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ORIGINAL PAPERS
Alkaline Reflux Esophagitis in Patients with Total Gastrectomy and Roux en Y Esojejunostomy

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Abstract

Background and Aims. Alkaline reflux esophagitis is a complication that might develop in patients with total gastrectomy. The aim of the study was to analyze the prevalence and severity of reflux esophagitis and the occurrence of complications (Barrett’s esophagus and esophageal stenosis) in patients with total gastrectomy and Roux en Y esojejunostomy. Methods. 92 patients with total gastrectomy performed for gastric cancer were included in the study. None of the patients had esophagitis prior to gastrectomy. The patients were assessed clinically and endoscopically after a certain interval from surgery. Results. An important number of patients (14 out of 92, 15.22%) had reflux esophagitis; 5.43% of the patients had also complications of reflux esophagitis (Barrett’s esophagus and benign esophageal stenosis) and 6.52% had local tumor recurrence. Of the 14 patients with reflux esophagitis, the majority (9/14) had Los Angeles (LA) grade C esophagitis. The mean interval between surgery and the endoscopic evaluation was 4.43 years. Barrett’s esophagus and benign stenosis were diagnosed after a longer period of time (10.33 and 8 years, respectively) as compared to reflux esophagitis (5.29 years). More than half of the esophagitis patients had reflux symptoms. Conclusions. Although Roux en Y esojejunostomy is a reconstructive technique which prevents the reflux, an important percentage of our patients developed alkaline reflux esophagitis. In most cases, the esophagitis was moderate or severe. Complications of alkaline reflux, i.e. benign stenosis and Barrett’s esophagus, also occurred after longer periods of time (8 to 10 years) in a small percentage of patients.

Key words
Alkaline reflux esophagitis - total gastrectomy - Roux en Y esojejunostomy - gastric cancer - Barrett’s esophagus - esophageal stenosis.
Association of Gastroesophageal Reflux Disease Symptoms with Exacerbations of Chronic Obstructive Pulmonary Disease

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Abstract

Background: Symptoms of gastroesophageal reflux disease (GERD) are common in various chronic respiratory diseases, but little is known about GERD in the setting of chronic obstructive pulmonary disease (COPD). The aim of this study was to determine the effect of GERD symptoms on COPD exacerbations and subsequent hospitalization and drug usage. Methods: This retrospective study was conducted from December 2008 to February 2009 in the Pulmonary Clinic of Dr. Shariati University Hospital, Isfahan, Iran. Consecutive patients who were diagnosed with COPD based on clinical features and pulmonary function tests were included. Patients were categorized in GERD positive and GERD negative groups based on the Mayo GERD questionnaire. Exacerbation of COPD, hospitalization, and drug usage were compared between the two groups. Results: During the study period, 110 patients with COPD (mean age = 68.0 ± 8.4 years, 87.3% male) were included; 59 (53.6%) patients were GERD positive. There was no significant difference between the GERD positive and GERD negative patients in age, gender, tobacco use, or body mass index. GERD positive patients experienced significantly more acute exacerbations of COPD than patients who were GERD negative (p<0.001). The rate of hospitalization due to COPD exacerbations was significantly higher in GERD positive patients and they had a more severe COPD (p<0.05) and more concurrent use of multiple therapies as compared with GERD negative patients (p<0.05). Conclusion: Patients with GERD symptoms have more COPD exacerbations and subsequent hospitalizations and drug usage. Clinical trials and preventive strategies for GERD in patients with COPD are warranted.

