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Impaired Esophageal Function in Patients with Irritable Bowel Syndrome

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A B S T R A C T

The aim of the study was to determine prevalence of the signs and symptoms related to esophageal dysfunction in irritable bowel syndrome (IBS) patients, and to investigate sensorimotor function impairment based on the esophageal manometry study, thus to determine the correlation between them. The study included 30 patients with IBS, 14 of them with diarrhea (IBSd) and 16 with constipation (IBSc) as a predominant discomfort. Control group consisted of 30 healthy subjects. The patients were included in the study on the basis of the Rome criteria for IBS. In addition to thorough history and physical examination patient underwent esophagogastroduodenoscopy and esophageal manometry. The values of esophageal manometry obtained in healthy subjects served as controls in manometry studies. The patients with IBS suffered a great number of both colonic and extracolonic signs and symptoms, however, there was no statistically significant difference in the prevalence of particular symptoms between the two patient subgroups. In comparison with healthy subjects, the patients suffering from IBS showed pathologically altered values in the majority of parameters of esophageal motility. Comparison of the two subgroups of IBS patients according to esophageal motility characteristics yielded differences in only few of them. The results obtained in the study could explain why the patients with IBS quite commonly complain of the symptoms related to upper gastrointestinal tract, such as heartburn and chest pain of noncardiac genesis. The results also suggest that the IBS might be associated with considerably more extensive smooth muscle or innervation changes than presumed before.

Key words: *irritable bowel syndrome, Rome criteria, esophageal motility, esophageal manometry*

Introduction

Irritable bowel syndrome (IBS) is a functional disorder of the gastrointestinal system characterized by abdominal pain related to bowel emptying, defecation impairment, and abdominal distention[1]. In 1988, the Rome criteria for functional gastrointestinal disorders were presented by an expert group at the XIII International Congress of Gastroenterology[2]. In 2006 expert group presented Rome III criteria which are the current standard. According to these criteria, the diagnosis of IBS is made on the basis of characteristic signs and symptoms of the disease, i.e. 'positive diagnosis' rather than by elimination of other diseases. These criteria define IBS as a pathologic entity with three different clinical forms: syndrome subgroup predominated by diarrhea, subgroup predominated by constipation, and subgroup with abdominal distension and/or abdominal pain[3] (Table 1).

IBS is one of the most common and at the same time least known diseases in gastroentrology[4–9]. The prevalence of IBS in West European countries and USA has been estimated to range between 5% and 25%, and is more common in female population[2–5]. In a large epidemiologic study conducted in the American population, 9.4% of subjects met the Rome criteria for IBS[1,6,9–11]. Unfortunately, complete epidemiologic data on IBS in Croatia have been lacking to date. There was only one study carried out in 2002 in 500 subjects recruited from the Zagreb population, which found the prevalence of IBS to

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TABLE 1
ROME III CRITERIA FOR THE DIAGNOSIS OF IRRITABLE BOWEL SYNDROME

1. For at least 12 weeks, which need not be consecutive, of the preceding 12 months, the patient must have abdominal discomfort or pain associated with at least 2 of the folowing 3 features
   a. Pain relieved by defecation
   b. Onset associated with change in stool frequency
   c. Onset associated with change in stool form
2. Positive two or more of the following items on at least ¼ episodes or days:
   a. Changes in stool frequency (more than 3 per day or less than 3 per week);
   b. Changes in stool consistency (pelleted/hard or loose/liquid);
   c. Changes in stool passage (straining, urgency, incomplete evacuation);
   d. Mucous stool; and/or
   e. Abdominal distension

be 28%. The figure is relatively high in comparison with the results reported elsewhere, however, the author attributes it to the impact of war and postwar stressors[8].

The pathogenesis of IBS remains unknown. These patients are considered to suffer from disturbances in the bowel sensorimotor function, central nervous system (CNS) impairments, psychologic disturbances, and effects of stress; in addition, the role of certain intestinal (luminal) factors has also been suggested. Anyhow, there is no specific, unique pathophysiologic disorder to differentiate the disease from organic diseases of the gastrointestinal system[1,2,10].

