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Gastroesophageal reflux disease and irritable bowel syndrome - prevalence and overlap

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Abstract

Introduction

Irritable bowel syndrome (IBS) belongs to the group referred as functional gastrointestinal disorders. IBS is manifested by abdominal pain or discomfort in association with frequent diarrhea or constipation and a change in bowel habits, which are not caused by organic or biochemical changes. Because of the lack of specific markers or tests, diagnosis is based on

the symptoms. In recent years there have been many reports about patients with IBS also presenting gastroesophageal reflux symptoms more commonly than healthy population.

Aim of the study
The aim of our study was to determine the prevalence and possible theories about irritable bowel syndrome and gastroesophageal reflux disease (GERD) overlap.

State of knowledge
Analyzed studies proves significant overlap of IBS and GERD. Theories explaining the co-existence of IBS and GERD says that both disorders are presented in significant number of patients, which is related with smooth muscle motor disorder in gastrointestinal tract. Other theories suggests that IBS-like symptoms are part of the spectrum of GERD manifestation, due to relief of IBS-like symptoms in GERD patients who are receiving anti-reflux treatment. Our study collect main reports about co-existence and common causes of GERD and IBS.

Conclusions
Studies highlights the importance of identifying overlapping functional gastrointestinal conditions as a therapeutic strategy for better management of GERD. Because of the strong association of IBS with GERD, it has been recommended that physicians who recognize, and treat IBS patients should also screen them for the co-existence of GERD.

Key words: Irritable bowel syndrome; Gastroesophageal reflux disease; Rome Criteria; Functional bowel disease

Introduction

Irritable bowel syndrome (IBS) belongs to group of diseases referred as functional gastrointestinal disorders, which are the most common diagnosis in gastroenterology. Except IBS this group includes functional constipation, functional diarrhea, functional abdominal bloating/distension, unspecified functional bowel disorder, opioid-induced constipation and is describing as functional bowel disorders. They are characterised by occurrence of motility disturbance, visceral hypersensitivity, altered mucosal and immune function, modified gut microbiota, and central nervous system processing. [1] Due to differences in diagnostic criteria, applied methodology and size of analyzed population, the prevalence of irritable bowel syndrome varies depending on the study, however, it is claim that this disease may affect around 11% of the global population.There are also differences of prevalence among geographic regions - the lowest number of IBS occurring in South Asia (7.0%) and the highest in South America (21.0%). IBS occurs in all age groups, but half of the patients present their first symptoms before 35 years old. Symptoms are more common in women (14%) than men (8.9%). The impact of socioeconomic status on this disease is not clear. [2,3] The pathogenesis of irritable bowel syndrome is multifactorial. At the beginning of the 20th century, a relation between bowel activity and psychological states like stress or aggression

was noticed, which proved that gut is associated with emotion and environmental stimulators. [1] Current theories about pathogenesis of this disease include: disorders of gut-brain interactions, abnormal gastrointestinal motility, visceral hypersensitivity, impaired immune function of the intestinal mucosa and dysregulation at the level of the central nervous system. There are also reports about changes in gene polymorphism associated with regulation of the serotonergic system. Gut microbiota plays important role in maintaining normal bowel function. Patients with IBS has reduction in the number of Lactobacillus and Bifidobacterium bacteria, and increase in the number of Streptococcus, Escherichia coli, Clostridium spp. There are also changes in the proportion between Firmicutes and Bacteroidetes bacteria. Acute infections can be related with higher incidence of IBS due to immune activation of the mucosa which is considered to be the main factor leading to post-infectious irritable bowel syndrome (PI-IBS). It is also believed that diet affects the symptoms occurring in IBS. [4] For many years it was difficult to define criteria for functional diseases. Manning's research from 1978 revealed that from many symptoms that have been suggested as being characteristic for IBS only distension, relief of pain with a bowel movement, more frequent and looser stools at the onset of pain were significantly more common in patients with IBS than organic disease. [5] The Rome Foundation was created in the late 1980s, and played important role in coordination of the research, and spreading knowledge about functional gastrointestinal disorders. It became the main organization providing guidelines for diagnosis and treatment this group of diseases, which resulted in development of Rome criteria first presented in 1994, Rome II - 1999–2000, Rome III - 2006, and Rome IV - 2016. [1] Based on current data IBS is diagnosed by identifying recurrent abdominal pain on average ≥1 day a week for the last 3 months having at least 2 of the following criteria: is related with defecation, frequency of bowel movements or change in the formation (appearance) of the stool. There are four main IBS subtypes: with predominant constipation (IBS-C), predominant diarrhea (IBS-D), mixed bowel habits (IBS-M) and unclassified IBS (IBS-U). Diagnosis of IBS should be preceded by collection of medical history, physical examination, performing necessary laboratory tests. Colonoscopy is not required but in justified situations might be performed. [6] Bristol Stool Form Scale (BSFS) is standardised instrument for stool assessment. Type 1 refers to stool forms as separate hard lumps, like nuts (hard to pass), type 2 – sausage-shaped but lumpy, type 3 – like sausage with cracks on the surface, type 4 – like an sausage or snake, smooth and soft, type 5 – soft blobs with clear cut edges (passed easily), type 6 – fluffy pieces with ragged edges, a mushy stool, and type 7 – watery, no solid pieces, entirely liquid. [7]

