

PECULIARITIES OF THE REALIZATION OF PSYCHOSOMATIC DISORDERS IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE WITH CONCOMITANT DIABETES MELLITUS TYPE 2 IN YOUNG PEOPLE

Oparin AA¹, Oparin AG¹, Kudriavtsev AA¹, Pavlov SB²

¹ Department of therapy, rheumatology and clinical pharmacology of Kharkiv medical academy of postgraduate education, Kharkiv, Ukraine

² Central research laboratory, Kharkiv Medical Academy of Postgraduate Education, Kharkiv, Ukraine

Received 15.05.2019; accepted for printing 07.03.2019

ABSTRACT

Objective. To study the peculiarities of the realization of psychosomatic disorders in patients with gastroesophageal reflux disease with concomitant diabetes mellitus type 2 and to develop methods for their correction.

Materials and methods. In order to obtain the results we conducted a study of two groups of patients suffering from GERD with concomitant mild to moderate diabetes mellitus type 2 and isolated GERD. The survey program included: determining the degree of carbohydrate metabolism compensation; state of aggression factor. For the evaluation of gastric secretion we used the daily pH-metry. Also, all patients underwent an ultrasound investigation with water load. Indices of oxidative stress were assessed by the diameter of the celiac trunk and blood flow velocity in it. Psychosomatic disorders and quality of life of the patients were estimated by conducting a survey using unified questionnaires.

Results. We established that in patients with GERD with concomitant diabetes mellitus there was a clear tendency towards stabilization of the glycemic profile. In patients of both groups, episodes of heartburn, frequency and intensity of belching, and dyspeptic phenomena decreased.

We found that, after a 4-week course of therapy, oxidative stress levels in patients of both treatment groups decreased. The findings suggest that psychosomatic disorders are factors that not only make the course of GERD and DM type 2 more difficult, but also take a direct part in the formation of GERD itself in DM type 2.

The results of our studies also clearly indicate that the additional assigning of actovegin in the general scheme of treatment for patients with DM type 2 with concomitant GERD has an evident positive effect on the reduction of the onset of clinical remission of both DM type 2 and concomitant GERD.

Conclusions. The inclusion of actovegin in the general treatment scheme of patients with GERD and DM contributes to a significant reduction in the recrudescence period of both DM and concomitant GERD.

KEYWORDS: gastroesophageal reflux disease, diabetes mellitus type II, psychosomatic disorders, state of aggression factor, actovegin.

INTRODUCTION

Nowadays diabetes mellitus (DM) is one of the most important medical and social problems. This is connected with the continued increase in the

number of patients suffering from this serious disease and the increase in the number of its complications [Thakkar B et al., 2013; Karabouta Z et al., 2014; Grinova VV, Glugovska SV, 2016].

Peer assessments of the International Diabetes Federation (IDF) in 2011 predicted that by 2030 the number of cases would reach 520 million people, and diabetes would become the 7th cause of death worldwide [Sun H et al., 2014; Bezrukov YuN, 2015; Dedov II et al., 2015]. For today, more

ADDRESS FOR CORRESPONDENCE:

ANTON A KUDRIAVTSEV

Kharkiv medical academy of postgraduate education,
Amosova street, 58, Kharkiv 61176, Ukraine

Tel. : (+38095) 633 49 86

Email: dtdn10@gmail.com

than 422 million people suffer from this disease. According to the estimates of modern diabetes specialists, by 2040 the number of patients will reach 642 million people worldwide [Medical care in diabetes.].

It is worth noting that over the past few years not only the number of patients suffering from this disease has increased, but also the percentage of diabetes type 2 in all patients has increased [Natalini J et al., 2014; Tkach SM, 2016]. There is a tendency towards an increase of the disability level, since patients have increasingly been diagnosed comorbid cases, among which gastroesophageal reflux disease (GERD) occupies a special place [Song Y, 2015; Oparin AA., Beziazychna NV, 2016].

According to numerous studies, the incidence of GERD in DM (from 18.8 to 26.7%) is significantly higher than in patients not suffering from DM (10-17%). Moreover, it should be noted that GERD is observed much more often in people with the second type of DM than in those who were diagnosed with the first type of the pathology (31.1% vs. 18.6%) [Wang X et al., 2015, Kostitska IO, 2017].

