

## ORIGINAL ARTICLE

# MECHANISMS OF THE FORMATION OF MOTOR-SECRETORY DISORDERS IN PATIENTS WITH GERD WITH CONCOMITANT AIT

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## ABSTRACT

**The aim:** The aim of this work was to study the effect of thyroid hormones on motor-secretory dysfunction in patients with GERD with concomitant AIT.

**Materials and methods:** The study involved three groups of patients: with isolated GERD, GERD with AIT at the stage of hypothyroidism and GERD with AIT at the stage of hyperthyroidism. The control group consisted of 15 practically healthy individuals. GERD and AIT were diagnosed on the basis of ICD-10. All patients underwent a comprehensive examination, including ultrasound examination of the motor-evacuation function of the esophagus and stomach. Quality of life of patients was assessed by using the GIQLI questionnaire.

**Results:** The most expressed complaints and low quality of life are observed among patients with combined pathology. The results of pH-metry indicate more severe course of GERD among patients with concomitant AIT. The most pronounced decrease in the tone of the lower esophageal sphincter and increased regurgitation were observed in the second group.

**Conclusions:** 1. It was found that more reliable motor-secretory disorders were observed among patients with GERD with concomitant AIT. 2. A close correlation was established between the severity of the clinical picture, the level of increased thyroid hormones and the degree of impairment of motor-secretory disorders among patients with GERD with concomitant AIT; 3. The results obtained indicate that changes in the metabolism of thyroid hormones are one of the factors involved in the mechanisms of GERD formation.

**KEY WORDS:** gastroesophageal reflux disease, motor secretory disorders, autoimmune thyroiditis, thyroid hormones

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## INTRODUCTION

In recent years, there has been a tendency towards an increase in the incidence of gastroesophageal reflux disease (GERD). This pathology occupies a leading place in diseases of the upper gastrointestinal tract (GIT), displacing gastric ulcer and chronic gastroduodenitis into the background. According to statistics, worldwide, the prevalence of GERD ranges from 8 to 33%, depending on the country. [1]

According to the WHO classification, GERD is a chronic recurrent disease caused by a violation of the motor-evacuation function of the gastroesophageal zone and characterized by spontaneous or regularly recurring throwing of gastric or duodenal contents into the esophagus, what leads to the damage of the distal esophagus with the development of erosive-ulcerative, catarrhal and / or functional disorders. From a pathophysiological point of view, GERD is an acid-dependent disease that develops against the background of a primary impairment of the motor function of the upper digestive tract. [2]

Despite the fact that the main pathogenetic significance in gastroesophageal reflux disease (GERD) is the contact of the esophageal mucosa with hydrochloric acid, as a result of a prolonged decrease in pH in the esophagus below 4.0, GERD is considered as a disease with primary impairment of esophageal and gastric motility. Secondary

motility disorders with delayed emptying can occur in other diseases (peptic ulcer, dermatomyositis, amyloidosis, hypothyroidism). [3]

At the core of the pathogenesis of GERD lays a violation of the motor function of the esophagus and stomach as a result of a decrease in the tone of the lower esophageal sphincter, which in turn leads to disruption of the normal functioning of the antireflux barrier and a decrease in esophageal clearance. According to the literature, these reasons predominate 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 refluent and the duration of contact with it.

Almost all organic diseases of the gastrointestinal tract as well as some general diseases in which hormonal imbalances are observed (diabetes mellitus, thyroid pathology, etc.) are accompanied by a decrease or increase in the motor activity of the digestive tract, changes in its muscle tone and peristalsis, that can be intensified or weakened. There is a close relationship between the level of gastric secretion and the motility of various parts of the gastrointestinal tract.

In the pathogenesis of this disease, the role of spontaneous relaxation of the lower esophageal sphincter (LES) is consid-

ered, that under normal conditions provides a barrier function and prevents the retrograde flow of stomach contents during active peristalsis of this organ caused by the initial phase of the digestive process. Up to this day, a huge amount of data has been accumulated, indicating that in the vast majority of patients with GERD reflux episodes occur mainly in the process of the so-called transient relaxation of the lower esophageal sphincter (TRLES). The tone of the lower esophageal sphincter is only one of the components of the antireflux barrier and accordingly its change is one of the components of the TRLES. Using sensitive methods for verifying reflux (both liquid and gas in the distal part of the esophagus) it can be found that 90% of episodes of TRLES in healthy individuals are accompanied by signs of gastroesophageal reflux. Pathological GERs are regarded refluxes with a pH in the esophagus less than 4.0 or more than 7.0 lasting longer than 5 minutes, more than 50 episodes per day, a total duration of more than 1 hour and existing for at least 3 months. Among patients with GERD, the latter are observed in 87% of cases of PRNPS, and refluxes in them turn out to be acidic (pH <4) or slightly acidic (4 < pH <7) more often than within healthy persons. Slowing of the gastric evacuation increases intragastric pressure, and this in itself provokes reflux. Therefore, there are differences in the mechanism of TRLES between these categories of subjects, which determine that in healthy people at the time of TRLES only gas enters the esophagus from the stomach, in contrast to patients with reflux disease. [4]