Gastroesophageal reflux disease (GERD) is divided into ‘‘erosive GERD’’ with esophageal mucosal break and ‘‘non-erosive GERD’’ with symptoms alone. The main factor involved in pathophysiology of this disease include transient lower esophageal sphincter (LES) relaxation. Heartburn and regurgitation are typical symptoms related with increased

acid exposure, but beyond them, there is also the possibility of extraesophageal expression of this disease like chronic cough, non-cardiac chest pain, bronchial asthma, discomfort of the pharyngolarynx or pharyngalgia. They may be the only symptoms, and it is important to take them into consideration during diagnostic process. [8] In recent years a lot of attention has been paid to frequent co-occurrence of IBS and GERD.

Aim of the study

The aim of our study was to determine the incidence of GERD and IBS overlap and possible hypotheses of this state.

State of the knowledge

The incidence of abdominal diseases in the Polish population is high, and does not differ significantly data from other countries. The prevalence of GERD was estimated for 36% and IBS for 13%. [9] Recent years showed many reports of frequent co-occurrence of IBS and GERD. In Yarandi analysis, from 6476 patients of Gastro-intestinal (GI) clinic, 1419 patients met Rome II or Rome III criteria. From them, 63.6% (69.0% women, 31.0% men) also had GERD, whereas 34.7% of the non-IBS patients had GERD [odds ratio (OR) = 3.2, 95% confidence interval (CI): 2.9-3.7, $P < 0.0001$]. Among patients with GERD, 33.9% of them met Rome criteria compared to 13.5% of non-GERD patients (OR = 3.6, 95% CI: 3.1-4.3, $P < 0.0001$). [10] The questionnaire study performed on Japanese population examining the prevalence of gastroesophageal reflux disease, functional dyspepsia (FD), and IBS based on Rome III criteria and their overlap rates revealed that form 2680 patients, 207 (7.7%) were diagnosed with GERD, 269 (10.0%) with FD, and 381 (14.2%) with IBS. Overlaps were present in 46.9% in GERD, 47.6% in FD, and 34.4% in IBS. Patients with IBS had significantly lower prevalence of overlap compared with those among GERD or FD. All patients with overlaps had significantly poorer quality of life compared with controls. [11] Assessment of prevalence and risk factors for GERD and IBS overlap show that predictors of irritable bowel syndrome–GERD overlap vs. irritable bowel syndrome alone, and separately GERD alone, include insomnia and frequent abdominal pain. An additional predictor of irritable bowel syndrome–GERD overlap vs. GERD alone was higher somatization, and for irritable bowel syndrome–GERD overlap vs. irritable bowel syndrome alone was a higher body mass index. [12] Analysis of the common symptoms of gastroesophageal reflux disease (GERD) with functional bowel diseases (FBD) was performed by filling Chinese Reflux Disease Questionnaire. From 1074 patients, 107 (10%) were diagnosed as GERD and 206 (19.2%) as FBD including 63 irritable bowel disease (IBS) patients. The incidences of chronic bloating, chronic constipation, IBS and functional constipation in patients with gastroesophageal reflux disease were statistically significant higher than in non-GERD patients [25.2% (27/107), 14.0% (15/107), 10.3% (11/107), 7.5% (8/107)] compared with [16.6% (160/966), 7.1% (69/966), 5.4% (52/966), 3.3% (32/966), all $P < 0.05$]. [13] On the other hand Lee study revealed anxiety as a factor significantly associated with GERD overlap (OR 2.73, 95% CI 1.13–6.57), dyspepsia overlap (OR 3.19, 95% CI 1.33–7.63) and IBS overlap (OR 4.92, 95% CI 2.04–11.84), compared with GERD, dyspepsia and IBS alone. [14]