However, so far many issues related to the formation of this comorbid state remain not fully disclosed or studied. This contributes to the fact that today diagnostic and treatment methods of such patients require further research.

The basis of the mechanisms for GERD development in DM is diabetic polyneuropathy, which leads to a decrease and delay in gastric secretion, which causes inadequate work of the peristaltic motions of the stomach that become asynchronous, their amplitude decreases, and as a result, they become ineffective, and the stomach is slower dispensed of food. All this contributes to throwing the contents of stomach into esophagus lumen [Shestakova MV et al., 2016].

In its turn, a persistent increase in blood sugar level entails an increase in relaxation time of the lower esophageal sphincter, which is another reason for the formation of gastroesophageal reflux [Xiao-Meng S et al., 2015].

It is also important that taking hypoglycaemics pills, such as sulfonylureas secondaries, which include amaril, glimepiride, glibenclamide, as well as posprandial regulators (metformin), contribute to the development of dyspeptic symptoms, which are one of the signs of GERD [Oparin A, Vnukova

A, 2017]. These facts significantly reduce the quality of life of such patients, which contributes to the development of anxiety, apathic and depressed mood, and sleep breakdowns, which, in their turn, aggravate the course of both GERD and DM type 2 [Oparin AA et al., 2018]. Therefore, the study of the mechanisms of psychosomatic realization in comorbid GERD and DM type 2 is of scientific and practical interest, which determined the objectives of our study.

Objective. To study the peculiarities of the realization of psychosomatic disorders in patients with gastroesophageal reflux disease with concomitant diabetes mellitus type 2 and to develop methods for their correction.

MATERIALS AND METHODS

In order to obtain the results we conducted a study of two groups of patients suffering from GERD with concomitant mild to moderate diabetes mellitus type 2 and isolated GERD.

The first main group included 24 patients – 13 men and 11 women aged 21-44 years (average age 36.7 ± 0.91 years) suffering from GERD with concomitant diabetes mellitus type 2 who received standard therapy – metformin. The dose was calculated taking into account the level of the glycemic profile. The treatment also included omeprazole 20 mg twice a day and actovegin 200 mg twice a day.

The second group consisted of 23 patients of the same age of 19-43 years (mean age 34 ± 0.56 years) and gender — 11 men and 12 women – with GERD without comorbidities. Their therapy included omeprazole 20 mg twice a day during 1 month.

The third control group included 20 healthy individuals of the same sex and age.

All studies were conducted in accordance with the Helsinki Declaration, the procedures were approved by the local ethics committee. All patients gave informed consent to participate in the study.

The diagnosis of diabetes mellitus type 2 was determined in accordance with the criteria proposed by WHO experts, including the determination of the glycemic profile, as well as the study of carbohydrate metabolism compensation for the level of glycated hemoglobin HbA1c using affinity chromatography according to the ICD-10 classification.

The diagnosis of GERD was determined ac-

cording to the Montreal Consensus (2006) taking into account the clinical picture and fibro-gastroduodenoscopy data (FGDS), and ICD-10 classification. With FGDS in all patients of both groups first and second, edema and hyperemia of the esophageal mucosa were detected. So both groups of patients were homogeneous and practically did not differ from each other by sex, age and clinical picture.

The exclusion criteria were: the presence of other diseases of internal organs and the neuroendocrine system, as well as the patient's refusal to participate in the study.

The average indices of 20 healthy individuals of the same age and gender were adopted as the norms.

The duration of gastroesophageal reflux disease in both groups did not exceed 5 years, the severity of symptoms was moderate, signs of Barrett's esophagus or atrophy of the esophagus and stomach mucosa were not detected during FGDS.

The survey program included: determining the degree of carbohydrate metabolism compensation by the level of blood glucose and glycosylated hemoglobin HbA1c by the chromatographic method; state of aggression factor – by the level of pH-metry in the body and antrum of the stomach.

