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EC GASTROENTEROLOGY AND DIGESTIVE SYSTEM

Research Article

Gastroesophageal Reflux Disease as a Polymorbid Disease

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Received: February 20, 2024; **Published:** March 01, 2024

Abstract

Introduction: The prevalence of gastroesophageal reflux disease (GERD) varies from 8.8 to 33.1%, and the incidence has a steady upward trend in all regions of the world. GERD is observed in the USA in 29.8% of men and 32.5% of women and in 30% of adults in Western European countries. Dyskinesia of the upper digestive tract accompanies the development of GERD. However, GERD as a polymorbid disease has not been studied enough.

Aim: The aim is to investigate the clinical and diagnostic features of GERD as a polymorbid disease.

Materials and Methods: The examination of 32 patients included clinical, electromyographic and dental examinations. The control group consisted of 16 patients. Statistical analysis was performed using the Statistica-16 software package at $p < 0.05$.

Results: Electromyographically, there is an increase in retrograde motility of the stomach and esophagus, as well as hypermotor dyskinesia of the duodenum, jejunum and colon. Stomatologically, the presence of carious cavities and gingivitis was revealed.

Conclusion: The features of GERD as a polymorbid disease are the presence of heartburn, motor evacuation disorders indicating an increase in the evacuation function of the stomach. esophagus and the presence of predominantly acid reflux, which determines the development of pathology of the oral cavity.

Keywords: *Gastrointestinal Motor Function; Gastroesophageal Reflux Disease; Dental Manifestations*

Introduction

Of all the variety of diseases of the gastrointestinal tract (GI tract), GERD is one of the most common diseases and is comparable in frequency to peptic ulcer and gallstone diseases. Gastroesophageal reflux disease (GERD) - this is a chronic recurrent disease caused by a violation of the motor evacuation function of the organs of the gastroesophageal zone and characterized by regularly repeated throwing of gastric and in some cases duodenal contents into the esophagus, which leads to the appearance of clinical symptoms that worsen the quality of life of patients, damage to the mucous membrane of the distal esophagus with the development of dystrophic changes in the non-corneating multilayer squamous epithelium, catarrhal or erosive ulcerative esophagitis (reflux esophagitis), and in some patients with cylindrical cell metaplasia [1-3].

Epidemiology

The true prevalence of GERD is difficult to assess, since only about a quarter of GERD patients seek medical help [4,5]. Epidemiological data indicate that the prevalence of the disease varies from 8.8 to 33.1%, and the incidence has a steady upward trend in all regions of the world [6,7]. The highest prevalence rates are recorded in Europe and North America, and the lowest in Asian countries [7,8]. According to the latest meta-analysis published in 2018, the global prevalence of GERD is 13.3% (95% CI: 12,0 - 14,6%) [9]. At the same time, the incidence of the disease is higher in people over 50 years of age (OR 1.32; 95% CI: 1.12 - 1.54), smokers (OR 1.26; 95% CI 1.04 - 1.52). In Russia, the prevalence of GERD varies from 11.3 to 23.6%, and the described risk factors are typical for the global population [10,11]. In the general population, the prevalence of esophagitis is estimated at 5 - 6%; at the same time, 65 - 90% of patients have slightly pronounced and moderate esophagitis, 10 - 35% have severe esophagitis [12-16].

