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THE FREQUENCY AND SPECTRUM OF ESOPHAGEAL DYSMOTILITY DISORDERS IN SUPRAESOPHAGEAL MANIFESTATIONS OF GERD.

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Esophageal motility problems have been demonstrated in patients with noninflammatory typical gastroesophageal reflux disease (GERD) and esophagitis; however, the frequency of dysmotility disorders in patients with supraesophageal manifestations of reflux has not been studied systematically. The purpose of this study was to assess the frequency and spectrum of esophageal dysmotility disorders in patients with laryngopharyngeal reflux (LPR) or upper aerodigestive disorders. Study subjects were 112 consecutive new patients (79 females, 33 males, aged 18-81 years) with LPR symptoms and laryngeal findings consistent with LPR, who were studied prospectively between November 1998 and November 1999. They were divided into the following diagnostic categories: hoarseness, 43% (n=48); dysphagia, 21% (n=24); chronic cough, 20% (n=22); globus pharyngeus, 12% (n=13); and paroxysmal laryngospasm, 4% (n=5). Of these 112 patients, 81 (72%) underwent pH-metry and esophageal motility studies, 12 (11%) had only pH-metry studies, and 19 (17%) had only motility studies. The 12 patients who underwent only pH-metry were excluded from data analysis. Of the 100 patients who underwent motility studies, 29% had normal esophageal motility and 71% had motility disorders: hypertensive lower esophageal sphincter (LES), 10; ineffective esophageal motility (IEM), 48; achalasia, 4; and nutcracker esophagus, 9. No patient had diffuse esophageal spasm. Of 81 patients who underwent both pH-metry and motility studies, 65 (80%) had abnormal pH-metry studies and 55 (68%) had abnormal motility findings. Abnormal pH-metry findings in these patients were as follows: pharyngeal or proximal probe only, 31 patients (38%); esophageal probe only, 3 patients (4%); and both pharyngeal and esophageal probe, 31 patients (38%). Abnormal motility findings were hypertensive LES in 8 patients (10%), IEM in 36 (44%), achalasia in 3 (4%), and nutcracker esophagus in 8 (10%). Based on our findings, it appears that a significant number of patients with supraesophageal manifestations of GER demonstrate primary esophageal motility disorders with and without positive pH studies. We are now undertaking a retrospective analysis of these patients to examine the possible relationship between esophageal motility disorders and specific supraesophageal complications of GER.

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THE EFFECT OF Z-338, A NEW GASTROPROKINETIC AGENT, ON THE ISOLATED SEGMENT OF THE OPOSSUM LOWER ESOPHAGEAL SPHINCTOR.

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Z-338 is an orally administered prokinetic agent that enhances postprandial gastroduodenal motility. It has been reported that Z-338 produced the increase in lower esophageal sphinctor (LES) pressure in dogs. We investigated the effect of Z-338 on the isolated circilar muscle segment of opossum lower esophageal sphinctor, and compared with the effect of the prokinetic agent cisapride. Z-338 (10^{-9}-10^{-5} M) increased the basal tone of the LES in a concentration-dependent manner. Cisapride (10^{-8}-10^{-6} M) produced a lesser increase on the basal tone. Z-338 induced greater contractions compared to equivalent concentrations of cisapride. Contractions caused by Z-338 were not influenced by the nitroric oxide synthase inhibitor L-nitro-L-arginine (L-NNA, 10^{-4} M) or by the selective serotonin 5-HT_4 antagonist GR113808 (10^{-5} M). Atropine (10^{-5} M) partially inhibited the contractions induced by Z-338. The increased basal tones caused by Z-338 were inhibited by tetrodotoxin (TTX, 10^{-6} M), and TTX plus the N-type calcium channel antagonist omega-conotoxin GVIA (omega-CTX, 10^{-6} M). On the other hand, contractions caused by cisapride were inhibited by GR113808. Contractions induced by cisapride were not affected by L-NNA, atropine, TTX, and TTX plus omega-CTX. These results suggest that Z-338 acts neurotransmission mediated by excitatory postganglionic nerve endings. On the other hand, cisapride acts directly on the smooth muscle of the opossum LES. It has been reported that cisapride has a human ether-a-go-go-related gene (HERG) K^+ channel blocking action. E-4301, a selective HERG-K^+ channel blocker, also produced a small increase in the basal tone of opossum LES. It is possible that cisapride-induced contractions were caused by directly blocking action of HERG-K^+ channel on the smooth muscle. Thus mechanisms of Z-338 are different from those of cisapride in the opossum LES.