For the evaluation of gastric secretion we used the daily pH-metry, conducted by the Gastroscan-24 apparatus (Russia) using the standard method, since this method allows to measure the pH directly in the esophagus and stomach, as well as intragastric pH-metry with antisemic-colomel electrodes (antral and corpus) on the ICZH-2 apparatus (made in Ukraine) using the standard procedure, since this intragastric pH-metry allows to measure pH directly in the stomach during the basal period, with continuous registration of pH changes in different parts of the stomach and esophagus. Also, all patients underwent an ultrasound investigation with water load, which determined width of the lower third of the esophagus, diameter of the diaphragmatic opening, thickness of the esophagus wall and duration of gastroesophageal reflux (about the time of fluid flowing from the stomach cavity into the esophagus) on the ULTIMA pro-30 device (made in Ukraine).

Indices of oxidative stress were assessed by the diameter of the celiac trunk and blood flow velocity in it, since the protective function of the esoph-

ageal mucosa is provided by normal regeneration of the epithelium with an adequate state of regional blood flow. The study of regional blood flow was carried out using ultrasound, performed on the apparatus ALOKA SSD-750 (made in Japan) and ULTIMA pro-30 (made in Ukraine).

Psychosomatic disorders and quality of life of the patients were estimated by conducting a survey using unified questionnaires: New effective depression scale [Salokangas, RK et al., 1994], Clinical anxiety scale [Snaith RP et al.1982]. Patients were also surveyed with GEDR-Q questionnaires.

Statistical processing of the data was performed using Windows program Statistica 6.0. Comparison of indices in groups was carried out by the method of parametric (t - Student's criterion) statistics.

The relation between the indices in the groups was assessed using the Pearson correlation analysis (r - is the correlation index). For all types of analysis of statistical significance differences were considered at $p < 0.05$.

The work was performed in accordance with the research work of the Department of Therapy, Rheumatology and Clinical Pharmacology of Kharkov Medical Academy of Postgraduate Education: "Pathogenetic formation mechanisms of comorbid pathology in students suffering from GERD and their correction" (state registration No. 1010U002441).

RESULTS

In the process of the research we established that in patients with GERD with concomitant diabetes mellitus there was a clear tendency towards stabilization of the glycemic profile. In patients of both groups, episodes of heartburn, frequency and intensity of belching, and dyspeptic phenomena decreased.

Moreover, in patients of the first group who received additional actovegin, these periods were shorter by 1-2 days, and on average were 5.4 ± 0.63 days, while in patients of the second group who received only standard therapy, these periods of the onset of clinical remission were extended to 8.3 ± 0.76 days and were statistically significantly longer ($p < 0.05$) than in patients of the main group.

At the same time, we found that, after a 4-week course of therapy, oxidative stress levels in patients of both treatment groups decreased.

In particular, diameter of the celiac trunk increased,

and blood flow velocity in it improved. However, in patients of the main group suffering from GERD with concomitant diabetes mellitus type 2, the diameter of the celiac trunk did not increase and was 0.65 ± 0.05 cm, and the blood flow velocity in it increased from 7.12 ± 0.42 to 7.96 ± 0.75 cm/sec.

While in patients of the second control group with isolated GERD, the dynamics of blood flow in the celiac trunk were significantly intensive, and the diameter of the celiac trunk increased from 0.67 ± 0.03 cm to 0.68 ± 0.06 cm, and the blood flow velocity on average increased from 9.36 ± 0.74 cm/sec to 10.45 ± 0.96 cm/sec ($p > 0.05$). However, on average, after treatment these indices remained below the norm ($p < 0.05$) (table 1).

In patients of both groups on the background of a 4-week treatment course, the acidity of gastric juice decreased. In particular, in the group of patients with isolated GERD, the pH values increased on average from 1.41 ± 0.17 to 1.62 ± 0.25 and

almost came close to those of the control group (1.67 ± 0.3) ($p < 0.05$). In patients with GERD with concomitant diabetes mellitus, there was also a tendency to a decrease in gastric acidity in the body and antrum of the stomach.

