

Examination and treatment of patients with gastroesophageal
reflux disease in primary care.

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Purpose: to test the effectiveness of treatment of gastroesophageal reflux disease (GERD) by dilation of the lower esophageal sphincter (LES) and pyloric sphincter by a large tablet (LT).

Material and methods. The study involved 37 patients who had at least one of the symptoms characteristics of GERD. Patients filled in the questionnaire. They were divided into 2 groups. The first group consisted of 20 patients. They had reflux index (RI), which is proportional to the severity of GERD, less than 10 (5.4 ± 0.4). The average age was 30 years, and the duration of the disease ranged from 3 to 39 months. In 17 patients of the second group, RI was equal to or more than 10 (20.1 ± 1.6). The average age was 51 years, and the duration of the disease ranged from 5 to 35 years. Patients swallowed 3 tablets with a diameter of 2.0 - 2.5 cm. After 0.5 - 1 month. patients re-filled the questionnaire.

Results. In patients of the 1st group after taking the tablets RI decreased to 0.6 ± 0.2 ($P < 0.001$). The effect of treatment lasted from 1 to 7 months. In patients of the 2nd group after swallowing the tablets RI decreased to 10.1 ± 2.8 ($P < 0.01$). In 3 cases, there was no effect on taking the tablets. The positive effect lasted 1-3 weeks.

Conclusion. We believe that patients of both groups represent different stages of GERD. Stretching of sphincters with the help of LT is safe and effective method of GERD treatment, especially if treatment is started at an early stage.

Keywords: diagnosis; gastroesophageal reflux disease; large tablet; lower esophageal sphincter; pyloric sphincter; sphincter dilation.

Gastroesophageal reflux disease (GERD) is a multifaceted disease affecting approximately 35-40% of the adult population in developed countries [1,2]. Among the clinical symptoms, heartburn, regurgitation and pain in the epigastrium or behind the sternum predominate. Extra-esophageal symptoms include cough, laryngitis, asthma and dental erosion [3]. These symptoms are considered clinically relevant if they are observed at least twice a week. Meanwhile, in 10-30% of the population in Europe and North America, these symptoms occur 1 time per week [1,4].

Until recently, the most reliable method for diagnosing GERD was the 24-hour pH monitoring (Gold Standard) [5]. However, over the past few years, it has been proven that the pH meter gives false-negative results in the endoscopy-negative reflux disease or non-erosive reflux disease [6,7]. To overcome the contradictions between the need for early treatment, and the lack of the possibility of mass referral to special methods of examination, questionnaires with clinical tests are suggested [9-12].

The purpose of this work to test the effectiveness of treatment of gastroesophageal reflux disease (GERD) by stretching the lower esophageal sphincter (LES) and pyloric sphincter by a large tablets (LT).

Material and methods. We had in outpatient treatment 37 patients who had at least one of the symptoms that occur when GERD. Other causes of the chest pain or chronic cough were excluded. Patients filled out a table with the most common symptoms of GERD (Table 1). Most of the symptoms are taken from the questionnaire proposed for the diagnosis of laryngopharyngeal reflux [9,10]. Patients chose a figure reflecting the severity of each of the symptoms. The sum of the marked numbers is a reflux index (RI).

Based on the RI value, all patients were divided into 2 groups. The first group included 20 patients whose RI was less than 10. The age of patients in this group ranged from 19 to 37 (average of 30 years). The duration of the disease ranged from 3 months up to 3 years (average of 1 year).

The second group included 17 patients, in whom RI was 10 or more. The age of the patients was within the range of 41-60 (average 51 years). The duration of the disease ranged from 5 to 35 years (average 23 years).

Table 1. Questionnaire for the screening of gastroesophageal reflux disease

How concerned are you with the symptoms described below? There is no symptom - 0. A strong symptom is 5.						
Hoarseness or alteration of voice	0	1	2	3	4	5
Sore throat or a desire to get rid of the irritant in the throat	0	1	2	3	4	5
Abundant sputum secreted from the back of the nose, or runny nose.	0	1	2	3	4	5
Difficulty in swallowing food, liquids or tablets	0	1	2	3	4	5
Cough after drinking, eating or resting in the horizontal position	0	1	2	3	4	5
Dyspnea or cases of sudden asphyxiation	0	1	2	3	4	5
Importunate cough	0	1	2	3	4	5
Sensation of foreign body in throat	0	1	2	3	4	5
Heartburn, chest pain or sensation of acid in the throat or mouth	0	1	2	3	4	5
Reflux Index (RI)	$\Sigma =$					

Each patient was offered to swallow large tablets (LT) with a diameter of $\approx 2.0-2.5$ cm and a thickness of 0.5-0.7 cm. It was recommended to swallow 3

tablets. One tablet a day. Starting with a smaller tablet and ending with the largest one. Tablets were prepared from an equal amount of flour and barium sulfate. They were dried and covered with a thin layer of agent, to improve the slip in the pharynx. Only three patients could not swallow LT. They are not included in this study.

