CHANGES IN CHOLECYSTOKININ LEVEL IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE ON THE BACKGROUND OF TYPE II DIABETES

ZMIANY STĘŻENIA CHOLECYSTOKININY U PACJENTÓW Z CHOROBĄ REFLUKSOWĄ PRZEŁYKU W PRZEBIEGU CUKRZYCY TYPU 2

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ABSTRACT

Introduction: The question of the combination and combined influence of the gastroesophageal reflux disease (GERD) and many other chronic diseases of internal medicine, including diabetes, have not been studied enough.

The aim: To investigate the changes in cholecystokinin (CCK) levels in blood serum of patients with GERD on the background of type II diabetes.

Materials and methods: On the basis of the propaedeutics of internal diseases department of the medical faculty of the SHEI "UzhNU" during the period of 2016 – 2017, 48 patients were examined for type II diabetes with GERD (main group: group I). The comparison group comprised 18 patients with GERD (group II). All of the patients had their blood serum cholecystokinin levels examined with the help of enzyme-linked immunosorbent assay (ELISA) using the test system of the "Peninsula Laboratories" (USA) company.

Results: The gathered data points to an increase of the CCK levels in blood serum in patients with GERD, as compared to the indices of the control group. This being said, we can highlight that in patients with the background of combined pathology, type II diabetes and GERD in particular, the level of CCK exceeds the average by 6 times, whereas in patients with GERD (comparison group) it exceeds only by 2.4 times. Further analysis of the gathered results points out an interesting pattern in the changes of blood serum CCK levels in patients with GERD on the background of type II diabetes depending on the BMI, in particular – the maximal indices were observed in patients with excess body weight.

Conclusions: In patients with GERD an increase of CCK level is observed, as compared to the indices of healthy individuals. The combination of GERD and type II diabetes is accompanied by a more prominent increase of CCK in blood serum, with a correlation between the disorder of the nutritional status and the CCK level had been established, namely – its maximal indices in patients with excess body weight.

KEY WORDS: gastroesophageal reflux disease, type II diabetes, cholecystokinin.

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INTRODUCTION

Diabetes is recognized by the World Health Organization (WHO) as a noninfectious disease and is a serious health and social problem. According to the world statistics, every 13-15 years the number of people with diabetes doubles. In the year 2000 the number of people with diabetes was 175 million, in 2010 – 240 million, and, according to predictions of the International Diabetes Institute (Melbourne, Australia) in 2030 this number will be 300 million people [1]. A similar tendency is also observed in Ukraine. It is worth keeping in mind that type II diabetes comprises 85-90% of all people with diabetes. Therefore, diabetes, and also complications, accompanying diseases, which are connected with diabetes are relevant and large-scale [2].

Diabetes is a special disease on the background of which disorders of metabolism occur, and, as a result, to a certain degree, all organs and systems of the body are affected, including the system of digestive organs (esophagus, stomach, intestines, liver, pancreas). An important role in the development of these organ-lesions is played by metabolic disorders, which are found in patients with diabetes [3]. In 75% of the cases, diabetes is accompanied by disorders of the digestive organs. These are both gastrointestinal changes (dysfunction of the esophagus, gastropathy, inhibition of the voiding function of the stomach, diabetic diarrhea, constipation, fecal incontinence) are all based on diabetic neuropathy [4], as well as conditions, connected with hormonal and metabolic disorder, which is the result of a disordered tissue metabolism.

Gastroesophageal reflux disease (GERD) is one of the most common diseases of the digestive organs. Lately, it has been drawing the attention of scientists and medical practitioners from many countries in the world, which is due to the increase in the frequency of disclosure of the given pathology, the variety of clinical manifestations, which include extraesophageal signs. The variety of symptoms and syndromes leads to a large number of diagnostic mistakes, when GERD is mistaken with stenocardia, pneumonia, anemia, etc. The clinical picture of this chronic disease is pleomorphic with a variety of "masks" of other diseases [5].

Table I. Indicators of anthropometric study in examined patients with type II diabetes and GERD

Indicator	Control group (n=20)	Examined patients with type II diabetes and GERD I group (n=48)	Examined patients with GERD II group (n=18)
BMI, kg/m^2	21,43± 3,22	36,21 ± 4,15 ^	27,3 ± 2,85
WHI, con.units	0,81 ± 0,55	1,22 ± 0,46 ^	0,96 ± 0,35

Note:
The difference between the indicators in patients and the control group is reliable:
^ – p<0,05.