In patients of both groups, on the background of a 4-week treatment course, gastrography performance improved. In particular, in the group of patients with isolated GERD, the number of maxima decreased from 5.33 to 4.98, and the average amplitude decreased from 334.5 to 267, and the degree of arrhythmia decreased from 1.21 to 0.97. In patients with GERD with concomitant diabetes mellitus there also was a tendency to normalizing gastrography indices — the number of maxima decreased from 5.29 to 4.95, the average amplitude decreased from 314.08 to 264.44, and the degree of arrhythmia decreased from 1.28 to 1.00 (table 1).

Also, in patients of both groups on the background of a 4-week treatment course, there was a

TABLE 1.

Dynamics of blood flow indices in patients and Indices of gastrography in patients with isolated GERD and GERD with concomitant diabetes mellitus

Indices		Treatment groups of patients with concomitant GERD			Norm	p
		First group	Second group	Control		
Dynamics of blood flow indices in patients						
Diameter of the celiac trunk, <i>cm</i>	Before treatment	0.65 ± 0.05	0.67 ± 0.03	0.97 ± 0.35	0.93 ± 0.07	
	After treatment	0.65 ± 0.05	0.68 ± 0.06			p2 <0.001
	p	p1 <0.001	p1 <0.05			p3> 0.05
Blood flow velocity in the celiac trunk, <i>cm / sec</i>	Before treatment	7.12 ± 0.42	9.36 ± 0.74	14.50 ± 0.82	13.5 ± 0.92	
	After treatment	7.96 ± 0.75	10.45 ± 0.96			p2 <0.001
	p	p1 <0.001	p1 <0.05			p3> 0.05
Indices of gastrography in patients						
Number of maxima	Before treatment	5.33	5.29	4.08	3.6-4.8	
	After treatment	4.98	4.95			p ₂ <0.001
	p	p ₁ <0.001	p ₁ <0.05			p ₃ >0.05
Average amplitude	Before treatment	334.5	314.08	171.43	100-250	
	After treatment	267.0	264.44			p ₂ <0.001
	p	p ₁ <0.001	p ₁ <0.05			p ₃ >0.05
Degree of arrhythmia	Before treatment	0.97	1.28	0.68	<0.8	
	After treatment	1.21	1.00			p ₂ <0.001
	p	p ₁ <0.001	p ₁ <0.05			p ₃ >0.05

Notes:

p_1 – degree of reliability of the difference data before and after treatment;

p_2 – degree of reliability of the difference between the data of patients of the first group after treatment and the norm;

p_3 – degree of reliability of the difference between the data of patients of the second group after treatment and the norm.

TABLE 2.

Ultrasound indices of the lower third of the esophagus with water load in patients with isolated GERD and GERD with concomitant diabetes mellitus

Indices		Treatment groups of patients with concomitant GERD			p
		First group	Second group	Control	
Width of lumen of esophagus (<i>mm</i>)					
3 minutes after water load	Before treatment	27.43	29.34		1
	After treatment	24.00	25.77	22.78	p ₂ <0.00
	p	p ₁ <0.001	p ₁ <0.05		p ₃ >0.05
5 minutes after water load	Before treatment	27.25	29.16		
	After treatment	23.81	25.57	22.63	p ₂ <0.001
	p	p ₁ <0.001	p ₁ <0.001		p ₃ >0.05
10 minutes after water load	Before treatment	27.03	29.00		
	After treatment	23.60	25.39	22.70	p ₂ <0.001
	p	p ₁ <0.001	p ₁ <0.05		p ₃ >0.05
15 minutes after water load	Before treatment	26.82	28.78		
	After treatment	23.39	25.17	22.30	p ₂ <0.001
	p	p ₁ <0.001	p ₁ <0.001		p ₃ >0.05
Diameter of esophageal opening of diaphragm (<i>mm</i>)					
3 minutes after water load	Before treatment	18.17	19.29		
	After treatment	14.28	15.15	14.26	p ₂ <0.001
	p	p ₁ <0.001	p ₁ <0.001		p ₃ >0.05
5 minutes after water load	Before treatment	17.99	18.99		
	After treatment	14.29	14.98	14.17	p ₂ <0.001
	p	p ₁ <0.001	p ₁ <0.05		p ₃ >0.05
10 minutes after water load	Before treatment	17.78	18.81		
	After treatment	13.90	14.81	14.02	p ₂ <0.001
	p	p ₁ <0.001	p ₁ <0.001		p ₃ >0.05
15 minutes after water load	Before treatment	17.56	18.63		
	After treatment	13.69	14.61	13.79	p ₂ <0.001
	p	p ₁ <0.001	p ₁ <0.001		p ₃ >0.05

