METHODS OF TREATMENT OF REFLUX ESOPHAGITIS IN PATIENTS WITH METABOLIC SYNDROME

Tojiaxmedov Musoxon Habibullo ogli
Tashkent Pediatric medical institute therapy direction Master's student 3rd year
Tashkent Pediatric Medical Institute
Muminov Shavkat Kadirovich
Therapy chair assistant, Candidate of Medical Sciences

Annotation: In the past few decades, the prevalence of such oncological forms as gastro esophageal reflux disease and obesity has been increasing throughout the world. The combination of these types of pathology is more often noted in patients with problems in nutrition and lifestyle, as well as a genetic predisposition for this nosology. It is noted that obese patients have an increased predisposition to the occurrence of diaphragmatic hernias and mechanical damage to the gastro esophageal junction, which occurs against the background of increased intragastric pressure and an increased pressure gradient between the stomach and esophagus, as well as due to stretching of the proximal stomach.

Key words: World Health Organization, epidemiological studies, gastrointestinal tract, pathophysiological mechanisms, prophylactic measures.

One of the main pathogen etic moments of gastro esophageal reflux disease is spontaneous relaxation of the lower esophageal sphincter. According to recent studies, in obesity, the frequency of postprandial spontaneous relaxation of the lower esophageal sphincter increases even in the absence of diaphragmatic hernias, non-erosive gastro esophageal reflux disease and reflux esophagitis. The variety of metabolic disorders observed in these patients suggests an integrated approach to treatment aimed at both effective reduction of acid-peptic factor and correction of excess body weight. Among the main directions of treatment of both components of this combined pathology, both non-drug and drug treatment methods are distinguished. An important role in therapy is assigned activities that promote a healthy lifestyle smoking cessation, weight loss, dietary nutrition, health-improving physical education.

Particular attention among drug therapy in patients with gastro esophageal reflux disease and obesity, allowing achieving an optimal acid-lowering effect. It is given to the group of proton pump inhibitors (inhibitors of H +, K + -ATPase), which have a lower affinity for the hepatic cytochrome P450 enzyme system, not influence on its activity and does not give clinically significant cross-reactions with other drugs.

According to the classification of the World Health Organization, gastro esophageal reflux disease (GERD) is a chronic relapsing disease caused by impaired motor-evacuation function of the gastro esophageal zone and characterized by spontaneous and / or regularly repeated throwing of gastric or duodenal contents into the esophagus, which leads to damage to the distal esophagus. GERD is a widespread chronic relapsing disease; typical GERD symptoms include heartburn and regurgitation. The incidence of GERD among the population of Western countries, according to various estimates, ranges from 10 to 20%, in Asian countries the level of this indicator is slightly lower.

GERD is a consequence of the rise of gastric or duodenal contents above the gastro esophageal junction, which leads to the manifestation of symptoms of the disease and a significant deterioration in the quality of life of patients. Analysis of the results of clinical and epidemiological studies, in which assessed the frequency of manifestations of the disease - heartburn or belching - at least one time per week. The reported prevalence of GERD ranged from 18.1 to 27.8% in the United States of America, from 8.8 to 25.9% in Europe, from 2.2 to 7.8% in East Asia, 11.6% in Australia, 23% in Argentina. When analyzing the prevalence of the disease in Latin America, in particular in Brazil and Mexico, the prevalence of the disease ranged from three to 11.9%.

In the international study DIGEST, it was shown that the prevalence of GERD symptoms is 7.7%, while heartburn is the most frequent manifestation of the disease (13.5%) from the gastrointestinal tract. During endoscopic examination of the Chinese population, reflux esophagitis was diagnosed in 5% of cases,

heartburn was noted in 22.5% of those examined, and, for example, in the Iranian population, the incidence of reflux esophagitis ranges from 1.77 to 2.80%. In some regions, In Russia, according to sample studies, up to 48.5% of men and 51.4% of women periodically experience heartburn. In the first population epidemiological study in Russia, initiated by the president of the Scientific Society of Gastroenterologists of Russia, director of the Central Scientific Research Institute of Gastroenterology L.B. Lazebnik within the framework of the MEGRE program (Multicenter study "Epidemiology of gastro esophageal reflux disease in Russia").

It was shown that the prevalence of GERD (presence of heartburn and / or acid belching once a week and more often during the last 12 months) was 23.6%. Another multicenter study ARIADNA (analysis of the prevalence of heartburn: a national epidemiological study of the urban adult population) showed that the main symptom of GERD - heartburn - was detected in 59.7% of respondents, frequent heartburn (2-3 times a week or more) - in 22.7 %. The most important risk factors for the development of GERD are heredity, overweight, visceral obesity, smoking, alcohol use and pregnancy. At the same time, according to a number of authors, risk factors for GERD should be differentiated from factors that contribute to the development and progression of gastro esophageal reflux, which include the consumption of fatty foods, chocolate, coffee, alcohol and gastric banding.