Key words

COPD - exacerbation - gastroesophageal reflux - hospitalization.
Faecal Lactoferrin, Capsule Endoscopy and Crohn’s Disease. Is there a Three Way Relationship? A Pilot Study

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Abstract

**Background & Aims:** Capsule endoscopy has been shown to be useful in diagnosing small bowel Crohn’s disease. Faecal lactoferrin has been shown to have a high sensitivity and specificity in discriminating between inflammatory bowel disease and irritable bowel syndrome. There have been no studies on the use of faecal lactoferrin in the setting of suspected Crohn’s disease using capsule endoscopy. Our aim was to investigate the clinical utility of lactoferrin in patients with suspected Crohn’s disease using capsule endoscopy. **Methods:** Data was collected prospectively on patient symptoms, family history and blood parameters. Patients were requested to return a stool sample and quantitative analysis using sandwich ELISA was performed for faecal lactoferrin. **Results:** Seventeen patients were recruited with all patients having had more than one criterion for referral. The diagnostic yield for capsule endoscopy was 41%, of which 71% of patients had an elevated faecal lactoferrin (correlation coefficient 0.56, p=0.01). The sensitivity, specificity, positive predictive value and negative predictive value of faecal lactoferrin were 71%, 100%, 100% and 83%, respectively. **Conclusion:** Faecal lactoferrin has a high positive and negative predictive value for the diagnosis of small bowel Crohn’s disease, detected by capsule endoscopy. Faecal lactoferrin is a useful marker (in conjunction with clinical parameters) to determine which patients should be referred for capsule endoscopy.

**Key words**

Faecal lactoferrin - Crohn’s disease - capsule endoscopy.
Outcome of Antiviral Treatment in Patients with Chronic Genotype 1 HCV Hepatitis. A Retrospective Study in 507 Patients

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Abstract

Background and aim: The current standard of care in chronic HCV genotype 1 hepatitis is the combination of pegylated interferon (PegIFN) with ribavirin for 48 weeks. The aim of our paper was to verify if there are significant differences regarding the sustained virologic response (SVR) in patients treated with PegIFN alfa-2a vs. those treated PegIFN alfa-2b, both in combination with ribavirin.

Method: We performed a retrospective study on 507 patients with chronic viral C hepatitis treated with PegIFN alpha-2a 180 μg/kg/week or PegIFN alpha-2b 1.5 μg/kg/week plus ribavirin in the recommended doses according to weight, following the current treatment guidelines. We evaluated the SVR defined as PCR RNA-HCV undetectable 24 weeks after the end of treatment.

Results: There were no differences regarding the baseline characteristics among the subgroups of patients treated with PegIFN alpha-2a or PegIFN alpha-2b concerning the pretreatment viral load (p=0.2445), the severity of fibrosis (p=0.2403), the mean age of the patients (p=0.9597) and the women/men ratio (p=0.2087). The SVR rates in patients treated with PegIFN alpha-2a were similar to those in patients treated with PegIFN alpha-2b: 208/338 (61.5%) vs. 94/169 (55.6%) (p=0.2129).

Conclusion: Sustained virologic response rates were similar in HCV genotype 1 patients treated with PegIFN alpha-2a and with Peg-IFN alpha-2b.

Keywords

HCV hepatitis - sustained virologic response - early virologic response - pegylated interferon - ribavirin - genotype 1 HCV.
Effects of Pro-Inflammatory Cytokines on the Production of Soluble Fractalkine and ADAM17 by HepG2 Cells

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Abstract

Background & Aims: Soluble fractalkine is increased in the liver during times of injury; however the effect of pro-inflammatory cytokines in this process is currently unknown. The aim of this study was to determine whether pro-inflammatory cytokines elevated in patients with hepatocellular carcinoma influence fractalkine shedding from HepG2 cells and whether ADAM17 was involved in this process. Methods: In vitro experiments were performed in the human hepatocellular carcinoma cell line HepG2. Soluble fractalkine was detected using an ELISA. ADAM17 expression was investigated using quantitative real time (reverse transcription)-polymerase chain reaction and flow cytometry. Short interfering RNA transfection was used to down-regulate ADAM17 expression. Results: Soluble fractalkine was present in supernatants of HepG2 cells, and was significantly increased by interleukin-1β (p≤0.005) and tumour necrosis factor-α (p≤0.043), but not by interleukin-6 (p≥0.316). This corresponded to minor increases in ADAM17 protein, but not ADAM17 mRNA, following the same treatments. However, the down-regulation of ADAM17 protein did not affect fractalkine shedding. Conclusions: This study showed that soluble fractalkine is up-regulated under inflammatory conditions associated with hepatocellular carcinoma development, but ADAM17 does not appear to be responsible for regulating this process.

