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GHRELIN LEVEL AND TYPES OF EATING BEHAVIOR WHEN COMBINED WITH IRRITABLE BOWEL SYNDROME, ARTERIAL HYPERTENSION AND OBESITY

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Abstract

Introduction. Regulation of gastrointestinal motility and eating behavior is one of the well-known ghrelin's effects. However, its cardioprotective effect, as well as vasodilatory action and participation in arterial pressure regulation, are not sufficiently studied.
Objectives. To study fasting and postprandial ghrelin levels and eating behavior in patients with comorbidities such as irritable bowel syndrome, arterial hypertension, and obesity.
Materials and methods. The study included 24 patients with irritable bowel syndrome, constipation and normal body mass index, 18 patients with arterial hypertension and obesity, and 54 patients with irritable bowel syndrome, constipation, arterial hypertension, and obesity. Blood pressure monitoring was performed in all patients and fasting and postprandial ghrelin levels in blood serum were measured, as well as eating behavior type, using the Dutch Eating Behavior Questionnaire.
Results. Results of 24-hour blood pressure monitoring showed a more significant rise in blood pressure,

Résumé

Le niveau de la ghréline et les types d'habitude alimentaire lors de la combinaison du syndrome de l'intestin irritable, de l'hypertension artérielle et de l'obésité

Contexte. La ghréline régule la motilité du tractus gastro-intestinal, la nature du comportement alimentaire, a un effet cardioprotecteur, augmente la vasodilatation et régule la tension artérielle.
Objectif. Etudier le niveau de la ghréline basale et postprandiale chez les patients présentant une combinaison de l'hypertension, le syndrome du côlon irritable sur le fond de l'obésité et du comportement alimentaire .
Méthodes. L'étude a porté sur 24 patients avec syndrome du côlon irritable, constipation, poids normal, 18 patients avec de l'hypertension de 2-ème degré sur le fond de l'obésité et 54 patients souffrant de troubles concomitants (syndrome du côlon irritable avec constipation sur le fond de l'hypertension et l'obésité I-III).

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as well as a predominance of the non-dipper profile, encountered in 40.0% of patients with the association of irritable bowel syndrome-constipation, arterial hypertension and 2nd degree obesity, and in 70% of patients with 3rd degree obesity. The increased level of postprandial serum ghrelin in patients with this comorbid pathology contributes to the predominance of external and emotional types of eating behavior, which were found in 37.5% and 34.2% of patients with the combination of these pathologies with obesity the 1st degree, 45.0% and 40.0% – with 2nd degree obesity and 60.0% and 40.0% – with 3rd degree obesity.

Conclusions. The studied combined pathology (irritable bowel syndrome with constipation, arterial hypertension, and obesity) is accompanied by higher blood pressure, non-dipper blood pressure profile predominance, increased postprandial ghrelin level and eating disorders.

Keywords: ghrelin, irritable bowel syndrome, arterial hypertension, obesity, comorbidity.

Abbreviations BS-C – irritable bowel syndrome with constipation; AH – arterial hypertension; BMI – body mass index; BP – blood pressure; SBP – systolic blood pressure; DBP – diastolic blood pressure; 24H BP – 24 hour average blood pressure; BPI – 24 hour blood pressure index.

Tous les patients ont subi une surveillance de la pression artérielle ambulatoire, et les niveaux de ghréline postprandiale dans le sérum et la nature du comportement alimentaire ont été mesurés à l'aide d'un questionnaire néerlandais Dutch Eating Behavior Questionnaire.

Résultats. Les résultats de la surveillance quotidienne pendant 24 heures ont montré une augmentation significative de la pression sanguine ainsi qu'une prédominance du profile non-Dipper, rencontrés en 40,0% des patients avec la combinaison entre le syndrome du côlon irritable et la constipation, l'hypertension artérielle et l'obésité de deuxième degré et en 70% des patients avec de l'obésité de troisième degré. Le niveau élevé de la ghréline postprandiale dans le sérum chez les patients atteints du syndrome du côlon irritable avec constipation, hypertension et obésité contribue à la domination des types externes et émotionnels dans le comportement alimentaire .

Conclusions. La pathologie étudiée associée syndrome du côlon irritable avec constipation, hypertension artérielle et obésité) manifeste des taux plus élevés de la pression artérielle, un profil quotidien à prédominance des concentrations non-Dipper, l'augmentation postprandiale de la ghréline et violations du comportement alimentaire.