The purpose of this work is to study the literature data of two-combined nosology: GERD and obesity.

The urgency of the problem is because the steady increase in the prevalence of GERD and associated complications, along with generally recognized risk factors for GERD. May be due to a change in the nature of the diet towards the predominant consumption of fats, smoking, alcohol consumption, as well as an increase in the number of overweight people. In addition, obesity, which significantly increases the risk development of the clinical picture of GERD, erosive esophagitis, esophageal adenocarcinoma.

The results of multivariate analysis show that GERD is more often detected in male patients with high socioeconomic status. GERD is a multifactorial pathological process in which the development of the disease is based on the process of transient relaxation of the lower esophageal sphincter. Relaxation of the lower esophageal sphincter is considered as transient relaxation of the lower esophageal sphincter. And more than 1 mm Hg. per second for at least 10 s with a minimum pressure of less than 2 mm Hg. without swallowing for 4 s before and 2 s after the onset of relaxation of the lower esophageal sphincter. In addition, the most important pathophysiological mechanisms of GERD can be various violations of esophageal clearance caused by mechanical (changes in peristalsis) and chemical (changes in saliva composition) factors, violations of the ant reflux barrier (hiatal hernia, decreased pressure of the lower esophageal sphincter), delayed gastric emptying and duodenal-gastric reflux.

Extra esophageal manifestations of the disease develop because of the direct effect of acidic gastric contents on the pharyngeal mucosa, episodes of micro aspiration, as well as stretching of the esophagus with activation of the vasovagal reflex and the development of bronchospasm with corresponding symptoms.

It is now generally accepted that the treatment of obese GERD patients should be aimed at correcting both components of this combined pathology. Reducing body weight with dietary food in combination with exercise contributes to a significant reduction in the symptoms of GERD. Diet therapy is used in all weight loss programs. When treating GERD, it is necessary to adjust lifestyle and diet for best results. Drug treatment.

The evidence for the need to exclude various foods in GERD is currently highly controversial. Therefore, earlier in a number of studies it was shown that the consumption of food rich in fats and chocolate leads to a decrease in the tone of the lower esophageal sphincter. In a crossover study of 915 patients, it was demonstrated that there is a direct relationship between high fat intake and the development of GERD, while consumption Eating fiber-enriched foods can help reduce symptoms of GERD. This relationship between the composition of food and the severity of symptoms is clearly traced in patients with obesity or increased body weight. Several studies have shown that alcohol consumption is a risk factor for the development of GERD.

Despite the contradictory data on diet correction in GERD, obtained in a number of studies, recommendations on the regimen and composition of the diet continue to remain within the limits clinical guidelines for the treatment of GERD. With GERD, moderate physical activity, recreational exercise, eating

in small portions, excluding fatty and spicy foods are recommended. You should not go to bed after eating. The head of the bed should be raised by 150 ° to prevent stomach contents from being thrown into the esophagus during sleep. It should also be noted that recreational exercise could reduce body weight in patients with overweight and GERD. In a study by M.A. Mocanuet.

It has been demonstrated that physical activity-induced weight loss allows for better correction of adipocyte levels and insulin resistance in obese men compared with diet. It is recommended to quit smoking. All this serves as an important adjunct to drug therapy for GERD, which may be ineffective if these recommendations are not followed. The most effective drugs for treating GERD in obese patients are inhibitors proton pump inhibitors (inhibitors of H +, K + -ATPase), which can also be used in combination with prokinetics and antacids, while proton pump inhibitors should be chosen with low affinity for the cytochrome P450 system. Pharmacotherapy of obesity is recommended in the presence of concomitant diseases - metabolic syndrome, type 2 diabetes mellitus, hypertension, dyslipidemia and GERD.

Orlistat is a potent selective lipase inhibitor that has been shown to not only reduce body weight, but also a decrease in cholesterol, low-density lipoprotein and glucose levels, which is especially important for patients with GERD and metabolic syndrome.

When choosing a drug for the treatment of GERD, first, one should be guided by the algorithm for prescribing drugs depending on the type of GERD: non-erosive reflux disease or erosive reflux disease. The leading direction in the treatment of GERD is the conduct of acid suppressive therapy using proton pump inhibitors to eliminate acidification in the esophagus, as well as creating a barrier between aggressive gastric reflux ate and the esophageal mucosa using antacids or alginates. This standard of management of patients with GERD is substantiated by the results of many randomized trials, during which not only clinical, but also morphological efficacy of the mentioned groups of drugs was proved. Acid suppressive therapy is a mandatory component in the treatment of GERD in overweight patients. According to A.S. Trukhmanova (2008), for a complete relief of symptoms, longer therapy is needed, since the duration of treatment is director proportionally to the patient's body weight ($r = 0.45$, $p = 0.01$). If in people with normal body weight, the relief of heartburn occurs on the 3rd day from the start of therapy, then in overweight patients - only by the 9th day.