IBS patients frequently also have symptoms that are not characteristic of the distal part of the gastrointestinal system. The upper gastrointestinal system symptoms such as heartburn, early satiety, nausea and vomiting occur in 25% to 50%, and intermittent dyspepsia (pain or discomfort localized in the upper abdomen) in as many as 90% of patients[12]. Dyspepsia is so common in IBS that some authors consider it a component of the IBS clinical picture. One third of patients with dyspepsia are free from defecation problems, whereas others exhibit similar motility impairments and hypersensitivity of the small and large intestine and upper gastrointestinal system[13].

There are relatively many studies dealing with small and large intestine motility impairments. Although clinical observations on the high prevalence of the upper gastrointestinal tract symptoms in IBS patients are beyond any doubt, reliable studies and definite data on the rate of esophageal motility impairments in these patients are still lacking.

TABLE 2
GENERAL CHARACTERISTICS OF STUDY GROUP

	IBS (n=30)	Control (n=30)	p
Age (yrs)	46.9 ± 10.21	46.2 ± 9.45	ns
Sex			
Male	11 (36.6%)	12 (40.0%)	ns
Female	19 (63.4%)	18 (60.0%)	ns
Education			
Elementary	9 (30.0%)	11 (36.6%)	ns
Secondary	15 (50.0%)	14 (46.7%)	ns
idctlparUniversity	6 (20.0%)	5 (16.6%)	ns
BMI	27.37 ± 3.15	28.33 ± 4.9	ns

IBS – irritable bowel syndrome, BMI – body mass index

The aim of the present study was to assess the prevalence of the signs and symptoms related to esophageal dysfunction in IBS patients, and to investigate the esophageal sensorimotor function impairment based on the esophageal manometry findings, thus to determine the correlation between the clinical picture and manometry finding.

Subjects and Methods

Subjects

Thirty IBS patients (19 female and 11 male) aged >18, suffering from upper gastrointestinal tract discomforts, and 30 healthy age-matched subjects (18 female and 12 male) were included in the study (Table 2). IBS patients were included on the basis of Rome criteria and exclusion of a potential organic gastrointestinal disease. Therefore, normal findings of the following tests were required for patient entry in the study: complete blood count, erythrocyte sedimentation rate, basic biochemistry parameters (potassium, sodium, blood glucose, urea, creatinine, hepatic transaminases, serum amylases), negative stool bacteriology and parasitology, negative blood in stool, and normal upper abdomen ultrasonography. IBS patients were divided into two subgroups: IBSd – IBS predominated by diarrhea (10 women and 6 men), and IBSc – IBS predominated by constipation (9 women and 6 men, Table 3).

Methods

Besides thorough history and physical examination, the following diagnostic methods were performed: esophagogastroduodenoscopy[14] and esophageal manometry with 6-channel catheter[15].

Esophageal manometry was performed by computed manometry (Albyn Medical, Griffon) in fasting state and after 48-hour medicamentous therapy interruption. The

TABLE 3
GENERAL CHARACTERISTICS OF IBS SUBGROUPS

	IBSd (n=16)	IBSc (n=14)	p
Age (yrs)	47.3 ± 10.25	46.4 ± 10.15	ns
Sex			
Male	6 (37.5%)	5 (35.7%)	ns
Female	10 (62.5%)	9 (64.3%)	ns
Education			
Elementary	5 (31.3%)	4 (28.6%)	ns
Secondary	6 (37.5%)	7 (50.0%)	ns
University	5 (31.3%)	3 (21.4%)	ns
BMI	28.7 ± 3.8	26.5 ± 4.3	<0.05