Mots-clés: ghréline, syndrome du côlon irritable, l'hypertension, l'obésité, comorbidité.

Introduction

Ghrelin is a peptide consisting of 28 amino acids, synthesized by the X/A cells of stomach mucous membrane, and acts as an endogenous ligand for the receptors of secretory growth hormone, affecting food ingestion, energy homeostasis, and gastrointestinal motility[1]. Ghrelin has a cardioprotective effect in cases of ischemia, it also increases vasodilation and regulates arterial pressure[2]. Receptors capable of expressing ghrelin are found in endothelial and smooth muscle cells of blood vessels, as well as in the right atrium and left ventricle's myocardium[3].

Negative correlations were found between plasma ghrelin level, body mass index (BMI) and blood pressure (BP), especially between the latter indicator and des-acyl ghrelin in patients suffering from arterial hypertension[4]. There was detected a baseline ghrelin level decrease in obese patients with arterial hypertension, compared to the healthy ones with a normal BMI, although there was no significant correlation between the level of this hormone and arterial pressure. There was observed a significant increase in ghrelin's concentration after the treatment of patients with cilazapril and its decrease due to the influence of bisoprolol[4]. In the opinion of Tokudome et al, ghrelin may regulate blood pressure through the stimulation of autonomic nervous system[5]. The risk of cardiovascular events is also associated with ghrelin level according to the SCORE assessment system for countries with higher cardiovascular risk, especially at a low peptide level[6].

Ghrelin level also positively correlates with obesity, though this dependence is not gender-specific. Excess body weight serves as a basis for the development of arterial hypertension[7]. Obesity also serves as a background for the development of irritable bowel syndrome with constipation (IBS-C), whose frequency, according to Aasbrenn et al[8], is twice higher in people with excess body weight than in those with normal BMI. Other researchers point to a more frequent combination of IBS-C and obesity, as well[9]. However, it still remains unknown which of the two diseases is primary[10].

There can be often observed a combination of gastrointestinal diseases and primary arterial hypertension, in particular, the combination of the latter and IBS-C, which defines some new clinical features

in the course of both diseases and reduces the effectiveness of their treatment and prognosis[11]. This kind of combination is likely to be caused by substantial incidence of these diseases, their clinical and social significance. Among the common risk factors for both pathologies are genetic factors, nutritional features, changes in gastro-entero-pancreatic functions, increased tone of the sympathetic nervous system, or imbalance of both parts of autonomic nervous system, decreased number and functional activity of ghrelin-producing cells, vasointestinal polypeptide, which plays the role in neuro transmissivity processes and regulation of gastrointestinal functions. All of these mechanisms depend on ghrelin level in one way or another[12,13].

It can be seen from the data above that the ghrelin's effect on the course of irritable bowel syndrome combined with arterial hypertension and obesity has not been adequately studied and certain statements are contradictory.

The objective of our study was to evaluate the basal and postprandial ghrelin levels and the type of eating behavior in patients with irritable bowel syndrome and constipation, arterial hypertension and obesity.

Materials and methods

The group of study included 24 patients with irritable bowel syndrome with constipation (IBS-C) and normal BMI, 18 patients with stage 2 arterial hypertension (AH) and obesity without intestinal function disorders, and 54 patients with comorbid pathology of IBS-C, obesity, and stage 2 AH.

The prospective study took place in the University Clinic of Ivano-Frankivsk National Medical University, Ukraine, between January 2016 – December 2017. All the patients were hospitalized in the clinic. In all the patients, clinical examination, laboratory tests and other paraclinical investigations (electrocardiogram, ultrasound, 24-hour blood pressure monitoring) have been performed. The Roman criteria III were used to establish the diagnosis of IBS-C. The body mass index was determined in all the patients.

The exclusion criteria were uncontrolled AH (malignant), heart failure functional class NYHA III-IV, organic bowel disease (Crohn's disease, ulcerative colitis, cancer), mental illnesses.