Notes:

p_1 – degree of reliability of the difference data before and after treatment;

p_2 – degree of reliability of the difference between the data of patients of the first group after treatment and the norm;

p_3 – degree of reliability of the difference between the data of patients of the second group after treatment and the norm.

positive trend in the ultrasound of the lower third of the esophagus with water load. In particular, in the group of patients with isolated GERD the width of the lumen of the esophagus and the diameter of the esophageal opening of the diaphragm were close to normal after treatment. In patients with GERD with concomitant diabetes mellitus, there was also a tendency to a decrease in the width of the esophageal lumen and the diameter of the esophageal opening of the diaphragm (table 2).

All patients were surveyed according to the unified questionnaires of the New effective depression scale [Salokangas, RK et al, 1994], Clinical anxiety scale CAS [Snaith RP Et al., 1982]. Patients were also surveyed with GEDR-Q questionnaires.

In patients of both groups on the background of a 4-week treatment course, there was a significant decrease in the scores on the GERD-Q questionnaire, as well as the total score. Thus, in the group of patients with isolated GERD, the average score

before treatment was 7.22, and after treatment – 3.80. In the second group, positive dynamics were also observed on the background of the treatment – 11.96 before and 4.11 after the treatment. The average score of the control group was 0.14.

In patients of both groups on the background of a 4-week treatment course, there was a significant decrease in the average amount of points in the new effective depression scale, as well as in individual questions of the questionnaire. In patients with isolated GERD, the depression score before treatment was 10.08, which corresponded to the state of mild depression, after treatment – 4.08, which corresponded to the norm. In patients of the second group the average score before treatment was 12.03, which indicated a more evident depression in patients, after treatment – 3.01, which corresponded to the norm. The average score of the control group was 0.05.

In patients of both groups on the background of a 4-week treatment course, there was a significant decrease in the amount of points in the clinical anxiety scale CAS, as well as in individual questions of the questionnaire. In patients with isolated GERD the anxiety level before treatment was 6.96 points, after the treatment – 3.68 points. In patients suffering from GERD with concomitant diabetes mellitus type 2, the anxiety level before treatment was 7.93 points, after treatment – 3.46 points.

Moreover, in 5 patients of the group of patients suffering from GERD with concomitant DM type 2 after a 4-week treatment course blood sugar levels increased periodically, though slightly, and this increase was accompanied with heartburn and acid regurgitation, which was not present in patients of the group suffering from isolated GERD.

The findings suggest that psychosomatic disorders

are factors that not only make the course of GERD and DM type 2 more difficult, but also take a direct part in the formation of GERD itself in DM type 2.

The latter is carried out by reducing the trophic and absorption functions of the mucous membrane of the esophagus and stomach, disorders of hydrochloric acid production, asynchrony and reduced motility of the esophagus and stomach, that is, those basic factors that underlie the formation of GERD.

The results of our studies also clearly indicate that the additional assigning of actovegin in the general scheme of treatment for patients with DM type 2 with concomitant GERD has an evident positive effect on the reduction of the onset of clinical remission of both DM type 2 and concomitant GERD while simultaneously normalizing level of oxylytic stress (an increase in the diameter of the celiac trunk and an increase in its blood flow velocity).

CONCLUSIONS

It was shown that in patients with GERD with concomitant DM type 2, there are noted evident psychosomatic disorders, first of all due to a significantly higher average score in the depression and anxiety scale, as compared to the control group and patients with isolated GERD.

A close correlation between the severity of psychosomatic disorders, the clinical features, and the severity of motor-secretory disorders was established.

The inclusion of actovegin in the general treatment scheme of patients with GERD and DM contributes to a significant reduction in the recrudescence period of both DM and concomitant GERD, while simultaneously normalizing oxidative stress, motor-secretory disorders and psychosomatic disorders.

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