Table II. Distribution of examined patients with type II diabetes and GERD depending on BMI

Indicator	Examined patients with type II diabetes and GERD I group (n=48), %	Examined patients with GERD II group (n=18), %
Normal weight (BMI: 18,0 – 24,9)		55,6 %
Excess weight (BMI: 25,0 – 29,9)	35,7 %	44,4 %
I degree obesity (BMI: 30,0 – 34,9)	39,6 %	
II degree obesity (BMI: 35,0 – 39,9)	22,9 %	

Still, the question of the combination and common influence of GERD and many other chronic diseases of internal medicine, including diabetes, have not studied well enough.

THE AIM

To study the changes in cholecystokinin (CCK) levels in blood serum in patients with GERD on the background of type II diabetes.

Scientific research is a fragment of a state-funded topic of the SHEI "UzhNU" medical faculty department of surgical diseases and propaedeutics of internal diseases № 815 "Mechanisms of complications formation in liver and pancreas diseases, methods of their treatment and preventive measures" (state registration number: 0115U001103).

MATERIALS AND METHODS

On the basis of the SHEI "UzhNU" medical faculty department of surgical diseases and propaedeutics of internal diseases (gastroenterological and endocrinological department of TRCH n.a. A. Novak) during 2016 – 2017, 48 patients with type II diabetes with GERD were studied. The patients with type II diabetes were 26 males (54.2%) and 22 females (45.8%). The average age was 47.9±7.8 years. These patients comprised the main study group (group I).

The comparison group comprised 18 patients with GERD (group II). Of these 11 were males (61.1%) and 7 were women (38.9%). The average age was 48.3±5.7 years. The control group comprised 20 practically healthy individuals (12 males (60.0% and 8 females (40.0%)). The average age was 47.6±5.8 years.

All of the studies were conducted with patient consent, and the methodology of conducting the study complied with the Helsinki declaration of the year 1975 and its revision of the year 1983.

All of the studied patients were subjects to anthropometric, general clinic, laboratory and instrumental methods of investigation. For the verification of the diagnosis, attention was paid to the nature of the complaints, anamnesis of the disease. During the anthropometric investigation the body mass index (BMI), waist circumference (WC), hips circumference (HC) were measured and the waist/hip index (WHI = WC/HC) was calculated.

The diagnosis of type II diabetes has been made according to the recommendations of the International Diabetes Federation (IDF, 2005). The level of severity of type II diabetes has been evaluated according to the level of glycated hemoglobin (HbA1c, %), which was determined by a chromogenic assay on the Sysmex 560 apparatus (Japan) using Siemens reagents.

GERD was diagnosed according to the criteria of the unified clinic protocol (Ministry of Health order №943 from 31.01.2013) taking into account complaints, endoscopic examination data, etc. The patients had esophagogastroduodenoscopy (EGD) conducted with the help of the endoscopic equipment with "Pentax" EPM-3300 video processor using "Pentax" E-2430 elastic fiberscopes GIF-K20. The Helicobacter pylori (HP) disease was diagnosed with the help of rapid urease test (CLO-test) and C^{13}-urea breath testing (C^{13}-UBT) (IZINTA, Hungary). The patients also had daily pH-monitoring (according to prof. V. N. Chernobrovov), ultrasound examination of abdominal cavity organs (HDI-1500 device, USA), electrocardiographic examination.

All of the patients had their blood serum cholecystokinin levels examined with the help of enzyme-linked immunosorbent assay (ELISA) using the test system of the "Peninsula Laboratories" (USA) company.