24 patients of the group with comorbid pathology were diagnosed with 1st degree obesity (BMI 32.7±0.24 kg/ m^2), 20 patients with 2nd degree obesity (BMI 37.3±0.3 kg/ m^2) and 10 patients with 3rd degree obesity (BMI 42.6±0.5 kg/ m^2). The BMI of patients with IBS-C was 21.7±0.4 kg/m^2, and 34.3±0.7 kg/m^2 in patients with AH and obesity. 18 obese patients with stage 2 AH, without functional bowel disorders, have also been examined. We studied ghrelin level in the blood serum of fasting patients and 1 hour after eating, by immunoassay method, using Ray Biotech Human Ghrelin EIA (USA) sets. At the same time, eating behavior type was studied in all the patients, using DEBQ (Dutch Eating Behavior Questionnaire)[14].

The study protocol was approved by the Ethics Committee of Ivano-Frankivsk National Medical University (the protocol N° 8 of 24.10.2014). All patients signed the informed consent to participate in the study. The study was conducted in accordance with the principles of the Helsinki Declaration of the World Medical Association "Ethical Principles of Medical Research with the Involvement of a Human as a Research Object" dated 01.10.2008, No. 900_005.

24-hour blood pressure (24H-BP) monitoring was carried out with the help of the "Cardiosens AD" device (produced by the National Aerospace University M.Y. Zhukovskyi, Ukraine). The protocol included BP measurements every 15 minutes during daytime (from 6.00 a.m. to 11.00 p.m.) and every 30 minutes during the nighttime period (from 11 p.m. to 6.00 a.m.). The results of the study involved more than 50 qualitative measurements during 24-hours. With the help of the computer program accompanying this device, 24 hours average blood pressure (24H-BP) was calculated; nighttime average blood pressure (nighttime BP); daytime average blood pressure (daytime BP); pressure time index (PTI) – % of measurement results, exceeding the norm > 50%; morning BP rise and 24 hours average blood pressure index (24H BPI). The patients whose nighttime fall of SBP and DBP equaled 10-20% were considered dippers, those with less than 10% nighttime fall – non-dippers, more than 10% – over-dipper, less than 0% – night – peaker.

There were 58.3% women and 41.7% men patients, having IBS-C and normal BMI, and 59.3% women, 40.7% men patients with combined pathology. The stool frequency of patients with combined pathology and 1st degree obesity was 1.9±0.1 acts of defecation per week. Patients with 2nd and 3rd degree obesity had 1.5±0.1 and 1.4±0.2, respectively, acts of bowel defecation per week. Dull or colicative pain in the lateral parts of the abdomen disturbed 66.7% of patients with comorbid pathology and 1st degree obesity, 90.0% of patients with 2nd degree obesity, and 87.5% of 3rd degree obese patients. 54.2% of patients with IBS-C and normal BMI suffered from pain in the lateral parts of the abdomen. The feeling of incomplete defecation was noted by 79.1% of patients with comorbid pathology and 1st degree obesity,

90.0% of patients with 2nd degree obesity, and all patients with 3rd degree obesity.

The results of ghrelin measurements, values of 24H blood pressure monitoring, and questionnaire of patients were processed statistically, using the standard package of Statistica 8.0 program for Windows and the package of statistical functions of the Microsoft Excel program. The reliability of dependent and independent variables was estimated by using the t-criterion of Student, and the difference was considered to be significant at $p<0.05$. A pairwise correlation analysis of basal ghrelin and 24H average systolic blood pressure values was performed, with calculation of Pearson correlation coefficient –r.

Results

The analysis of 24H-BP monitoring results showed the rise of both systolic (SBP) and diastolic (DBP) blood pressure values with the increase of obesity degree in patients with combined pathology (Table 1). The SBP values were 1.3, 1.45 and 1.5 times higher ($p_{1,2,3}<0.05$) in obese patients with IBS-C and AH than in non-obese patients with IBS. The DBP values were also 1.1, 1.2 and 1.3 times higher ($p_{1,2,3}<0,05$), respectively. The bowel function disorders in the form of prolonged constipation also contributed to the rise of 24H-BP values in patients with 2nd and 3rd degree obesity, contrasting to the values of patients with AH and 1st degree obesity, by 11.3-15 mm Hg (SBP) and 10.5 –18.8 mm Hg (DBP), respectively.