Etiology and pathogenesis

Gastroesophageal reflux disease is an acid-dependent disease in which hydrochloric acid of gastric juice acts as the main damaging factor in the development of clinical symptoms and morphological manifestations of GERD. Pathological reflux occurs due to insufficiency of the lower esophageal sphincter (NPS), that is, GERD is a disease with an initial violation of the motor function of the upper gastrointestinal tract (GI tract) [17-20]. A key factor in the pathogenesis of GERD is the pathologically high frequency and/or duration of episodes of gastric contents being thrown into the esophagus. The integrity of the mucous membrane of the esophagus is due to the balance between the factors of aggression and the ability of the mucous membrane to resist the damaging effect of the thrown contents of the stomach during gastroesophageal reflux (GER). A violation of this balance in a large proportion of patients is accompanied by a significant slowdown in the recovery of the pH of the distal part of the esophagus after each episode of reflux. Violation of esophageal clearance develops due to a combination of several factors: weakening of peristalsis of the thoracic esophagus, decreased secretion of saliva and mucin [21]. The first barrier having a cytoprotective effect is the mucus layer covering the epithelium of the esophagus and containing mucin [22]. The mucous layer is one of the key components of the chemical clearance of the esophagus and the restoration of pH in the esophagus to normal values, the violation of which contributes to the deterioration of the purification of the esophagus from acidic, slightly acidic or slightly alkaline contents that have entered it. It was found that mucin secretion in mucus in GERD decreases depending on the severity of esophagitis, which is an additional factor predisposing to the development of erosive esophagitis in conditions of ongoing GER. Therefore, an additional increase in the protective properties of the mucous barrier, along with acid suppression, is an important component of the treatment of GERD [31-33]. A significant increase in gastric hydrochloric acid secretion significantly increases the risk of GERD. In the vast majority of GERD patients, reflux episodes occur mainly during transient relaxation of the lower esophageal sphincter (PRNPS). During PRNPS, the antireflux barrier between the stomach and esophagus usually disappears for 10 - 15 seconds, regardless of the act of swallowing [14]. PRNPS as a fundamental mechanism of reflux is carried out through the same pathways from the dorsal nucleus of the vagus nerve (nucleus dorsalis and nucleus ambiguous), which mediate esophageal peristalsis and relaxation of the NPS in a healthy person. Mechanoreceptors located in the upper part of the stomach react to an increase in pressure inside the organ and send signals to the posterior brain along the afferent fibers of the vagus nerve. In the centers of the posterior brain, which perceive these signals, motor programs of the PRNPS are formed, reaching the NPS in descending ways. Efferent pathways are carried out through the vagus nerve, where nitric oxide (NO) is a postganglionic neurotransmitter. The contraction of the diaphragm legs is controlled by the respiratory center in the brainstem and the nucleus of the diaphragmatic nerve. An increase in intra-abdominal pressure when coinciding with PRNPS significantly increases the likelihood of reflux. Currently, in understanding the mechanism of GER, one should be guided by the paradigm of the mutual influence of PRNPS and the consequences of the destruction of the esophageal-gastric junction. The weakness of the diaphragm legs leads either to a delay in the onset of action, or to a significant degradation of the actual compression effect of diaphragm contraction on the NPS. A hernia of the esophageal orifice of the diaphragm, depending on its size and structure, has a mechanical effect on the NPS: it worsens the

antireflux function during PRNPS and/ or reduces the actual tonic component of the sphincter. The most important consequence of the destructurization of the esophageal-gastric junction zone is the throwing of relatively large volumes of liquid contents from the stomach into the esophagus during the PRNPS period [14,26]. In a significant number of patients, GER episodes develop at normal NPS pressure levels. The mechanism of GER is associated with a high pressure gradient between the stomach and esophagus, due to various reasons: in some patients, this is a violation of the evacuation of contents, in another part - high intra-abdominal pressure. In these cases, GER develops due to the inability of the locking mechanisms to counteract the high pressure gradient in the stomach [27,28]. Indeed, half of patients with GERD show symptoms of functional dyspepsia (FD) and 40 - 52% of patients with FD show concomitant GERD [29]. The high frequency of the combination of GERD and PD is explained by the fact that disturbances in the accommodation of the fundal part of the stomach and a slowdown in its emptying contribute to an increase in the frequency of episodes of PRNPS [30]. The results of studies conducted in recent years indicate changes in the microbiota of the esophagus and stomach in patients with GERD, Barrett's esophagus and ACP. Potential mediators of inflammation and carcinogenesis are toll-like receptors, cytokines, nuclear factor kB, cyclooxygenase-2, the expression of which can be modified depending on the composition of the microbiota. Currently, there is little convincing data on the effect of certain changes in bacterial composition on the functional and structural state of the esophagus and stomach, and further research in this direction is needed [31-33]. Thus, from a pathophysiological point of view, GERD is an acid-dependent disease that develops against the background of a primary violation of the motor function of the upper digestive tract and affects the organs of the oral cavity with high reflux.