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NON-ACHALASIA HYPERTENSIVE LOWER ESOPHAGEAL SPHINCTER: EGG PROFILE.

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AIMS: The hypertensive lower esophageal sphincter (HLES) is an uncommon primary motility disorder characterised by elevated sphincter pressure and normal sphincter function. Proximal gastric dysfunction and neuromuscular sphincter abnormalities have been documented in Achalasia. The aim of this study was to compare EGG patterns pre and post prandially in symptomatic patients with a hypertensive sphincter. METHODS: EGG studies were carried out in the upright position, pre and post prandially. 17 Normal volunteers were compared with 11 patients with HLES. Stationary manometry was performed on all patients, HLES was defined as lower esophageal pressure >30mmHg. The Basal Electrical Rhythm (BER) was recorded for a minimum of 30 minutes during fasting. All subjects then consumed a 447 kCal meal and the recording was continued for 60 minutes post prandially. Bradygastria (Brady) was defined as less than 2 cycles per minute (cpm), Normal BER as 2-4cpm, and Tachygastria (Tachy) as 4-9cpm. The Power Ratio (PR) was also measured. RESULTS:(See Table below) The basal electrical rhythm was normal for both groups, however there was significant increase in the incidence of Tachygastria post prandially in the HLES group. The power ratio was significantly less than the normal values, and the Dominant Frequency(Dom Freq) pre and post prandially was unaltered. The combination of elevated LES pressure and gastric dysrhythmia may contribute to the symptoms experienced in patients with Hypertensive Lower Esophageal Sphincter.

Normal vs HLES patients

	Brady		3cpm		Tachy		PR	Dom Freq	
	Pre	Post	Pre	Post	Pre	Post		Pre	Post
Normal (17)	13.6	11.9	84	87	2.4	1.3	5.9	3.03	2.97
SEM +/-	3.5	2.9	3.6	2.9	1.4	0.6	1.1	0.6	0.09
HLES (11)	15.3	15.2	85.4	80.8	0.77	3.85	2.96	2.88	3.02
SEM +/-	5.9	4	6.2	4.7	0.5	1.2	0.95	0.2	0.6
Wilcoxon p values	ns	ns	ns	ns	ns	<0.05	<0.01	ns	ns

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HEARTBURN-LIKE SYMPTOMS ARE NOT ONLY INDUCED BY ABNORMAL GASTRO-ESOPHAGEAL REFLUX, BUT ALSO ASSOCIATED WITH IMPAIRED GASTRIC MOTILITY.

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Background: Delayed gastric emptying is a frequent finding in patients with functional dyspepsia, but it is also a contributing factor in the pathogenesis of gastro-esophageal reflux disease (GERD). Aim of the study was to investigate gastric emptying and the presence of abnormal gastro-esophageal reflux (aGER) in patients with predominant heartburn in conjunction with other upper abdominal symptoms. Methods: 45 consecutive patients with heartburn were investigated. Patients with PPI in the last 2 weeks were excluded. In all patients a 24h-pH-metry was performed and after placement of the catheter a standardised ^{13}C-octanoic acid breath test was performed. An aGER was defined by the DeMeester-score > 14.7. During a 4h period breath samples were collected every 15 min. after ingestion of a standard solid test meal containing 91 mg ^{13}C-octanoic acid. Lag phase (LP) and half gastric emptying time (t½) were calculated. Results: 23 of 45 (51%) patients presented with aGER. 11 of 45 (24%) patients had a normal half gastric emptying time based on the reference values of an European study. 16 (36%) patients have both abnormal t½ and aGER. Discussion: Heartburn is not specific for abnormal gastro-esophageal reflux but often associated with a delayed gastric emptying. This raises the question if heartburn-like symptoms in several patients are induced by viceral hypersensitivity associated with a motility disorder.

	mean±sem	n	t1/2 (min)	LP (min)
pts. with abnormal t1/2 (n=34)	aGER	16	207±20	154±16
	no aGER	18	184±14	123±7
pts. with normal t1/2 (n=11)	aGER	7	93±5	59±6
	no aGER	4	92±4	53±2

aGER = abnormal gastroesophageal reflux