Keywords
Analysis of the Common Vasoactive Intestinal Peptide Receptor 1 Polymorphism in Gallstone Patients

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Abstract

Background and aim: Cholesterol gallstone disease is caused by both genetic and environmental factors (e.g., deranged motility of the gallbladder wall). Recently, a single nucleotide polymorphism (SNP) of the vasoactive intestinal peptide receptor 1 (VIPR1) gene has been linked to late onset of achalasia, a lower esophagus dysmotility disorder. As VIPR1 is expressed in the gallbladder wall as well, and patients with achalasia exhibit extraesophageal motility disorders, the influence of VIPR1 SNP on cholelithiasis was investigated. Methods: We analyzed 254 gallstone-free controls (confirmed by ultrasound, age 21-78 years, 88% women, BMI 16-43 kg/m²) and 226 individuals from 107 families with gallstones (age 24-80 years, 87% women, BMI 17-55 kg/m²). All individuals were genotyped for the VIPR1 rs437876 SNP (intron 4) with PCR-based 5'-nuclease and fluorescence detection assays (TaqMan). We performed nonparametric linkage (NPL) analysis in affected sib-pairs (ASP), association tests, and regression analyses. Results: Controls were significantly younger (P < 0.01) and leaner than ASP and cases (P < 0.01), and both age as well as BMI significantly increased the risk of developing gallstones (P < 0.001). Allele frequencies were in line with database entries and no deviation from Hardy-Weinberg equilibrium was detected. Neither allele and genotype distributions nor NPL scores or the restriction of analysis to individuals older than 50 years provided evidence for association or linkage of the VIPR1 SNP and cholelithiasis. Conclusion: The VIPR1 polymorphism, previously linked to gastrointestinal dysmotility disorders, does not represent a common risk factor for gallstones in the general or in an elderly population.

Key words
Achalasia - cholelithiasis - gallbladder motility - single nucleotide polymorphism.
Prevalence of Gastroparesis in Type 1 Diabetes Mellitus and its Relationship to Dyspeptic Symptoms

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Abstract

Background and Aim: Gastroparesis and/or dyspeptic symptoms occur in around 50% of type 1 diabetic patients. The aim of our study was to evaluate the prevalence of gastroparesis in patients with type 1 diabetes using \(^{13}\)C-octanoic acid breath test (\(^{13}\)C-OBT) and the relationship between dyspeptic symptoms and gastric emptying. Methods: Gastric emptying of solids was evaluated prospectively in euglycemic conditions in 69 type 1 diabetic patients (male/female: 36/33; mean age 49.5 ± 14.2 years; mean duration of diabetes 20.4 ± 8.2 years) and 40 healthy volunteers (male/female 17/23; mean age 34.3 ± 16 years) using \(^{13}\)C-OBT. Dyspeptic symptoms, autonomic nerve function and Helicobacter pylori (H. pylori) status were assessed. Results: Solid gastric emptying was slower in diabetic patients (T1/2=125.36 ± 31.5 min) than in healthy subjects (T1/2=88.5 ± 27.3 min) (p<0.05). Gastric emptying was slower in diabetic female compared to diabetic male patients (p<0.05). Body mass index (BMI) was the only independent predictor for delayed solid gastric emptying in a logistic regression model testing HbA1c, BMI, age, diabetes duration, H. pylori status, peripheral neuropathy, retinopathy, nephropathy, and autonomic neuropathy. Abdominal bloating and upper abdominal pain were associated with delayed gastric emptying. Conclusions: We found that 33.7% of type 1 diabetic patients had delayed gastric emptying that correlated with female gender, increased BMI, abdominal bloating and upper abdominal pain.