IBSd – irritable bowel syndrome with predominant diarrhea, IBSc – irritable bowel syndrome with predominant constipation, BMI – body mass index

measurements were done by use of a 6-channel catheter with distal openings distributed at variable distance, 5 cm apart (3 openings) or radially distributed at the same level (3 openings). Each of the catheter lumina was perfused with distilled water flowing at a rate of 1.36 ml/min. Pressure converters were connected to the free ends of the catheter for computer recording of pressure curves. The tip of the catheter, previously introduced through the nose to the stomach was slowly pulled out through the esophagus while continuously recording pressure values at rest in various projections. The lower esophageal sphincter pressure was measured by stationary and rapid pull-through technique. The catheter was left for 5 min in place in the lower esophageal region to record the number of spontaneous contractions not induced by deglutition and expressed as number of contractions per minute. The occurrence of simultaneous contractions and incomplete propagation contractions was also recorded. Then the catheter was so placed as to cover the complete body of the esophagus with its openings, the most distal opening placed 5 cm above the upper edge of the lower esophageal sphincter. Contraction waves after 10 gulps of 5 ml water each were determined. The upper esophageal sphincter pressure was recorded by use of the stationary method of catheter withdrawal. The dynamics of all esophageal pressures was recorded and stored in a computer, allowing for subsequent analysis of the data obtained[1,16]. The esophageal manometry parameters are: position, length, resting pressure, ability of relaxation upon deglutition of upper and lower esophageal sphincter; contractions (normal, repetitive, absent), mean peristaltic peak pressure for upper, medial and lower esophagus, peristaltic activity (coordinated, simultaneous, incomplete propagation) and mean rate of peristaltic wave.

Statistics

A number of statistical methods were employed in the study. The methods of descriptive statistics were regularly used for all variables according to defined groups, and included arithmetic mean, standard deviation, minimal and maximal values, and Kolmogorov test of distribution normality. Depending on the characteristics of the data obtained, the methods of parametric or nonparametric statistics were used to determine the significance of between-group differences (t-test, analysis of variance, correlation test, χ^2-test, Pearson's χ^2-test with Yates correction in 2 × 2 tables). The Statistica Version 10 software was used in statistical analysis.

Results

There was no statistically significant difference between the group of IBS patients and control group of healthy subjects according to age, sex, level of education and body mass index. There was a female predominance in both IBS and control group (M/F ratio: 63%/37% and 60%/40%, respectively, Table 2). The two IBS subgroups did not differ significantly according to age, sex and level of education, however, they did differ according to body mass index in favour of the IBSd subgroup (Table 3).

Considering the upper gastrointestinal tract symptoms occurring in IBS patients, dyspepsia present in 87% of study patients showed highest prevalence, followed by

TABLE 4
PREVALENCE OF UPPER GASTROINTESTINAL TRACT SIGNS AND SYMPTOMS IN IBS PATIENTS

	IBS (n= 30)	IBSd (n=16)	IBSc (n=14)	p
Epigastric pain	14 (47%)	7 (44%)	7 (50%)	ns
Pain posteriorly to sternum	6 (20%)	4 (25%)	2 (14%)	ns
Heartburn	21 (70%)	12 (75%)	9 (64%)	ns
Regurgitation	12 (40%)	7 (44%)	5 (36%)	ns
Dysphagia	3 (10%)	2 (13%)	1 (10%)	ns
Eructation	21 (70%)	11 (69%)	10 (71%)	ns
Vomiting	5 (17%)	3 (19%)	2 (14%)	ns
Globus sensation	23 (77%)	12 (75%)	11 79%)	ns
Dyspepsia	26 (87%)	13 (81%)	13 (93%)	ns

IBSd – irritable bowel syndrome with predominant diarrhea, IBSc – irritable bowel syndrome with predominant constipation, BMI – body mass index