When choosing a proton pump inhibitor, one should take into account the fact that all inhibitors are lipophilic drugs. With obesity, the degree of metabolism of these drugs by liver enzymes changes. A decrease in the monoxides activity of cytochrome P450 isoforms is the basis of medicinal interactions and possible side effects of proton pump inhibitors. The advantages of using orlistat in patients with GERD and obesity should be considered the fact that this drug acts in isolation in the intestine, without affecting other organs and systems.

Relatively recently, sympathomimetic, norepinephrine reuptake inhibitors and others - benzfetamine, diethylpropion and phentermine - have been proposed for use in clinical practice. Most often, the prescribed drug in this group is phentermine, which is the only drug for short-term use (up to 12 weeks). It is effective and safe, as demonstrated in a randomized controlled trial involving 74 patients. Since one of the diagnostic criteria for metabolic syndrome, in addition to abdominal obesity, is an increase in fasting blood glucose levels, it is necessary to correct disorders of carbohydrate metabolism as for prevention the development of type 2 diabetes mellitus, and to reduce body weight, and, accordingly, reduce the severity of GERD symptoms. In metabolic insulin resistance, which occurs in obesity, the response of cells to the action of insulin is insufficient.

At the same time, the concentration of insulin in the blood is not reduced. Adiponectin, synthesized by adipose tissue, is involved in the regulation of glucose and lipid metabolism. With a decrease in adiponectin levels in obesity, insulin resistance increases, while level of insulin resistance in men is higher than in women. The drug of choice for correcting insulin resistance is metformin, a drug from the iguanid group. In a double-blind, randomized study of 100 obese women (body mass index 30-40 kg / m2), there was a significant decrease in insulin resistance and a decrease in body mass index by an average of 1 kg / m2 in the group receiving metformin at a dose of 1700 mg / day.

Despite the limited the number of drugs for the treatment of obesity, it should be noted that the off-label prescription of metformin to patients without diabetes mellitus in order to reduce body weight is widespread throughout the world. According to the results of a meta-analysis of 31 studies from 1966 to

2006, which included 4570 patients with an average study duration of 1.8 years, metformin reduced body mass index by an average of 5.3%.

It is important to note that metformin not only reduces body weight, but also promotes healthy distribution of fatty tissue in the body, which is confirmed by a study using radionuclide scanning. According to the results of which metformin reduced body weight by 4% after 6 months of treatment, and adipose tissue weight decreased by 9 %, the loss of visceral fat was 15%, the mass of subcutaneous adipose tissue decreased by 7%, there was no decrease in muscle mass. Another, fine Glucagon-like peptide-1 receptor agonists, or incretion mimetic, have proven themselves in clinical practice as a group of hypoglycemic drugs for the treatment of type 2 diabetes mellitus with obesity or overweight.

The action of these drugs is based on the incretion response, mediated by the effect on the β-cells of the pancreas, and a decrease in the secretion of glucagon by α-cells. The peculiarity of incretinomimetics is the positive dynamics of body weight against the background of their administration, which leads to a decrease in the volume of visceral fat, a decrease in insulin resistance and lepton resistance. S.R. Norris et al., Who systematized the results of 17 studies, emphasize that therapy with incretin-mimetics for 16– 30 weeks not only improves glycemic control, but also leads to a decrease in body weight by 1.0– 2.5 kg.

Analysis of the LEAD study showed a significant reduction in body weight with a combination of type 2 diabetes mellitus and obesity. In that, the study also involved obese volunteers, whose results allow considering liraglutide as a drug for drug therapy and obesity. Of undoubted interest is a new class of drugs for the treatment of type 2 diabetes mellitus - inhibitors of sodium-glucose cotransporters-2. An increase in the excretion of glucose in the urine under their action leads to a loss of about 60– 80 g of glucose per day, which corresponds to 240– 320 calories per day. Currently have published data from randomized trials showing a decrease in body weight by 2.5– 3.0 kg during 6 months of therapy with sodium-glucose cotransporter-2 inhibitors. It is important to note that weight loss is associated with the loss of visceral as well as subcutaneous adipose tissue.

It is known that α-glycosidase inhibitors slow down the absorption of complex carbohydrates in the small intestine, preventing the development of postprandial hyperglycemia. When studying the effect of the α-glycosidase inhibitor agarose on glucose metabolism in patients with impaired glucose tolerance (n = 118), it was shown that after 3 years of agarose treatment, the post-meal blood glucose level decreased by 1.16 moll / L, and the risk of developing diabetes mellitus decreased by 6%.