After 2 weeks - 1 month, the questionnaire was re-filled, which allowed to evaluate the effectiveness of treatment. During this time, 31 patients received no other methods of treatment. Six continued to take omeprazole. Two of them during this period underwent a gastroscopy: one due to pain intensification after administration of one LT (duodenal ulcer), and the other due to lack of effect (erosive esophagitis and gastritis). We received information on the duration of the therapeutic effect by telephone or from patients when they asked to receive LT again.

Results

In the first group, the IR before treatment ranged from 1 to 9 (average 5.4 ± 0.4) (Table 2). In 16 (80%) of 20 patients were only symptoms typical of GERD: heartburn, belching, chest pain or epigastric pain. Only in 4 (20%) cases were mild symptoms from the nasopharynx. The average IR after taking LT was 0.6 ± 0.2 ($P < 0.001$). In 8 of them, complete disappearance of previously existing symptoms was noted. In 11 patients there was a significant improvement. A positive effect lasted from 1 to 7 months.

In 17 patients of the second group RI was on average, 20.1 ± 1.6 (Table 2). In 3 cases there was no effect. The less RI was before taking LT, the more pronounced the effect of treatment. So, for example, with RI up to "15" the symptoms of the disease after taking LT disappeared almost completely. Only in one patient was a minimal belch. The total RI in patients of the 2nd group after taking LT decreased to 10.1 ± 2.8 ($P < 0.01$). The effect of treatment in this group was less prolonged (one - five weeks).

Table 2. Results of examination and treatment of 37 patients with symptoms of GERD during primary care.

	1st group (RI <10)	2nd group (RI ≥ 10)
Number of patients	20	17
Average age	30 years	51 years
Duration of the disease	3 – 39 months	5 – 35 years
RI before treatment	5.4±0.4	20.1 ± 1.6
RI after taking the tablets	0.6 ± 0.2 (P <0.001)	10.1 ± 2.8 (P <0.01)
Duration of positive effect	1- 7 months	1-5 weeks

We have experience of using LT for the treatment of GERD in more than 100 patients. In the present work, only those observations are presented, where the results of the treatment could be estimated from the change in RI. We did not observe any complications. Moving through the intestines, the tablets disintegrate and decrease in size until they disappear completely. In two cases outside the present study: with ulcerative stenosis of the esophagus (1) and with achalasia (1), the tablets freely released during vomiting. Often after taking the LT, there is a feeling that it is stuck in the esophagus. At first, we took x-rays to make sure that the BT passed into the stomach. Subsequently, it was enough to swallow a piece of bread to promote the tablet and get rid of this sensation.

Figure 1 shows the arrangement of tablets in different parts of the digestive tract.