TABLE 5
ENDOSCOPICALLY VERIFIED LESIONS OF ESOPHAGUS, STOMACH AND DUODENUM IN IBS PATIENTS

	IBS	IBSd	IBSc	p
Normal finging	17 (57%)	8 (50%)	9 (64%)	ns
Reflux esophagitis*	13 (43%)	5 (31%)	8 (57%)	ns
Grade 1	10 (33%)	4 (25%)	6 (43%)	ns
Grade 2	3 (10%)	1 (6%)	2 (14%)	ns
Grade 3	0 (0%)	0 (0%)	0 (0%)	ns
Grade 4	0 (0%)	0 (0%)	0 (0%)	ns
Antral gastritis	11 (37%)	6 (38%)	5 (36%)	ns
Duodenitis	9 (30%)	5 (31%)	4 (29%)	ns
H. pylori positive	7 (23%)	3 (19%)	4 (29%)	ns

IBS – irritable bowel syndrome, IBSd – irritable bowel syndrome with predominant diarrhea, IBSc – irritable bowel syndrome with predominant constipation, BMI – body mass index; *Savary-Miller classification

globus sensation, heartburn and frequent belching. Dysphagia was the most infrequent symptom, present in 10% of study patients. There was no statistically significant difference between the two IBS subgroups in the prevalence of any of the symptoms determined (Table 4).

Endoscopic examination of the upper segment of the alimentary tract revealed normal findings in 57% of IBS patients. Reflux esophagitis according to Savary-Miller was endoscopically verified in 43% of IBS patients, none of them with the disease stage III or IV. There was no sta-

TABLE 6
MANOMETRY CHARACTERISTICS OF IBS PATIENTS AND NORMAL CONTROL SUBJECTS

	IBS (n= 30)	Control (n=30)	p
Lower esophageal sphincter			
Total length (mm)	35 ± 5	38 ± 7	ns
abdominal segment	15 ± 6	28 ± 6	p<0.05
thoracic segment	20 ± 8	10 ± 5	p<0.01
Resting pressure (mmHg)	11 ± 8	17 ± 7	p<0.01
abdominal segment	12 ± 8	18 ± 8	p<0.01
thoracic segment	10 ± 4	15 ± 6	p<0.01
Relaxation upon deglutition (mmHg)	2 ± 1	0 ± 2	ns
Body of esophagus			
Contraction (n=30)			
normal	123 (41%)	270 (90%)	p<0.01
repetitive	132 (44%)	30 (10%)	p<0.01
absent	45 (15%)	0 (0%)	p<0.01
Mean contraction duration (s)	3 ± 0.5	3.3 ± 0.4	ns
Mean peristaltic peak pressure (mmHg)			
upper esophagus	78 ± 12	74 ± 9	p<0.05
medial esophagus	95 ± 15	91 ± 13	p<0.05
lower esophagus	78 ± 11	76 ± 10	ns
Peristaltic activity (n=300)			
coordinated	210 (70%)	300 (100%)	p<0.01
simultaneous	45 (15%)	0 (0%)	p<0.01
incomplete propagation	45 (15%)	0 (0%)	p<0.01
Mean rate of peristaltic wave (cm/s)	5.2 ± 1.05	4.6 ± 0.9	ns
Upper esophageal sphincter			
Length (mm)	28 ± 10	30 ± 12	ns
Resting pressure (mmHg)	135 ± 16	129 ± 15	p<0.05
Relaxation upon deglutition (mmHg)	–3.9 ± 1.5	–3.5 ± 1.5	ns

IBS – irritable bowel syndrome

tistically significant difference between the two IBS subgroups in the prevalence of any of these endoscopic findings. *Helicobacter (H.) pylori* was isolated from gastric mucosa in seven (23%) IBS patients (Table 5).