The regulation of the motor-secretory function of the gastrointestinal tract is carried out by neuro-humoral mechanisms. The main role is played by the autonomic nervous system and gastrointestinal hormones. Activation of the vagus nerve with the subsequent release of acetylcholine, as well as blockade of dopamine (D2) receptors, increases esophageal peristalsis, gastric motor activity and sympathetic fibers have the opposite effect. [5]

In addition to gastrointestinal hormones, a number of other hormones, including thyroid hormones, also affect the motor secretory function of the gastrointestinal tract. One of the most common thyroid disorders is AIT.

GERD and AIT have several common pathogenetic mechanisms, the main of which are thyroid hormones, which regulate the processes of motility and secretion of the gastrointestinal tract. Disruption of the gastrointestinal tract in patients with AIT is caused by the influence of thyroid hormones. With a decrease in the level of thyroid hormones in hypothyroidism, mucinous edema of the gastrointestinal mucosa occurs, the secretion of gastric juice decreases, peristalsis and food passage slow down, the muscle tone of the stomach and lower esophageal sphincter decreases that contributes to the occurrence of GERD. When production of thyroid hormones increases, peristalsis and muscle tone of the stomach intensify and the secretion of gastric juice increases too.

## THE AIM

The aim was to study the effect of thyroid hormones on motor secretory dysfunction in GERD patients with concomitant AIT.

## MATERIALS AND METHODS

The study involved three groups of patients. The first group consisted of 25 patients with isolated GERD (15 women and 10 men, mean age  $20.5 \pm 1.8$  years). The second group included 20 patients with GERD in combination with AIT in the hypothyroid stage (12 women and 8 men, mean age  $21.2 \pm 1.7$  years). And the third group included 20 patients with GERD in combination with AIT at the stage of hyperthyroidism (11 women and 9 men, mean age  $21.0 \pm 1.5$  years). The control group consisted of 15 apparently healthy individuals of the same age and sex.

GERD was diagnosed in patients on the basis of ICD-10. All patients underwent a comprehensive examination which included the necessary set of clinical, laboratory and instrumental research methods according to local treatment protocols, such as collection of complaints and anamnesis, patient examination, physical examination, clinical and biochemical analyzes, ECG, EGD, intragastric pH-metry.

The patients underwent ultrasound examination of the motor-evacuation function of the esophagus and stomach with water load using the ULTIMA pro-30 apparatus (Ukraine). The patient had drunk 1.0-1.5 liters of water before the study. 3, 5, 10 and 15 minutes after taking the fluid, the patient underwent an ultrasound examination, during which the thickness of the esophageal wall, the diameter of the esophageal opening of the diaphragm, the diameter of the lower third of the esophagus were measured and the presence and duration of gastroesophageal reflux were established.

To diagnose AIT, ICD-10 and the American Thyroid Association's clinical guidelines for the diagnosis and treatment of hypothyroidism and hyperthyroidism were used. [6, 7] An increase in antibodies to thyroid peroxidase (TPO), an increase in thyroid-stimulating hormone (TSH) and changes in the ultrasound picture of the thyroid gland were taken into account. The patients underwent an ultrasound examination of the thyroid gland using the ULTIMA pro-30 apparatus (Ukraine). The functional activity of the thyroid gland was judged by determining the level of thyroid hormones (TSH, T4 free, T3) with ELISA method and the presence of antibodies to TPO by using a set of standard reagents from the "Vector-Best" company.

The evaluation of the quality of life of the patients was carried out on the basis of a survey of the patients using the GIQLI (Gastrointestinal Quality of Life Index) questionnaire. The GIQLI questionnaire was developed to evaluate the quality of life of the patients with gastroenterological profile and consists of 36 questions, which are grouped into five sections: functional state, emotional state, social activity, treatment effect and disease-specific questions. The proposed answers include a 5-rank scale - from 0 to 4, with 0 being the worst value, 4 being the best indicator. The maximum possible number of points is 144. The sum of points for all questions is the GIQLI-index for a given patient. Thus, the higher the GIQLI-index, the higher the quality of life of the respondent.