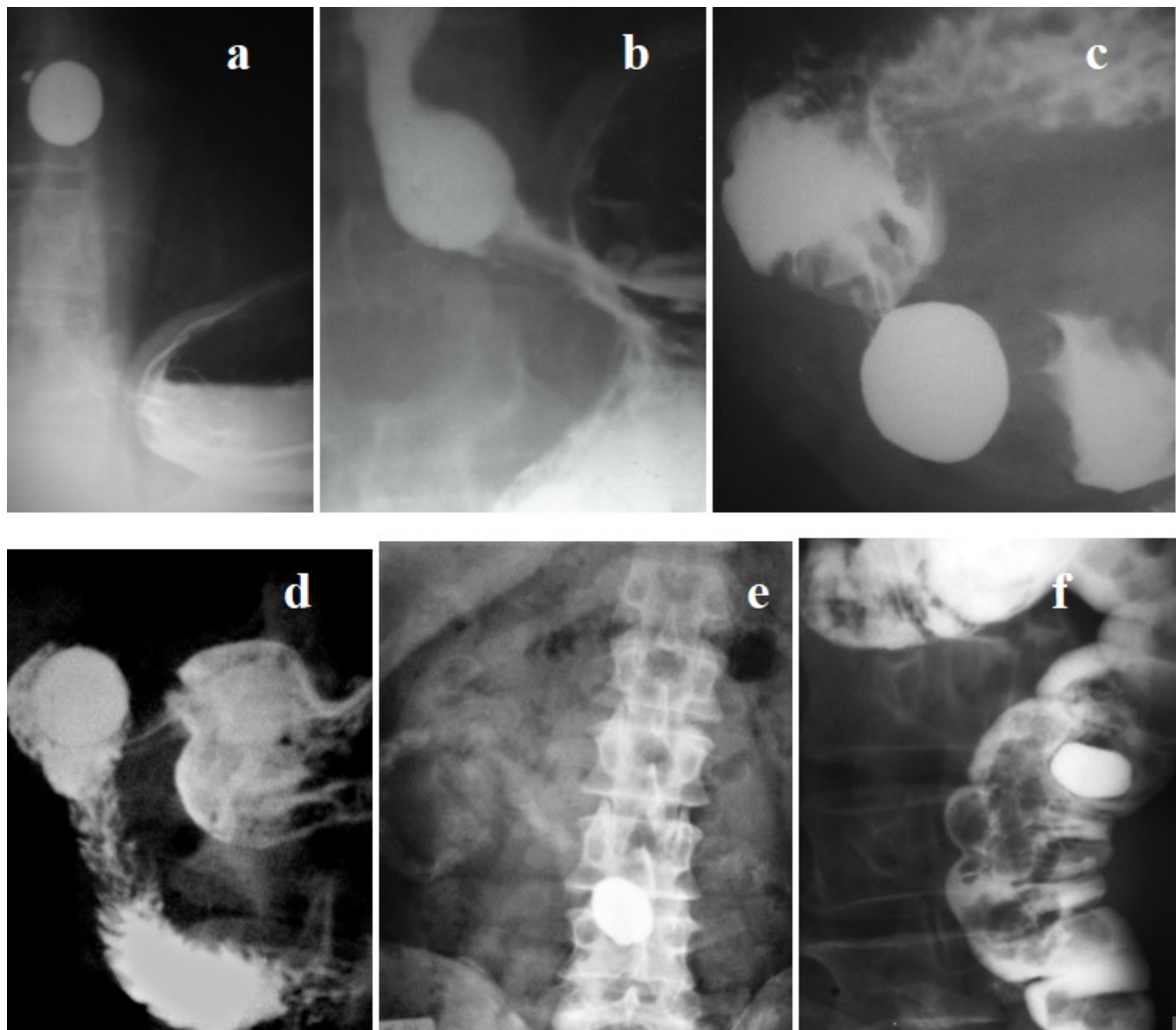


Figure 1. Radiographs of different patients who swallowed LT. **(a)** BT in the middle of the esophagus; **(b)** above the contracted lower esophageal sphincter; **(c)** in the antrum of the stomach during antral systole; **(d)** in the duodenal bulb; **(e)** an x-ray was taken 28 hours after swallowing the last LT. A reduced tablet is visible at the level L 3-4. Traces of barium from the disintegrated surface layer of the tablet are visible in the loops of the small intestine; **(f)** in the sigmoid colon.

Discussion

Until recently, the 24-hour pH monitoring is considered as Gold Standard. It is believed that pH <4 in the lower third of the esophagus > 4% of the time of the

study is a sign of GERD. Therefore, such morbid conditions as "physiological eructation" and "simple heartburn", which when examined by modern methods of diagnosis do not go beyond the limits of the norm, are referred to as pathologies that are not related to GERD [13]. However, in order to initially determine the normal pH limits, it was necessary to compare the pH-metry data with another method of investigation in healthy patients. There was no other more accurate method of investigation. Consequently, these boundaries were established based on correlation with clinical symptoms and endoscopy data. First, the selection of the norm based on clinical symptoms is not possible, since GERD may have preclinical form, and periods of asymptomatic disease are possible. In recent years, many researchers have concluded that GERD in adult begins in early childhood. The disappearance of symptoms after treatment of children does not mean recovery, i.e. there are subclinical forms of the disease [14,15]. It has been shown that in children older than one year, in whom the symptoms of GERD after treatment disappeared, histological studies revealed pathological changes [15].