Key words

Diabetic gastroparesis - \(^{13}\)C-octanoic acid breath test - gastroparesis - symptom questionnaire - diabetes mellitus type I - gastric emptying coefficient - breath tests.
Survival and Quality of Life of Cholangiocarcinoma Patients: a Prospective Study over a 4 Year Period

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Abstract

Background and aims: Cholangiocarcinomas (CCAs) are tumors with a poor prognosis and a lower quality of life (QoL). The aim of this study was to evaluate the survival rate and quality of life in CCA patients. Method: We prospectively enrolled 133 patients diagnosed with CCA in the 3rd Medical Clinic, Cluj Napoca, over a 4-year period (2005-2009). The QoL was evaluated by means of a QoL questionnaire (EORTC QLQ-C30). Results: The mean age of the patients was 65 ± 10.6 years: 55% were males. 71% of the patients had hilar tumor (Klatskin), 23% distal and 6% intrahepatic CCA (IH). Only 11.3% of the patients were eligible to receive curative treatment. The 1-year overall survival was 22.3 ± 4.4% and the 2-year survival was 3.4 ± 2.1%. The patients receiving metallic stents had better survival than those receiving plastic stents (40.4% vs 12.5% at 1 year, 9.1% vs 5.0% at 2 years, respectively). The 1-year survival was significantly improved for patients who underwent surgery plus adjuvant chemotherapy. The post-therapy QoL demonstrated a less improvement in Klatskin tumor patients than in patients with other types of tumors. Endoscopic palliative therapy allowed a faster community reintegration, but with variable evolution. Conclusions: The highest 2-year survival rate was 5.5%. Slightly longer survival was recorded when chemotherapy was added and also after endoscopic placement of metallic stents. Endoscopic biliary decompression improved the QoL faster than surgery.

Key words
REVIEWS

Dosing 6-Thioguanine in Inflammatory Bowel Disease: Expert-Based Guidelines for Daily Practice

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Abstract

Conventional thiopurines are considered to be effective and safe in the treatment of inflammatory bowel disease (IBD) patients; unfortunately more than 50% of patients discontinue thiopurine therapy, mainly due to the development of intractable adverse events. In recent years, the use of 6-thioguanine has been proposed as an alternative thiopurine in IBD patients failing to tolerate or to respond to conventional thiopurine therapy. In this clinical review, we describe the rationale for 6-thioguanine therapy and discuss the reported hepatotoxicity of 6-thioguanine (especially nodular regenerative hyperplasia). We propose expert-based guidelines for balanced treatment.

Key words
Cyclic Antibiotic Therapy for Diverticular Disease: a Critical Reappraisal

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Abstract

Different symptoms have been attributed to uncomplicated diverticular disease (DD). Poor absorbable antibiotics are largely used for uncomplicated DD, mainly for symptom treatment and prevention of diverticulitis onset. Controlled trials on cyclic administration of rifaximin in DD patients were evaluated. Four controlled, including 1 double-blind and 3 open-label, randomized studies were available. Following a long-term cyclic therapy, a significant difference emerged in the global symptoms score (range: 0-18) between rifaximin plus fibers (from 6-6.5 to 1-2) and fibers alone (from 6.7 to 2-3.8), although the actual clinically relevance of such a very small difference remains to be ascertained. Moreover, a similar global symptom score reduction (from 6 to 2.4) can be achieved by simply recommending an inexpensive high-fiber diet. Current data suggest that cyclic rifaximin plus fibers significantly reduce the incidence of the first episode of acute diverticulitis as compared to fibers alone (1.03% vs 2.75%), but a cost-efficacy analysis is needed before this treatment can be routinely recommended. The available studies have been hampered by some limitations, and definite conclusions could not be drawn. The cost of a long-life, cyclic rifaximin therapy administered to all symptomatic DD patients would appear prohibitive.

