ORIGINAL ARTICLE

CONTENTS

Level of cholecystokinin after cholecystectomy in patients with irritable bowel syndrome and obesity

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ABSTRACT

Aim: To investigate changes in cholecystokinin (CCK) levels after cholecystectomy in patients with IBS and increased on body mass index (BMI).

Materials and Methods: We examined and treated 57 patients. The examined patients were divided into two groups depending on the method of cholecystectomy: group 1 included 35 patients who underwent laparoscopic cholecystectomy (LCE), and group 2 consisted of 22 patients who underwent open cholecystectomy (OCE). The level of CCK was determined in blood serum.

Results: A correlation was established between BMI and the clinical form of IBS, namely, in patients of group 1, overweight correlated with IBS-D ($r=0.86$; $p<0.01$), while in patients of group 2, obesity of the 3rd degree correlated with IBS-constipation (IBS-C) ($r=0.90$; $p<0.01$). A significant increase in the level of CCK in the blood serum of the examined patients with IBS and anorexia was established even before the CE.

Conclusions: In patients with IBS and GSD, an increase in the level of CCK in the blood serum was found, which increases maximally during cholecystectomy, especially its open form. A positive correlation was established between the level of CCK and the form of IBS, namely $r=0.90$; $p<0.01$ for patients with IBS-diarrhoea and $r=0.96$; $p<0.01$ for patients with IBS-constipation after cholecystectomy.

KEY WORDS: gallstone disease, irritable bowel syndrome, cholecystectomy, cholecystokinin, body mass index, obesity

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INTRODUCTION

Gallstone disease (GSD) are a common gastrointestinal disease and one of the main causes of hospitalisation, which is associated with a significant burden on health and the economy. The prevalence and incidence rates are approximately 15.0 % and 0.6 % per year, respectively [1].

Gallstone disease is more common in patients with excess body weight [2]. The main risk factor associated with the development of this disease is central obesity, and given the increasing prevalence of overweight and obesity worldwide, the prevalence of GSD is expected to continue to rise. Gallstone disease has a high medical burden due to its treatment, which is mainly surgical [3].

Obesity is recognised as a major risk factor for gallstone disease, but this disease has also been described in patients who are not obese. Therefore, it should be noted that the development of GSD is determined by a combination of various modifiable risk factors, such as physical inactivity, diet, medication and body mass index (BMI), as well as non-modifiable risk factors, such as age, ethnicity, genetics, gender and number of births. The most common type of stones that form in obese and non-obese patients are cholesterol stones (>90%), which are formed as a result of cholesterol metabolism products and cholesterol oversaturation of bile. However, other processes are also involved in the pathophysiology of this disease [3, 4].

The development of GSD is also associated with an imbalance between the liver, gallbladder and intestine, where cholesterol synthesis occurs. Changes in these processes are caused by an imbalance in the transport of bile lipids, cholesterol esterification enzymes, regulatory signalling pathways, and gallbladder motility [3].

Epidemiological studies have shown that 12–43% of patients with irritable bowel syndrome-diarrhoea (IBS-D) have excessive bile acid excretion, and nearly 25% of patients with IBS-D suffer from bile acid malabsorption [5]. Analysis of bile acid profiles in the faeces of patients with IBS showed that bile acid levels were higher in patients with IBS-D and lower in patients with IBS-constipation (IBS-C) than in healthy control groups

[6]. Therefore, bile acids play an important role in the pathology of IBS [7, 8]. Cholecystectomy has a direct effect on bile acid metabolism [7, 9]. Studies have shown a higher incidence of IBS in patients with cholelithiasis and in those with a history of cholecystectomy [10].

Therefore, research into various biologically active substances that affect gastrointestinal motility in patients with obesity and IBS after cholecystectomy is relevant.

AIM

The aim to investigate changes in cholecystokinin levels after cholecystectomy in patients with IBS and increased BMI.

MATERIALS AND METHODS

We examined and treated 57 patients with GSD who had an increased BMI in combination with various clinical variants of IBS. All patients underwent cholecystectomy (CE) in the surgical department No. 1 of the Municipal Non-Profit Enterprise «St. Martin's Hospital».

Among the examined patients, there were 42 women (73.7%), whose average age was 38.9±5.3 years; there were 15 men (26.3%), whose average age was 42.5±4.4 years. The control group included 20 healthy individuals (15 (75.0%) women and 5 (43.3%) men). The average age of women in the control group was 41.7±5.1 years, and that of men was 39.3±4.7 years.