Aim of the Study

The aim is to investigate the clinical and diagnostic features of GERD as a polymorbid disease.

Materials and Methods

32 patients with gastroesophageal reflux disease were examined. In the study, the first group was dominated by women (69%), whose average age was 52.7 ± 1.1; men made up 31%, whose average age was 58.1 ± 1.3, with oral pathology. The control group consisted of 18 patients with gastroesophageal reflux disease, of which 36.1% were men, 63.9% were women, the age of the subjects ranged from 19 to 63 years, while this group of patients had practically no pathology of the oral cavity.

The main sign of GERD is heartburn (especially with physical exertion, bending, lying down, after eating or after a certain meal), which is one of the most common symptoms (in more than 80% of patients) and, often, the only symptom of the disease.

Electromyography of the gastrointestinal tract and esophagus of patients with GERD of the main and control groups was performed: electromyography (EMG) was performed in 32 patients of the main and 18 patients of the control group. EMG allows you to assess the state of the motor function of the esophagus, stomach and various parts of the small and large intestine., the power of phase and tonic contractions, characterizing, respectively, the contractile activity of the longitudinal and circular muscle layer, and propulsive activity.

Electromyography was performed continuously for 1.5 hours using silver electrodes placed on the anterior abdominal wall in the projection of the recorded gastrointestinal tract, followed by signal conversion using the Conan-M hardware and software complex.

Electromyography is a set of electrophysiological and related motor phenomena in smooth muscle tissue, which are characterized by the presence of biopotentials reflecting the processes of depolarization and repolarization. Numerous researchers have proven the existence of a close relationship between the electrical and contractile activity of the gastrointestinal tract [34].

Specific dental symptoms of GERD have been identified:(burning of the tongue, cheeks, impaired taste sensations, damage to the hard tissues of the teeth - thinning and erosion of tooth enamel, caries, periodontitis, granuloma.

Statistical processing of the obtained data was carried out using the Statistica-6 software package. All quantitative data obeying the normal distribution are presented in the form of M ± m. The Student's criterion (t) was used to process the obtained data, followed by the determination of the level of reliability of the differences (p) and the criterion χ^2. The differences between the mean values were considered significant at $p < 0.05$.

Results and Discussion

The most common complaints in patients of the main and control groups were nausea and bitterness in the mouth; heartburn, pain in the epigastric region and behind the sternum.

In patients of the main group with dental problems, complaints (as a percentage) were distributed as follows: heartburn occurred in 76.9%; nausea - 14%; epigastric pain was noted in 47.2%; chest pain occurred in 19.6% of cases. In patients of the control group with isolated GERD, the most common complaints were: heartburn - 48%; epigastric pain - 54%, chest pain - 7.3% of cases.

Thus, the clinical picture of GERD with dental pathology differed in the presence of heartburn in 76.9% of patients and the presence of pain syndrome in 66.6% of cases, whereas the leading clinical symptom in patients of the control group was pain syndrome (61.3%).

Specific dental symptoms of GERD were revealed (burning of the tongue, cheeks in 28% of cases, impaired taste sensations in 12% of cases, damage to hard tissues of teeth - thinning and erosion of tooth enamel, caries - in 48% of patients, periodontitis, granuloma. in 8% of cases) were isolated by a separate group among the extraesophageal clinical manifestations of the disease. The GERD Expert Group (Montreal, 2006) notes that reflux caries is a reliably associated extraesophageal symptom of GERD. Salivation due to vagotonia, characteristic of most patients with diseases of the upper digestive tract, is also a specific clinical symptom for GERD.