The analysis and processing of the patients' results were done with the help of a computer program "Statistics" for

Table III. Cholecystokinin level in the blood serum of examined patients

Examined patients	**Cholecystokinin level** (ng / ml)
Control group (n=20)	0,86 ± 0,12
I group: patients with type II diabetes and GERD (n=48)	5,16 ± 0,24 **
II group: patients with GERD (n=18)	2,08 ± 0,11 *

Note:
* p<0,05 the difference between the control group and group II is reliable;
** p<0,01 the difference between the indicators of the control and group I is reliable

Table IV. Change of CCK level in the blood serum of the examined patients depending on BMI indicators

Indicator	**CCK level** (ng/ml)	
	Examined patients with type II diabetes and GERD I group (n=48), %	Examined patients with GERD II group (n=18), %
Normal weight		1,78 ± 0,23
Excess weight	5,89 ± 0,42 *	2,41 ± 0,30
I degree obesity	4,29 ± 0,18 **	
II degree obesity	4,17 ± 0,29 **	

Note: * p<0,01 the difference between the indicators in patients of group I and group II with excess body weight is reliable;
** p<0,05 the difference between the indicators in patients of group I with excess body weight and patients with I degree and II degree obesity is reliable.

Windows v.7.0 *StarSoft Inc., USA) using parametric and non-parametric methods of gathered data evaluation.

RESULTS

In all of our patients with type II diabetes, the disease was diagnosed with an average degree of severity, i.e. the level of glucose in blood fasting did not exceed 8.5 mmol / l, after eating - 10 mmol / l, HbA1c - did not exceed 9%. In all 48 patients with type 2 diabetes, an excessive body weight or obesity of varying degrees was detected while analyzing anthropometric study results, which manifested itself in the increase of BMI, as well as WHI. In patients within a group comparing with GERD, 10 (55.6%) patients had normal body weight, and only 8 (44.4%) of those surveyed were overweight (Table I).

In addition, in patients with type II diabetes and GERD, excess weight was diagnosed in 37.5% of the examined patients, I degree obesity - in 39.6% of the examined patients, II degree obesity - in 22.9% of the examined patients. The distribution of the examined patients is presented in Table II.

EGD in all 48 examined patients with type II diabetes confirmed the diagnosis of GERD (main group), as well as - in all 18 patients of Group II (comparison groups). We have also identified the gastrointestinal hormone in serum, as CCK in the examined patients of both groups and healthy individuals. The results are presented in Table III.

The obtained data indicate an increase in CCK levels in the blood serum of patients with GERD compared with those of the control group. At the same time, attention should be drawn to the fact that patients with a combined pathology, namely type II diabetes and GERD, have a 6-fold increase in HCC levels, while patients with GERD (comparison group) experience only 2.4 times increase. We have analyzed the change in the level of CCK in the examined patients, depending on nutrition status (Table IV).

In patients with GERD (Group II - comparison), the reliable difference between the CCK indicators in normal-weight and overweight patients has not been determined. In case of GERD and type II diabetes combination, CCK levels in patients with excessive body weight was statistically significantly different from that of patients in the comparison group (5,89 ± 0,42 ng/ml in patients of group I, compared with 2,41 ± 0,30 ng/ml in patients of group II - p<0,01).

Further analysis of the obtained results indicates an interesting pattern of changes in the CCK level in the blood serum in patients with GERD on the background of type II diabetes, depending on BMI, namely, the maximum indicators were typical in patients with excessive body weight. In patients of group I with obesity I and II, the difference in CCK indices is not significant.

DISCUSSION

As it is known, the formation of GERD is predetermined by the imbalance between the protection factors (barrier function of the lower esophageal sphincter, effective esophageal clearance, normal resistance of the esophagus mucous membrane) and aggression (hydrochloric acid, pepsin, bile, pancreatic enzymes). Excessive weight and obesity in patients with type II diabetes, on the one hand, may cause the violation in the normal functioning of protective factors (failure of the lower esophageal sphincter), and, on the other hand, metabolic abnormalities in this contingent of patients can also provoke "excessive" influence of aggression factors, which result in GERD formation.

The high level of CCK detected in patients with GERD on the background of type II diabetes proves the violation of the chemical regulation of the digestive system function. The increase in CCK level negatively affects the motor function of the esophagus, which is especially pronounced in patients with excess weight and obesity suffering from type II diabetes. Further research on the role of CCK in the examined patients is necessary to provide a deeper understanding of the digestive disorders formation, including GERD in these patients, in order to develop effective prophylaxis and treatment regimens.

CONCLUSIONS

1. In patients with GERD an increase of CCK level is observed, as compared to the indices of healthy individuals.
2. The combination of GERD and type II diabetes is accompanied by a more prominent increase of CCK in blood serum, with a correlation between the disorder of the nutritional status and the CCK level had been established, namely – its maximal indices in patients with excess body weight.

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