All examinations were conducted with patient approval (written authorization for relevant diagnostic procedures and therapeutic interventions was secured from every patient and control participant), implementing comprehensive safeguards to maintain confidentiality of collected data. The research approach adhered to the 1975 Helsinki Declaration on Human Rights and its 1983 amendments, the Council of Europe's Convention on Human Rights and Biomedicine, as well as Ukrainian legal requirements.

The exclusion criteria were: age under 18 and over 75; BMI corresponding to normal body weight or reduced body weight; cholangiocellular carcinoma, pancreatic cancer, colon cancer; systemic autoimmune diseases, including primary sclerosing cholangitis; pulmonary tuberculosis; mental illnesses that prevent adequate assessment of the patient's health and signing of informed consent for diagnosis and treatment; pregnancy and lactation.

All examined patients underwent general clinical, anthropometric, instrumental, and laboratory examinations. To confirm the diagnosis, the nature of the complaints and medical history were described in detail.

IBS diagnosis was established according to Rome IV criteria and clinical recommendations from the Ukrainian Gastroenterological Association for irritable bowel syndrome patient management.

The anthropometric assessment involved measuring height, weight, and waist circumference, with subsequent BMI calculation. Based on WHO standards, subjects were classified according to BMI ranges: severe underweight (BMI ≤16.0); underweight (16.0-18.5); normal weight (18.5-24.9); overweight (25.0-29.9); Grade I obesity (30.0-34.9); Grade II obesity (35.0-39.9); and Grade III obesity (BMI ≥40.0).

All participants received abdominal ultrasound scanning following standard protocols, with particular focus on hepatobiliary and biliary tract structures. Measurements of gallbladder and common bile duct dimensions were obtained, along with identification of the presence or absence of gallbladder stones.

The examined patients were divided into two groups depending on the method of cholecystectomy: group 1 included 35 patients who underwent laparoscopic cholecystectomy (LCE), and group 2 consisted of 22 patients who underwent open cholecystectomy (OCE).

The level of cholecystokinin (CCK) was determined in blood serum using an enzyme immunoassay with a test system from „Peninsula Laboratories" (USA).

Patient data analysis and result processing were accomplished using STATISTICA 10.0 statistical software (StatSoft Inc, USA), applying parametric and non-parametric methods for statistical assessment of outcomes.

FRAMEWORK

The study was performed within the framework of the scientific topics "Intra-abdominal hypertension (symptoms, pathogenesis, prevention, treatment) and its impact on the occurrence and development of pathological syndromes and complicated course of surgical diseases" researched by the Department of Surgical Disciplines of State University "Uzhhorod National University".

RESULTS

Before performing CE, the main clinical and anthropometric features of the examined patients were characterized. After analyzing the anthropometric data, patients in both groups were divided according to their BMI (Table 1).

As the results indicate, the vast majority of patients in group 1 who underwent laparoscopic CE were overweight, while among patients in group 2, grade 3

Table 1. Indicators of BMI change in the examined patients

Indicator	Examined patients, Absolute number / %	
	1 group (n= 35)	2 group (n= 22)
Overweight	16 / 45.7 %	_
Obesity – grade 1	10 / 28.6 %	3 / 13.6 %
Obesity – grade 2	9 / 25.7 %	7 / 31.8 %
Obesity – grade 3	_	12 / 54.6 %

Source: compiled by the authors of this study

Table 2. Characteristics of clinical forms of IBS in examined patients

Clinical forms of IBS	Examined patients, Absolute number / %	
	1 group (n= 35)	2 group (n= 22)
IBS-diarrhoea	19 / 54.3 %	5 / 22.7 %
IBS-constipation	9 / 25.7 %	13 / 59.1 %
IBS-mixed	5 / 14.3 %	3 / 13.6 %
IBS-unclassified	2 / 5.7 %	1 / 4.6 %

Source: compiled by the authors of this study

obesity was more common. These arguments served in favor of open HE in patients in group 2.

We also assessed the clinical form of IBS in our patients with GSD against the background of increased BMI (Table 2).

It was found that in group 1 of the examined patients, IBS-D individuals predominated, while in group 2 of patients, IBS-C was more common. A correlation was established between BMI and the clinical form of IBS, namely, in patients of group 1, overweight correlated with IBS-D ($r=0.86$; $p<0.01$), while in patients of group 2, obesity of the 3rd degree correlated with IBS-C ($r=0.90$; $p<0.01$).