Results of the manometric studies of the lower esophageal sphincter obtained in the groups of IBS patients and healthy controls showed decreased resting pressure in the group of IBS patients. While total sphincter length showed no statistical difference between IBS patients and control group, lengths of thoracic and abdominal part were significantly different (Table 6). Analysis of two IBS subgroups revealed higher resting pressure of lower esophageal sphincter in the IBSc subgroup (Table 7). There was no statistically significant difference either between the IBS and control group or between the two IBS subgroups in the mean value of the lower esophageal sphincter relaxation to deglutition (Tables 6 and 7). Assessment of the esophageal body manometric characteristics revealed IBS patients to have statistically significant difference for all estimated manometric parameters besides mean rate of peristaltic wave. A completely normal motor activity was only present in 41% of the patient population versus 90% of the control group. The most pronounced changes included frequent repetitive contraction waves, elevated amplitude of contraction waves in the proximal two-thirds of the esophagus and increased prevalence of simultaneous peristaltic activity (Table 6). Some of this changes in motility parameters of esophageal body were more common in IBSd subgroup (Table 7). Considering the upper gastrointestinal sphincter motility, there was no significant between-group difference in the sphincter length, whereas resting pressure was higher in the group of IBS patients (Table 6). These changes were also more pronounced in the IBSd subgroup (Table 7).

Discussion

Based on the clinical experience indicating a great number of extracolic symptoms occurring in IBS patients, and postulating the existence of more or less generalized intestinal dysfunction, we embarked upon the present study to determine the prevalence of symptoms

TABLE 7
MANOMETRY CHARACTERISTICS OF ESOPHAGUS IN IBS PATIENTS ACCORDING TO IBS SUBGROUPS

	IBSd (n= 16)	IBSc (n=14)	p
Lower esophageal sphincter			
Total length (mm)	34 ± 5	36 ± 6	ns
abdominal segment	14 ± 5	16 ± 7	ns
thoracic segment	20 ± 8	20 ± 8	ns
Resting pressure (mmHg)	9 ± 7	13 ± 9	<0.05
abdominal segment	11 ± 8	15 ± 8	ns
thoracic segment	7 ± 4	11 ± 5	ns
Relaxation upon deglutition (mmHg)	2 ± 1	2 ± 1	ns
Body of esophagus			
Contraction (n=30)			
normal	48 (30%)	49 (35%)	ns
repetitive	84 (53%)	65 (47%)	ns
absent	28 (18%)	25 (18%)	ns
Mean contraction duration (s)	3.2±0.5	2.8 ± 0.5	ns
Mean peristaltic peak pressure (mmHg)			
upper esophagus	80 ± 13	76 ± 11	<0.05
medial esophagus	98 ± 14	95 ± 13	ns
lower esophagus	75 ± 11	80 ± 11	<0.05
Peristaltic activity (n=300)			
coordinated	88 (55%)	119 (85%)	<0.01
simultaneous	32 (20%)	14 (10%)	<0.05
incomplete propagation	40 (25%)	21 (15%)	<0.05
Mean rate of peristaltic wave (cm/s)	5.3 ± 1	5.1 ± 1.1	ns
Upper esophageal sphincter			
Length (mm)	30 ± 11	25 ± 9	ns
Resting pressure (mmHg)	147 ± 35	123 ± 38	<0.05
Relaxation upon deglutition (mmHg)	–1 ± 1.5	–1 ± 1.5	ns

IBSd – irritable bowel syndrome with predominant diarrhea, IBSc – irritable bowel syndrome with predominant constipation

associated with esophageal dysfunction, and to objectify them by use of endoscopy and esophageal manometry.

The study included two subgroups of IBS patients: those with IBS and diarrhea, and those with IBS and constipation as the predominant symptom of the disease. We embarked upon the study of the manometric and clinical features of these two IBS forms on the basis of literature reports identifying them as the two IBS extremes, which should thus be expected to differ significantly according to the motility parameter values[1,5,7]. It should be emphasized that the two subgroups of IBS patients differed according to body mass index, which was higher in IBS patients with diarrhea as the predominant symptom. This is consistent with literature data, attributing it to the higher žsusceptibility' to stress due to obesity in these patients[9].