The study followed the principles of the Helsinki Declaration adopted by the General Assembly of the World Medical Association (1964-2000), Council of Europe Convention on Human Rights and Biomedicine (1997), the

**Table I.** Dynamics of the quality of life in the studied groups according to the results of the GIQLI questionnaire

	Before treatment	After treatment	p
Group 1	83,25±10,2	103±7	p < 0,001
Group 2	77,3±15	98,6±12,3	p < 0,001
Group 3	75,2±11,3	94,7±10,7	p < 0,001

**Table II.** Functional state of the lower third of the esophagus during ultrasound examination with water load

Index	Group 1	Group 2	Group 3	Control group
Regurgitation	+	++	+	-
Width of the lumen of the lower third of the esophagus	25.3±0.7 mm	32.1±0.5 mm	29.7±0.6 mm	22.8±0.3 mm
Diameter of the esophageal opening of the diaphragm	16.8±0.6 mm	19.2±0.8 mm	17.9±0.5 mm	14.2 ±1.3 mm

relevant provisions of the WHO, of the International Council of Medical Scientific Communities, of the International Code of Medical ethics (1983) and the laws of Ukraine. The clinical part of the work was carried out on the basis of the Municipal Nonprofit Enterprise of Kharkiv Town Council "City Student Hospital" (Kharkov, Ukraine). The data was statistically processed by using Microsoft Excel 2007 and Windows Statistika 6.0. For all types of analysis, differences were considered statistically significant at  $p < 0.05$ .

## RESULTS

The clinical picture of GERD was characterized by the presence of complaints of heartburn during a long time, recurrent epigastric pain, heaviness in the abdomen, belching, sour taste in the mouth, occasional nausea, chest pain. The majority of patients noted the appearance of these complaints after dietary disturbances and / or stressful situations. Patients of the second group, along with standard dyspeptic complaints, noted the presence of constipation, drowsiness, mood swings, lethargy, apathy, and increased anxiety about their own health. Patients of the third group, in addition to the standard complaints inherent in GERD, showed complaints of diarrhea, hunger pain in the epigastrium, nausea, anxiety, weakness, sweating.

The quality of life of all patients, as measured by the GIQLI questionnaire, improved after the treatment (Table I).

According to the conclusion of EGDS, 90% of patients had a non-erosive form of GERD, 10% of patients had the initial stage of erosive esophagitis, among them, the majority of patients were with concomitant pathology.

According to the results of intragastric pH-metry among patients of the 1st group with isolated GERD a decrease in the acidity of gastric juice and alkalizing function of the antrum (pH in the body ( $1.22 \pm 0.03$ ), with the norm ( $1.8 \pm 0.09$ ), in the antrum - ( $6.3 \pm 0.7$ ) with the norm ( $7.3 \pm 0.8$ )) was found out. Among patients of the 2nd group there was a decrease in indicators of aggression of gastric juice with a simultaneous decrease in indicators of the alkalizing function of the antrum (pH in the body ( $2.9 \pm 0.8$ ), at normal ( $1.8 \pm 0.09$ ), in the antrum - ( $6, 5 \pm 0.75$ ) at the norm ( $7.3 \pm 0.8$ )). Among patients of the 3rd group an increase in indicators of gastric acid aggression (on average, pH in the body was  $1.10 \pm 0.01$ , with a norm of  $1.8 \pm 0.09$ )

and a decrease in indicators of alkalizing function of the antrum (on average, pH  $5.2 \pm 0.5$  at the norm of  $7.3 \pm 0.8$ ) compared with patients with isolated GERD were noted.

Among patients of the first group with isolated GERD, the indicators of thyroid hormones and antibodies to TPO were within the normal range: TSH 0.3–4.0 mIU / L, antibodies to TPO up to 35 IU / L. In the second and third groups, antibodies to TPO exceeded the norm several times. In the second group, the increase in TSH was on average up to  $11.0 \pm 1.2$  mIU / L. In the third group, TSH was reduced on average to  $0.12 \pm 0.05$   $\mu$ IU / ml.

Ultrasound examination of the thyroid gland among patients of the first group with isolated GERD showed that the structure of the gland was normal.

When studying patients of the second group with combined pathology of GERD with concomitant AIT in the hypothyroid stage, the following data were obtained:

- 90% had a heterogeneous structure of the thyroid gland due to fibrous inclusions, as well as a seal of the capsule;
- 9% of patients had single enlarged follicles in the structure of the thyroid gland;
- and in 3.5% of cases - areas of reduced echogenicity;
- an increase in the size of the thyroid gland was observed in 2% of patients.

