for chronic pancreatitis.** Br J Surg. 2010;97:1087–95.

Surgery is generally more effective than endoscopic therapy for relief of pain in patients with chronic pancreatitis (CP). Many patients of CP have an inflammatory mass in the pancreatic head and its resection is necessary to relieve pain.
Sixty patients (50 men, median age 36.5 y) diagnosed with CP (alcohol-52%, pancreas divisum-3%, idiopathic-45%) underwent Frey's procedure (resection of head of pancreas with lateral pancreaticojejunostomy [LR-LPJ]) for severe, persistent or recurrent pancreatic pain. Patients were evaluated using the Izbicki pain score (range 0–100) before surgery, and at intervals of 1, 2, 5 and 7 years after surgery. Pain relief during follow up was categorized as complete (score ≤10) or partial (score >10 after a decrease of over 50%). Fourteen (23%) patients had prior endoscopic pancreatic duct stenting, 26 (43%) had pancreatitis-related complications like pseudocyst, jaundice, segmental portal hypertension, duodenal obstruction, and 12 (20%) had undergone previous pancreatic surgery. Pain was continuous in 15 patients (25%) and recurrent in 45 (75%). The median pain score was 46.4 (40.5–55.8) and 19 patients (32%) needed opiate analgesics for pain relief. All patients had an enlarged pancreatic head (diameter 6 [5.1–7.9] cm), and 25 (42%) had an undilated pancreatic duct. The median hospital stay was 8 (7–9) days. Twenty-five patients (42%) developed early postoperative complications. Two patients died. The dose of insulin could be decreased in 5/19 patients; the prevalence of steatorrhea did not change during follow up. Over follow up of 6.4 (4.5–7.8) years, pain score decreased (46.4 [40.5–55.8] vs. 10.0 [9–21.5]; $p<0.001$). The reduction in pain score was immediate and sustained consistently throughout follow up. The number of events requiring hospital admission decreased (4 [0–6] vs. none) after surgery ($p<0.001$). At the end of follow up, pain relief was achieved in 45 patients (75%). Preoperative opiate medication use, continuous pain and occurrence of postoperative complications were independent predictors of failure to achieve sustained complete pain relief. In patients who required opiate medication before operation, the Izbicki pain score decreased (63.1 vs. 23; $p=0.001$), and number of hospital admissions for exacerbation of pain decreased from 5 to 0 after surgery ($p=0.008$).
Thus, LR-LPJ leads to pain relief in patients with CP. Early referral for surgery before opiate use is needed to relieve pain.

Somani SK, Verma N, Avasthi G, Ghosh A, Goyal R, Joshi N. **High pharyngoesophageal strictures after laryngopharyngectomy can also be treated by self-expandable plastic stents.** Gastroint Endos. 2010;71:1304–7.

Stricture of the neopharynx, or tumor recurrence causes late-onset dysphagia in patients who have undergone total laryngectomy. There may be recurrence of stricture and these patients require long-term feeding via a nasogastric tube or a gastrostomy. Placement of a self-expandable plastic stent (SEPS) is difficult because it is placed very high with the upper end of the stent at 9 to 10 cm from the incisors in the neopharynx.
Four patients (3 men, mean age 63.2 y) with advanced carcinoma of the larynx who had undergone total laryngectomy and radiotherapy developed stricture of the neopharynx and dysphagia. The stricture was dilated using Savary-Gilliard dilators under fluoroscopic guidance. All patients had recurrence of the stricture; 3 patients had grade IV and 1 had grade III dysphagia. Upper GI endoscopy showed a tight stricture at 9 to 14 cm from the incisors, starting from the base of tongue. After 3 sessions of dilation, a stent with a polyester-braided material encapsulated with silicone (Polyflex stent) 9 cm long and 23 mm flare with 20 mm body was placed across the stricture with the upper end and flare above the stricture. After stent placement, dysphagia score reduced to grade I in all patients and they were able to take solid meals. After 3 months the stent was removed endoscopically by using a foreign-body forceps. There was complete improvement of stricture in all 4 patients without recurrence in any of the patients at 6 months follow up. All patients had transient foreign body sensation, transient difficulty in swallowing and transient pain in the throat after stenting. One patient required stent repositioning for relief of neck pain. None of the patients had airway obstruction. There was no stent migration. Three patients remained symptom free after a median follow up of 14 months (range 9–18); one patient died of myocardial infarction 9 months after stenting. The authors conclude that placement of an SEPS is effective in postlaryngopharyngectomy dysphagia.

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