In the present study, discomforts in the upper gastrointestinal tract were reported by the majority, i.e. more than two-thirds of study patients. These recurrent discomforts pose great burden upon the patients and usually cause extensive diagnostic procedure in IBS patients. The high prevalence of the symptomatology otherwise primarily associated with esophageal and duodenal diseases in IBS patients points to generalized impairment of the gastrointestinal system motility[9,12,16].

According to Smart et al. study, the prevalence of reflux disease in IBS patients ranges between 22% and 48%[17]. Prevalence of reflux esophagitis in our IBS patients was 43%, mostly grade 1 and 2. 23% of IBS patients had positive test for H. pylori. It should be noted that in spite of transient improvement observed in patients after treatment for H. pylori eradication, the discomforts did not disappear completely, and exacerbation episodes were mostly related to patient exposure to stress events.

Analysis of esophageal motility changes detected by manometry in our IBS patients produced a highly heterogeneous picture of the impairments involved. Esophageal motility changes were found in as many as 85% of IBS patients. Analysis of the motility changes according to study subgroups showed no significant differences between IBS patients with predominant diarrhea and those with predominant constipation.

In contrast to some other related studies, we found significantly lower values of the lower esophageal sphincter pressure at rest and transient spontaneous sphincter relaxations in IBS patients as compared with healthy controls, and no difference between the two patient subgroups[18]. Also, the abdominal segment of the sphincter was shorter in IBS patients, with hiatal hernia verified in some of them. This finding is highly consistent with the significant prevalence of reflux disease in IBS patients.

Accordingly, IBS patients develop pathologic changes of several motility parameters, the IBS subgroups differing according to some of them. Esophageal manometry provides important diagnostic data that may influence the treatment strategy. Development of electrogastrography, diagnostic procedure for assessment of functional characteristics of stomach, will definitely help in establishing gastric function impairement in patients with IBS[20]. The results obtained in the present study suggest that IBS may be associated with by far more extensive smooth muscle or innervation lesions than it used to be believed before. However, a definite answer to these questions requires additional studies.

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POREMEĆAJ FUNKCIJE JEDNJAKA U BOLESNIKA SA SINDROMOM IRITABILNOG CRIJEVA

S A Ž E T A K

Cilj ove studije je bio odrediti prevalenciju znakova i simptoma povezanih s disfunkcijom jednjaka u bolesnika sa sindromom iritabilnog crijeva (IBS), utvrditi poremećaje senzorimotoričke funkcije jednjaka na temelju manometrijskog ispitivanja te na taj način utvrditi korelaciju među njima. 30 bolesnika sa IBS, 14 s proljevom i 16 s konstipacijom kao predominantnim simptomima je uključeno u studiju. Kontrolna grupa se je sastojala od 30 zdravih ispitanika. Bolesnici su uključeni u studiju na temelju Rimskih kriterija za IBS. Nakon temeljito uzete povijesti bolesti i fizikalnog statusa bolesnicima je učinjena ezofagogastroduodenoskopija i manometrija jednjaka. Vrijednosti manometrije jednjaka dobivene u zdravih ispitanika su služile kao kontrolne vrijednosti za manometrijsko ispitivanje. Bolesnici s IBS su se žalili na veliki broj kako koloničkih tako i ekstrakoloničkih simptoma i znakova, međutim, nije bilo statistički značajne razlike u prevalenciji ovih simptoma između dvije podgrupe IBS bolesnika. U usporedbi sa zdravim ispitanicima bolesnici s IBS imali su patološki promjenjene vrijednosti većine parametara motiliteta jednjaka. Komparacija dviju podgrupa bolesnika s IBS je pokazala razlike samo u pojedinim manometrijskim parametrima. Rezultati dobiveni u ovoj studiji bi mogli objasniti zašto bolesnici s IBS često imaju simptome povezane s gornjim dijelom gastrointestinalnog trakta, kao što su žgaravica i bol u prsima nekardiogenog uzroka. Rezultati također sugeriraju da bi IBS mogao biti povezan sa značajno proširenijim promjenama inervacije glatke muskulature nego što se dosada mislilo.