Key words
Diverticular disease - therapy - symptoms - rifaximin - diverticulitis - haemorrhage.
Abstract

The rates of the predominantly hospital acquired infection, *Clostridium difficile*, have increased throughout the world. Several risk factors and susceptible patient populations have been identified. Patients with pre-existing liver disease represent an important cohort; recent evidence suggests that *Clostridium difficile* infection (CDI) is associated with a worse outcome and increased health care costs. This review focuses on the epidemiology, risk factors, pathogenesis, treatment options and outcomes associated with CDI in patients with liver disease.

Keywords

*Clostridium difficile* - *Clostridium difficile* infection enterocolitis - pseudomembranous - epidemiology - liver diseases - risk factors and treatment.
An Unusual Cause of Dysphagia: Esophageal Tuberculosis

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Abstract

A 25-year old Indian exchange-student presented to our department with a three week history of dysphagia. Diagnostic evaluation by upper gastrointestinal endoscopy, endosonography and chest-CT revealed a tumor-suspect ulcerative lesion at the middle esophagus, and a mediastinal lymph node enlargement. Initial histopathological evaluation of multiple esophageal tissue biopsies showed an unspecific esophagitis without signs for malignancy. A positive T-spot®.TB assay result, together with the bronchoscopic detection of a small exophytic lesion at the right main bronchus depicting caseating epitheloid cell granulomas, provided evidence for a tuberculous etiology of the esophageal tumor. Multiple further deep submucosal biopsies were needed to finally detect epitheloid cell granulomas in the esophageal lesion. Microbacteriological or molecular tests were negative for M. tuberculosis. Tuberculostatic treatment resulted in a good response with complete remission of the esophageal lesion and the mediastinal lymph node enlargement. Esophageal tuberculosis is rare in developed countries, and its possible presence deserves consideration particularly in patients at risk.

Keywords

Dysphagia - ulcerating esophageal lesion - M. tuberculosis - esophageal tuberculosis.
Incomplete Deployment of an Expandable Metallic Stent in a Patient With Esophageal Malignant Stenosis

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Abstract

The use of self expandable metallic stents (SEMS) in the palliation of dysphagia due to malignant esophageal stenosis is a gold standard. Covered stents are used in all cases with overt air-digestive fistula or high potential for fistula development. The procedure is associated with a low incidence of procedure-related complications. We present a case with a major accident which developed during stent deployment. The delivery system became blocked and we found it impossible to fully deploy the stent, which remained attached to the introductory system. The stent was forcefully removed and replaced later on with a new stent. This is the first report of a SEMS related accident due to malfunction of the stent deployment system. Stent malfunction is unusual and unlikely to happen, but one should be aware and prepared for such unusual situations.

Key words
Self expandable metallic stent (SEMS) - esophageal malignant stenosis - incidents and accidents.
Rapid Recovery of a Rectovaginal Fistula with Infliximab in a Patient with Crohn’s Disease

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Abstract

We present the case of a female patient diagnosed with colonic Crohn’s disease, having a clinical evolution with many recurrences and in whom conventional therapy had failed. The patient was admitted in our department 4 years after the onset of the disease, with an altered general state, diarrhea, malnutrition, fever and fecaloid vaginal discharge. Investigations classified the patient in a severe activity flare of Crohn’s disease (CDAI 329), complicated with a rectovaginal fistula. Infliximab therapy was initiated. The evolution was rapidly favorable and the fistula closed after 4 weeks of therapy.

Key words
Crohn’s disease - endovaginal ultrasonography - rectovaginal fistula - infliximab.
Acute Spontaneous Chylous Peritonitis: Report of a Case

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Abstract

Acute abdominal pain with peritonitis due to sudden extravasation of lymph into the peritoneal cavity is a rare condition that is often mistaken for other causes of acute abdomen. The diagnosis of spontaneous chylous peritonitis is rarely suspected preoperatively, usually misdiagnosed with diverse common surgical emergencies. We report the case of an 81 year old female who presented with typical symptoms of acute abdomen, presumed as acute mesenteric ischemia. The diagnosis of chylous peritonitis was established during laparoscopy and treatment consisted of low fat diet and octreotide.

Key words

Acute abdominal pain - chylous peritonitis - somatostatin.