Secondly, it turned out that based on modern criteria of pH-metry, GERD without erosion of the esophageal mucosa are not diagnosed [6,7,16]. GERD with high gastric pH and bile reflux are also not detected [17]. The method of impedance pH-metry has been recognized as a more effective test [16]. But the criteria of truth remain the same.

Third, recent histological studies have shown that GERD begins with a weakening of the intra-abdominal part of the LES, as a result of which the mucous of this department alone is exposed to aggressive hydrochloric acid. Because of this, the squamous epithelium of the abdominal part of the esophagus is transformed into the cardiac epithelium. The authors believe that the intra-abdominal part of the esophagus according to modern concepts is mistakenly considered a cardiac department of the stomach. The changes in the mucosa of the abdominal part of the LES occur long before the signs of inflammation in the supra-diaphragm part of the esophagus and a decrease in

pH. Thus, the orientation towards pH-metry leads to a belated diagnosis of GERD and an increased risk of esophageal cancer [18].

If we compare the data of both groups, it becomes obvious that the older the patient and the longer the anamnesis of the disease, the more numerous and stronger the complaints. There is reason to believe that patients 1st and 2nd groups are in a different stages of the same disease .

As a result of this research and analysis of the literature, we have arrived at the following conclusions.

If the patient in primary care has even with one of the symptoms characteristic of GERD (heartburn, belching after a light breakfast; non-cardial pain behind the sternum or in the epigastric region; chronic cough without changes on the roentgenogram of the chest or asthma attacks that appeared in the adult state without any allergy), we consider it more likely that he has GERD. GERD, as a chronic progressive disease, begins to manifest itself with little expressed symptoms. Over time, new symptoms appear, and they become more severe.

We agree with the recommendations of Canadian gastroenterologists that patients with heartburn and acidic regurgitation can be treated empirically as GERD patients, without preliminary examination, if there are no alarm signal" [19]. An American and English gastroenterologist support this concept [20].

We consider it expedient to use screening of GERD according to the table in order to evaluate the severity of the pathological process and the effectiveness of treatment by the magnitude of RI.

Large diameter tablets are used to determine the degree of narrowing of the esophagus in patients with the Schatzki ring. For this, the patient was given a barium tablet with a diameter of 1.3 cm. If she lingered over the narrowing of the esophagus, this was an indication for treatment [21]. The therapeutic effect of LT with GERD was first described by us in 2005 [22]. At first it was assumed that this was due only to the expansion of the LES. This was evidenced by the disappearance or mitigation of clinical symptoms of GERD in young children and in infantile colic after the dilation of the LES by the inflated balloon of the

Foley catheter extracted from the stomach outward. With a manometric study performed immediately after this procedure, an increase in the tone of the LES and an increase in its response to stimulation were found in comparison with the indices before the LES stretching [23]. In the laboratory of Professor Shafik, an increase in the peristalsis of the esophagus and an increase in the tone of the LES in response to the stretching of this sphincter in healthy volunteers were observed [24]. Since LT is pushed by the peristaltic wave of the stomach through the pyloric sphincter and stretched it, a positive effect may also be due to an improvement in evacuation from the stomach. It is known that the stretching of the pyloric sphincter accelerates the evacuation from the stomach [25].

In patients with GERD the inflammatory process under the influence of hydrochloric acid, trypsin and bile gradually progresses not only in the esophagus, but, first, in the LES [18]. Initially, this process captures only the mucous membrane, and then spreads to the muscle layers. This is manifested by a stretching, edema and hypertrophy of muscle fibers with the gradual development of fibrosis. It leads to rigidity of the sphincter, which is not able to contract enough strongly, and not open wide. As a result, the rugal-like folds appear which easily mistaken for gastric folds. [18]. The same processes occur in the pyloric sphincter. We assume that a strong peristaltic wave of the esophagus, pushing LT through the LES, and then antral systole pushes LT through the pyloric sphincter. Dilation of the rigid muscles restores their elasticity. The older the patient, the more pronounced fibrosis, and the dilation of the LES less effective.