In the review performed by Nastaskin, where six electronic databases from 1966 through January 2005 were analyzed, from 15 studies included in the analysis, 7 determined the GERD maximum mean prevalence in patients already diagnosed with IBS to be 39.3% and the weighted mean 30.3%. The maximum mean prevalence of IBS in patients with known GERD was 48.8% and the weighted mean 60.5%. Research concluded that there is a strong overlap between GERD and IBS. In the absence of GERD, IBS is relatively rare. [15]

There are two main theories explaining the coexistence of IBS and GERD. First says that GERD and IBS are present in significant number of patients, which is related with smooth muscle motor disorder in gastrointestinal tract, which results from the fact that these two diseases are distinct, but share common pathophysiology. Second, suggests that gastroesophageal reflux disease contain IBS symptoms. [16] Progression of intestinal contents in colon is reached by high-amplitude propagated contractions (HAPCs). In the colon there are also present sporadic, and non propagating contractions. Changes in the balance of contractions in favour of the first, can lead to frequent bowel movements appearing in IBS with dominant diarrhea. The opposite situation occurs in the constipation type. [17] Gastrointestinal motility disorders in IBS has been proven in Smart research, were esophageal symptoms like dysphagia, and globus sensation were analyzed. The lower esophageal sphincter pressure was significantly reduced in the irritable bowel patients compared with the age and sex matched controls. There was no difference between the two groups studied in upper esophageal sphincter pressure or in peristaltic amplitude. [18] Central nervous system and stress are another factors affecting gastrointestinal diseases. Discovery of the enteric nervous system (ENS) enabled understanding of the physiological gut functions. Exposure to stress modifies the bacterial flora, which lead to changes in neurotransmitters and proinflammatory cytokine levels. Mast cells have receptors for corticotrophin releasing factor (CRF) on their surface which is evidence of their role in brain-gut axis. Stress plays important role in modification of the gut function by affecting gut motility, secretion, paracellular permeability, mucosal blood flow and visceral sensitivity. [19]

These factors are also involved in pathogenesis of gastroesophageal reflux disease. The main mechanism responsible for increased acid exposure is transient lower esophageal sphincter (LES) relaxation. Primary peristalsis and the presence of esophageal hiatal hernia are also important factors affecting occurrence of this disease. [8] Esophageal manometry performed on 20 patients with non-erosive reflux disease revealed that triggering of secondary peristalsis is significantly lower ($P < 0.0001$) in this group than that in healthy subjects. [20] Visceral hypersensitivity also seems to play a role in pathophysiology of the GERD. Studies show that esophageal exposure to mechanical stimulation and low or high pH resulting in visceral hypersensitivity. [21] Exposure to stress leads to increased sensitivity to reflux feeling. There is a need to examine the role of stress on patients resistant to typical anti-reflux therapy due to the presence of evidence that reduction of stress may lead to reduction of symptoms. [19]

The second theory is supported by reports about reduction of IBS symptoms among patient with GERD after proton pump inhibitors treatment, which could be evidence for the possibility of IBS coexistence. [22] On the other hand, it's important to remember that long-term proton pump inhibitors therapy can lead to the opposite effect. Patients with non-erosive reflux disease were treated with esomeprazole for 6 months. After 8 weeks of PPIs treatment, patients complained of bloating,

abdominal pain and diarrhoea. After 6 months, the incidence of bowel symptoms further increased. At the end of the research a significant ($P < 0{\cdot}05$) percentage of patients (8/42) met Rome III criteria for irritable bowel syndrome. [23]

Lacy analysis revealed that occurence of dyspepsia and gastroesophageal reflux disease was associated with more frequent diagnostic tests and procedures in patients with irritable bowel syndrome. More tests and procedures were performed in older patients, female and those who have more comorbidities like anxiety, depressive disorders, and somatization. [24]

Conclusions

Irritable bowel syndrome and gastroesophageal reflux disease share similarities in pathophysiology including visceral hypersensitivity, role of the stress, altered motor function of the gut which results in frequent overlapping. During diagnostic process increased number of symptoms characteristic for IBS and GERD shouldn't led to excessive number of diagnostic tests but led to conclusion about the possibility of coexistence two diseases. Doctors who diagnose IBS or GERD should pay attention to the possibility of the coexistence of these two diseases.

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