The data obtained, apparently, may be related to the fact that the pathogenesis of GERD is based on a change in the motor activity of the esophagus as a result of a decrease in the tone of the lower esophageal sphincter, which, in turn, leads to a violation of the normal functioning of the antireflux barrier, and a decrease in esophageal clearance. According to the literature, these causes prevail in the initial stages of GERD, further giving way to the damaging effect of a number of factors such as hydrochloric acid, bile acids, pepsin, etc. The compensatory capabilities of the esophageal mucosa depend on the degree of aggressiveness of the reflux and the duration of contact with it [35].

Evidence of the role of hypermotor dyskinesia of the esophagus and stomach in the development of GERD in patients with oral pathology can be provided by electromyography data (Table 1). Thus, the frequency of slow esophageal EMA waves increases from 14.6 ± 12 to 19.7 ± 0.8 per minute (34.5%, $p < 0.05$) with a stable amplitude. There was an increase in the frequency of spikes from 2.1 ± 0.18 to 3.4 ± 0.16 (55%, $p < 0.05$), propulsive activity was 26.6 ± 0.9 (an increase of 89%, $p < 0.05$), the magnitude of tonic contractions increased by 18.2% ($p < 0.05$), indicating an increase in the excitability of the longitudinal muscular layer of the esophagus. That is, there is an increase in the basic electrical rhythm of the esophagus with an increase in the excitability of its smooth muscles (MMC) mainly of the longitudinal layer.

Retrograde gastric dyskinesia is noted: the frequency of slow waves increases from 5.4 ± 0.3 to 8.4 ± 0.5 per minute (43.6%, $p < 0.05$) with a stable amplitude of slow waves. An increase in spike activity was detected from 1.9 ± 0.13 to 3.4 ± 0.21 (75%, $p < 0.05$), the power of tonic contractions was increased by 22.3% ($p < 0.05$), the power of phase contractions was reduced by 30% ($p < 0.05$) (Table 1), the propulsive activity was 14.1 ± 1.5 (increase by 83.3%, $p < 0.05$), which generally indicates an increase in the excitability of the longitudinal and partially oblique muscles of the stomach and the presence of both antegrade and retrograde contractions of the smooth muscles of the stomach. This leads to the development of GERD with the ingestion of acidic gastric contents into the oral cavity.

Hypermotor dyskinesia of the duodenum and jejunum is noted: the frequency of slow waves of the duodenum is reduced from 22.0 ± 0.8 to 19.6 ± 0.12 per minute (7.2%, $p < 0.05$) the power of tonic contractions is increased by 6.1% while phase contractions decrease by 10% ($p < 0.05$). The frequency of slow waves of the jejunum decreases from 20.0 ± 0.5 to 18.0 ± 0.6 per minute (10%, $p < 0.05$) with a relatively low amplitude of slow waves, the power of tonic contractions is increased by 20% ($p < 0.05$) (Table 1) at the same time, the propulsive activity of the duodenum was 26.0 ± 1.7 (an increase of 18.1%, $p < 0.05$), the propulsive activity of the jejunum was 27.0 ± 1.9 (an increase of 35%, $p < 0.05$). The spike activity in both parts of the small intestine is increased by half, which indicates the presence of pain syndrome when stretching the intestine. An increase in the propulsive activity of the small intestine, in particular, with the retrograde spread of arousal, contributes to the development of duodenogastric reflux with the ingestion of aggressive small intestinal contents into the esophagus and oral cavity: bile acids, enzymes that break down proteins, fats and carbohydrates and lysolecithins, which, along with acidic gastric contents, have a damaging effect on tooth enamel and oral mucosa.

A decrease in the slow-wave activity of the ascending colon is detected from 11.0 ± 0.2 to 9.5 ± 0.42 per minute (12.7%, $p < 0.05$) while maintaining the spike activity of smooth muscle cells, the power of tonic contractions is reduced by 4%, phase activity is reduced by 19% ($p < 0.05$) (Table 1) while the propulsive The activity was slightly increased from 11.0 ± 0.9 to 13.0 ± 1.5 (by 18.1%, $p < 0.05$).