The level of CCK in the blood serum of the examined patients was assessed before and after CE (Table 3).

A significant increase in the level of CCK in the blood serum of the examined patients with IBS and anorexia was established even before the CE. As the obtained results indicate, open CE contributes to a more pronounced increase in the level of CCK in these patients (Table 4).

The analysis conducted indicates a relationship between the change in the level of CCK in the blood serum and the clinical form of IBS in the examined patients. At the same time, in patients of group 1, the correlation was established with the predominance of diarrhea, while in patients of group 2 - constipation in the examined patients with IBS and GSD.

Therefore, the study of changes in the level of regulatory gastrointestinal hormone in patients with GSD and IBS may open new perspectives on the development and progression of comorbid pathology.

DISCUSSION

A study by Peng D. et al (2024) highlights the potential increase in the risk of developing IBS after cholecystectomy. The role of many factors in this regard remains unclear, requiring further research to confirm the causal relationship and study the underlying mechanisms [11].

The small intestine hormone CCK is known to be the primary stimulator of gallbladder contraction after a meal. Reduced gallbladder motility may lead to gallstone formation by nucleation of cholesterol into solid cholesterol monohydrate crystals when the cholesterol saturation index in gallbladder bile exceeds the solubility limit. In addition, impaired gallbladder motility has been observed in patients with cholesterol gallstones. These observations have led to the suggestion that reduced plasma CCK levels may contribute to the development of cholelithiasis [12].

On the other hand, Simrén M et al. (2018) found that mucosal and plasma CCK levels were significantly higher in IBS patients than in controls. Abdominal pain was identified as the dominant symptom in IBS patients, and pain scores, pain symptoms, and pain frequency were positively correlated with mucosal and plasma CCK levels [13, 14].

Another study evaluated the sensory impact on serosal and mucosal receptors in IBS (12 patients with IBS underwent a procedure of gradual rectal stretching during infusion of CCK and placebo in random order). Ten other healthy individuals from the control group and ten patients with IBS underwent intermittent stretching during infusion of CCK and placebo in random order. No differences in rectal elasticity during stretching were found between patients with IBS and the control group.

Table 3. Level if CCK in blood serum in examined patients

Examined patients	Level of CCK, ng/ml				
	Before CE	After CE			
		day 1	day 7	day 14	day 21
Control group (n= 35): 0.67±0.04					
1 group (n= 35)	0.98±0.05*	2.86±0.09	2.03±0.07	1.85±0.06	1.44±0.04
2 group (n= 22)	1.05±0.09**	3.41±0.08 +	4.11±0.10 ++	3.46±0.08 ++	2.96±0.07 ++

Note: the difference between the control group and the group examined is significant: * – $p<0.05$; ** – $p<0.01$; the difference between the groups of examined patients is significant: + – $p<0.05$; ++ – $p<0.01$

Source: compiled by the authors of this study

Table 4. Comparison of CCK levels with the clinical variant of IBS in examined patients

Clinical forms of IBS	Level of CCK, ng/ml			
	1 group (n= 35)		2 group (n= 22)	
	Before CE	After CE (day 1)	Before CE	After CE (day 1)
IBS-diarrhoea	r=0.76; p<0.01	r=0.90; p<0.01	_	_
IBS-constipation	_	_	r=0.84; p<0.01	r=0.96; p<0.01

Source: compiled by the authors of this study

CCK did not affect the perception of urge and pain in the control group and patients with IBS. Similar results were obtained during intermittent stretching, but at higher stretching pressures, CCK significantly increased rectal sensitivity in patients with IBS. The authors concluded that infusion of exogenous CCK to plasma levels typically observed in the postprandial state did not affect rectal motor function or sensation during distension, but significantly increased pain sensation in patients with IBS during rapid intermittent distension [15].

Our results also indicate an increase in the level of CCK in patients with IBS, especially in the early stages of the postoperative period in GSD. Therefore, the study of the level of gastrointestinal hormones may open new perspectives for a deeper study of the pathogenetic mechanisms of the course of comorbid pathology.

CONCLUSIONS

1. In patients with IBS and GSD, an increase in the level of CCK in the blood serum was found, which increases maximally during cholecystectomy, especially its open form.
2. A positive correlation was established between the level of CCK and the form of IBS, namely r=0.90; $p<0.01$ for patients with IBS-diarrhoea and r=0.96; $p<0.01$ for patients with IBS-constipation after cholecystectomy.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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