The echographic picture of patients of the group No. 3 is dominated by the presence of areas of reduced echogenicity (75%) and enlarged follicles in the structure of the thyroid gland (55%).

Ultrasound examination of the lower third of the esophagus and stomach in patients of all three groups in varying degrees showed the presence of regurgitation, expansion of the lumen of the lower third of the esophagus and an increase in the diameter of the esophageal opening of the diaphragm, in contrast to patients in the control group (Table II).

Thus, it can be noted that the most pronounced complaints are in patients with combined pathology. According to the results of the GIQLI questionnaire, it can be seen that the baseline quality of life among patients with the combined course of GERD and AIT was lower than among patients with isolated GERD.

According to the results of pH-metry, it can be concluded that among patients with isolated GERD and patients from the GERD group with combined AIT in the stage of thyroid hyperfunction, there are an increase in gastric acid aggres-

sion indices and a decrease in the alkalizing function of the antrum. However, in the group with combined pathology, this deviation from normal values is more expressed, which indicates more severe course of GERD in patients with combined AIT in the stage of thyroid hyperfunction. Among patients of the second group with combined GERD and AIT in the hypofunction stage, there is a decrease in the aggression of gastric juice, but at the same time the alkalizing ability of the antrum decreases too.

According to the results of ultrasound examination of the motor function of the lower third of the esophagus and stomach, the most pronounced changes are observed in the second group of patients, which is expressed in a decrease in the tone of the lower esophageal sphincter and increased regurgitation.

## DISCUSSION

Thus, summing up, it can be claimed that the presence of concomitant AIT worsens the clinical picture of GERD. Patients with this combined pathology have more expressed complaints and decrease in the quality of life, which is due to strengthening of the secretory function on the background of a more expressed decrease in the tone of the LPS, walls of the stomach and peristalsis of the digestive tract, caused by a malfunction of the thyroid gland.

Malfunction of the gastrointestinal tract among patients with AIT is caused by the influence of thyroid hormones. With a decrease in the level of thyroid hormones in hypothyroidism, mucinous edema of the gastrointestinal mucosa occurs, the secretion of gastric juice decreases, peristalsis and food passage slow down, the muscle tone of the stomach and lower esophageal sphincter decreases, which contributes to the occurrence of GERD [8].

As a result of overproduction of the thyroid gland, intensifies the motility of the esophagus and stomach and increase the acid-producing and enzymatic activity of the gastric mucosa. [9]

The data obtained in one way or another correlate with the studies carried out by other authors. However, Baranov I.V. and Maikova T.V. (2010) [10], as well as Shebalina A.O. (2017) [11] in their researches studied the course of GERD amid changes in the thyroid gland and did not take into account changes in the psychosomatic status of patients. Voodoo L.F. (2013) [12] and Masalova O.O., Gunes NA. (2020) [13] in their works highlight psychovegetative disorders in diseases of the thyroid gland, but do not take into account the diseases of the upper gastrointestinal tract. Kokurkin G.V., Akimova V.P. (2012) [14], Trofimov V.I., Bezrukov Y.N. (2015) [15] and Tkacheva N.V., Savenkova N.D. (2012) [16], studied psychovegetative disorders in diseases of the upper gastrointestinal tract, without taking into account the effect of the level of thyroid hormones. Thus, our study and the results obtained indicate a close pathogenetic relationship in the course of AIT and GERD, as well as the role of thyroid hormones in the mechanisms of the formation of motor secretory disorders in GERD.

Study limitations. The study was not conducted in case

of identified concomitant pathology of other organs and in case of patients refuse to participate in the study.

Prospects for further research. Further study of the effect of thyroid hormones on the clinical course of isolated GERD and GERD with combined pathology is important for the formation of treatment and prevention regimens for a particular patient, and at the same time it outlines new directions in approaches to both diagnosis and treatment of this pathology.

## CONCLUSIONS

1. It was found that patients with GERD with concomitant AIT have significant motor-secretory disorders. This is manifested in more expressed acidity of gastric juice with hyperproduction of thyroid hormones, decrease in the alkalizing function of the antrum, more pronounced decrease in the tone of the lower esophageal sphincter and increased regurgitation in patients with hypothyroidism, in contrast to patients with isolated GERD, who have these indicators shown to a lesser extent;
2. A close correlation was established between the severity of the clinical picture, the level of increased thyroid hormones and the degree of impairment of motor-secretory disorders in patients with GERD with concomitant AIT;
3. The results obtained indicate that changes in the metabolism of thyroid hormones are one of the factors involved in the mechanisms of GERD formation.

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