	Esophagus	Stomach	The duodenum	The jejunum	Ascending gut	The descending intestine	Sigmoid colon
Tonic contractions	1,755 ± 0,014	1,008 ± 0,071	2,34 ± 0,12	1,62 ± 0,13	1,056 ± 0,1,5	0,567 ± 0,032	0,58 ± 0,021
Phase reductions	0,066 ± 0,0032	0,07 ± 0,005	0,090 ± 0,005	0,06 ± 0,004	0,081 ± 0,006	0,057 ± 0,004	0,072 ± 0,006

Table 1: *Motor activity of the longitudinal (tonic) and circular (phase) muscle layers of the gastrointestinal tract in patients with gastroesophageal reflux disease.*

The stability of the slow-wave activity of the descending colon is 6.3 ± 0.3 per minute ($p > 0.05$) with spastic activity exceeding the norm by half, while tonic activity is reduced by 5.5% ($p < 0.05$), phase activity by 43% ($p < 0.05$), which may indicate the presence of a gastrocolytic reflex, which It is confirmed by an increase in propulsive activity from 6.0 ± 0.4 to 9.9 ± 0.6 (by 65%, $p < 0.05$).

Hypermotor dyskinesia of the sigmoid colon was revealed: the frequency of slow waves increased from 5.0 ± 0.25 to 6.3 ± 0.3 per minute (by 26%, $p < 0.05$) with a significant increase in the frequency of spike activity - from 2.0 ± 0.12 to 3.6 ± 0.2 (80%, $p < 0.05$), tonic activity increased by 16% ($p < 0.05$) the phase, on the contrary, decreases by 28% ($p < 0.05$), while the propulsive activity is increased by 59% ($p < 0.05$).

Thus, GERD, combined with damage to the organs of the oral cavity, occurs against the background of gradually decreasing hypermotor dyskinesia of the esophagus and stomach, duodenum and jejunum and additionally increasing propulsive activity of the colon.

The data obtained confirm the data described above on the predominance of changes in the motor activity of the esophagus with the development of both acid and alkaline reflux in the basis of the pathogenesis of GERD in patients with pathology of the oral cavity organs.

Consequently, in the pathology of the organs of the oral cavity, the mucous membrane of the esophagus is exposed longer to acidic and alkaline contents when GERD and DH occur, that is. The role of aggression factors is increasing.

Conclusion

In the last few decades, the prevalence of both GERD and its dental manifestations has been increasing worldwide. Despite a number of works devoted to the analysis of the possible connection of these diseases, the understanding of the mechanisms is still far from complete. When analyzing the association of GERD and dental pathology, it is necessary to take into account that both diseases develop in people with nutritional and lifestyle problems, as well as those with a genetic predisposition to the development of these nosologies [35]. At the same time, direct predisposing factors for the development of GERD with oral pathology, often associated with the presence of hernias of the esophageal orifice of the diaphragm, are clearly identified today.

Recent studies have confirmed the link between the pathology of the dental and maxillary apparatus and an increased risk of GERD. The relationship between the pathology of the oral cavity and GERD is based on changes in the structure and functioning of the esophageal-gastric junction, which develop in patients with GERD and the peculiarities of nutrition and mechanical processing of food. In the group of patients with GERD and oral pathology, hernia of the esophageal orifice of the diaphragm was more often observed, the presence of hyperacidity of the esophagus at various stages, which, along with impaired motor function of the esophagus, stomach and intestines, leads to the development of both acidic and alkaline GERD and impaired intestinal transit.

The conducted research allows us to identify one of the variants of GERD, typical for patients with dental problems. The features of this variant are: the predominance of heartburn, motor evacuation disorders of the gastrointestinal tract and esophagus.

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Volume 11 Issue 3 March 2024