It has been demonstrated that the use of agarose can increase the level of adiponectin and reduce insulin resistance in patients with diabetes mellitus and metabolic syndrome. Insulin secretogens stimulate formation and the release of insulin from β-cells. One of the most commonly used insulin secretogens, glimepiride (a sulfonylurea derivative), increases adiponectin levels and helps to reduce insulin resistance in patients with metabolic syndrome.

It has also been shown that the use of glimepiride decreases the levels of tumor necrosis factor α, interleukin-6 and C-reactive protein. Insulin therapy for metabolic syndrome is prescribed for unsatisfactory results correction of carbohydrate metabolism with drugs that reduce insulin resistance, α-glycosidase inhibitors, insulin secretogens; it is possible to prescribe insulin therapy, including in combination with the above drugs, with the most preferable combination of insulin and metformin. If it is impossible to reduce body weight with the help of diet and pharmacotherapy, the methods of bariatric surgery are used - gastric bypass with gastrojejunostomy according to Roux (the most effective a procedure that allows you to achieve remission of GERD in obese patients).

Thus, obesity is the most important problem of modern medicine; its prevalence is increasing every year and acquires the character of an epidemic. Obesity is a complex disease in the pathogenesis of which the gastrointestinal tract plays a key role. Metabolic syndrome and diseases of the gastrointestinal tract often complicate obesity. One of the most common types of pathology in this case is GERD, the prevalence of which is also has increased significantly in recent years. Despite the availability of a large number of effective drugs for the treatment of GERD, a number of patients fail to achieve remission of the disease.

The analysis shows that the therapy of GERD in patients with abdominal obesity must certainly be complex and include not only drugs, but also correction of diet and diet, lifestyle changes, which requires significant efforts on the part of the patient. GERD in obesity- a disease in the treatment of which the efforts of gastroenterologists and endocrinologists should be combined. Analysis of literature data suggests that the

presence of obesity and signs of GERD are significantly associated with each other due to several common anatomical and pathophysiological mechanisms.

The variety of metabolic disorders suggests an integrated approach to the management of such patients. As the analysis of the literature shows, a large number of clinical and fundamental research was devoted to identifying the mechanisms of occurrence of these pathological conditions, the search and creation of new drugs, the assessment of their effectiveness. Based on the results of these studies, the main guidelines for the development of our knowledge in the described area and their application in clinical medicine are determined.

The development of modern medical technologies makes it possible to combine the use of various methods of treatment for such a complex category of patients, such as patients with GERD against the background of obesity.... At the same time, it is obvious that there is a need for research in order to improve the complex of therapeutic and prophylactic measures in relation to this contingent of patients.

List of References:

1. Ivashkin V.T. Clinical variants of metabolic syndrome. V.T. Ivashkin, O. M. Drapkina, O. N. Korneeva. M.: Med. inform. Agency, 2011.
2. Katz P.O., Gerson L.B., Vela M.F. Guidelines for the diagnosis and management of gastroesophageal reflux disease. Am. J. Gastroenterol. 2013; 108: 308-328.
3. Krentz A.J. Management of type 2 diabetes in the obese patient current concerns and emerging therapies. Curr. Med. Res. Opin. 2008; 24 (2): 401-417.
4. Kurukulasuriya R., Banerji M.A., Chaiken R., Lebovitz H. Selective decrease in visceral fat is associated with weight loss during metformin treatment in African Americans with type 2 diabetes. Diabetes. 1999; A315.
5. Norris S.L., Lee N., Thakurta S., Chan B.K. Exenatide efficacy and safety: a systematic review. Diabet. Med. 2009; 26 (9):
6. Huerta-Iga F., Tamayo-de la Cuesta J., Noble-Lugo A. et al. Consenso mexicano de enfermedad por reflujo gastroesofбgico (Parte I). Rev. Gastroenterol. Mex. 2012; 77: 193-213...
7. Salis G. Systematic review: Epidemiology of gastro esophageal reflux disease in Latin America. Acta Gastroenterol. Latinoam. 2011;
8. Sandler B.J., Rumbaut R., Swain C.P. et al. One-year human experience with a novel endoluminal, endoscopic gastric bypass sleeve for morbid obesity. Surg. Endosc. 2015; 29: 3298-3303.
9. Cange L., Johnsson E., Rydholm H. et al. Baclofen-mediated gastrooesophageal acid reflux control in patients with established reflux disease. Aliment. Pharmacol. Ther. 2002; 16: 869-873. doi: 10.1046/j.1365-2036.2002.01250. x.
10. Delavari A., Morado G., Elahi E. et al. Gastro esophageal reflux disease burden in Iran. Arch. Iran Med. 2015; 18: 85-88. PMID: 25644795.