In the course of long-term observations, we were convinced that the effect of LES dilation did not depend on the number of swallowed LT, and in the recent time we give swallow one tablet with diameter 2.0 or 2.5 cm, depending on the patient's size. The following is one of the last cases. A 62-year-old woman had all the symptoms shown in table 1, except for difficulty of swallowing food. Most symptoms are marked with a "3". Dyspnea or cases of sudden asphyxiation

was marked with a "4". She took Esomeprazole 40 mg in the morning for 1 month without obvious improvement. The RI was 22. An X-ray study of GEJ was performed on an empty stomach. The patient drank a glass of water, and then in a horizontal position she was drinking a barium suspension through a straw from a glassful located near her head. The radiograph was taken when she drank 200 ml of barium and raised her straightened legs (**Figure 2. a**). After 3 minutes, an x-ray was taken to assess the degree of emptying of the esophagus (**Figure 2. c**).

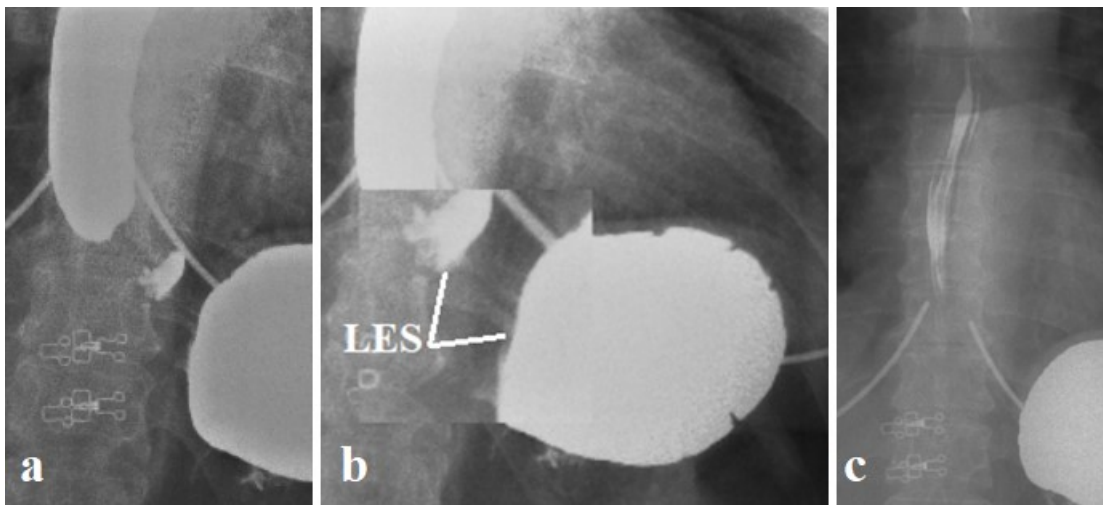


Figure 2. A GEJ study with the provocation of high pressure in the stomach. **(a)** A radiograph of GEJ; and **(b)** a diagram to it. The esophagus is dilated (2.5 cm) while the norm is 1.5 cm. There is no peristaltic wave. There is the contraction zone between the esophagus and the stomach in the middle part of which the pseudodiverticulum is determined. It divides the contraction zone into 2 parts. The lower part is a short LES. Its length is 1.7 cm, while the norm is 3.6 cm. The upper part is a contracted phrenic ampulla. A pseudo-diverticulum is a not completely contracted left base of an ampoule. **(c)** After 3 minutes, the esophagus was not completely cleared of barium. The folds in its upper part are determined. The lower part is represented by contracted phrenic ampulla and LES. This is a typical GERD picture.

The patient swallowed LT 2.5 cm in diameter, and she was recommended to take PPI twice a day. One weeks later, RI was 5. Improvement came immediately after taking LT. The patient herself began to take one PPI tablet per day a week after the examination. Endoscopic examination without histology revealed no pathology.

Conclusion. The pathogenesis of gastroesophageal reflux disease is due to the incompetent (weak) lower esophageal sphincter. This is a chronic disease that can progress despite the absence of severe symptoms. Therefore, the detection of even minor symptoms characteristic of GERD should be the basis for treatment, since the sooner treatment is started, the easier it is to prevent its progress. All symptoms of GERD are due to esophagitis. Acute esophagitis leads to an increase in the tone of the esophagus. The inflammatory process caused by damage to the walls of the esophagus and LES with hydrochloric acid, pepsin or bile leads to edema, hypertrophy and ultimately to fibrosis of all layers of the esophagus and LES. Gradually, the LES becomes rigid. Stretching of the LES with a large tablet increases tissue elasticity, especially in young patients who have few fibrotic changes.

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