The non-dipper BP profile was diagnosed more frequently in obese patients with association of IBS-C and AH, compared to obese patients with AH and without IBS-C, especially if a higher degree of obesity. In particular, the non-dipper profile was observed in 33.7% of patients with combined pathology and 1st degree obesity. The dipper profile was encountered in 8.3% of patients, and night peaker profile in 16.7%. In cases of combined pathology and 2nd degree obesity, the proportion of patients with non-dipper profile increased to 40.0% and night-peaker – up to 30.0%, while dipper and over-dipper profiles were registered in 20.0% and 10.0% of patients. In patients with IBS-C, AH and 3rd degree obesity, the non-dipper profile was encountered in 70.0% of cases, while night-peaker was observed in 10.0% and dipper – only in 20%. At the same time, in patients with 2nd stage AH without functional bowel disorder, the non-dipper, night – peaker, dipper and over-dipper profiles were diagnosed in 27.8%, 11.1%, 44.4 % and 16.7% cases, respectively.

Fasting ghrelin level in non-obese patients with IBS-C equaled 21.69±1.92 pg/mL, decreasing to 17.13±1.29 pg/mL after eating (fasting ghrelin level in healthy people equaled 46.15±4.89 and decreased by 2.7 times after eating, to 6.91±2.96 pg/mL), while SBP and DBP values increased. Patients with AH, IBS-C and 1st, 2nd or 3rd degree obesity had lower fasting ghrelin levels (25.43±2.96, 10.06 ±0.94 and 4.02±0.80 pg/mL, respectively). It was established a correlation between fasting ghrelin level and SBP values in patients with comorbid pathology and obesity ($r = –0,68$, $p<0,01$ in 2nd degree obesity and $r = –0,72$, $p<0,02$ in 3rd degree obesity).

Postprandial ghrelin level in patients with comorbid pathology increased by 1.5, 2.1 and 2.7 times in patients with 1st, 2nd and 3rd degree obesity, respectively (unlike in healthy and non-obese patients with IBS-C and AH).

The analysis of eating behavior type in obese patients with IBS-C and AH showed the predominance of the external and emotional type, revealed in 37.5% and 54.2% of patients with 1st degree obesity; 45.0 and 40.0% of patients with 2nd degree obesity; 60.0 and 40.0% of patients with 3rd degree obesity, respectively. 61% of obese patients with AH had eating behavior disorders, 45.5% of restrictive type, 36.3% of emotional type and 18.2% of external type of behavior. The restrictive type of behavior was dominant in 62.5% of surveyed patients with IBS-C, normal blood pressure and normal BMI.

Table 1. 24 hours blood pressure monitoring values in patients with different types of comorbid pathology

Groups of patients	*Values of 24H blood pressure monitoring*	
	Systolic (mmHg)	*Diastolic (mmHg)*
Patients with IBS-C and normal BMI	101.7±2.4	85.9±2.0
Patients with AH and obesity	136.2±2.5	90.2±2.1
Patients with AH + IBS-C + 1st degree obesity	136.6±2.7*	93.2±1.9*
Patients with AH + IBS-C + 2nd degree obesity	147.5±2.2*#	100.7±2.4*#
Patients with AH + IBS-C + 3rd degree obesity	151.2±3.4*#	109.0±1.7*#

*Legend: * reliable, compared to values in patients with IBS-C and normal BMI; # reliable, compared to AH with obesity and without functional bowel disorders.*

Discussion

The higher values of arterial pressure observed in patients with association of IBS-C and AH are to some extent consistent with the results of Holeski et al[15], showing that blood pressure parameters are also significantly higher in cases of abdominal obesity and arterial hypertension. The inverse relationship between elevated blood pressure and fasting ghrelin level with combined IBS-C, AH and obesity has also been discovered by other researchers[16]. However, in their opinion, this kind of inverse relationship requires further studies. As it is known, ghrelin level in healthy people decreases after eating. Our study' results indicate a rise of ghrelin level by 1.5, 2.2, and 2.7 times in patients with the comorbid pathology described and 1st, 2nd and 3rd degree obesity, respectively. The ghrelin level rise in obese patients after eating causes the loss of postprandial feeling of satiety and stimulates repeated eating of even bigger food portion[17].

The obtained data differ from the results of other authors[18], that established a predominance of the restrictive type of eating behavior in patients with hypertension, especially with its prolonged course. Such divergence can be explained by the fact that these authors investigated patients with hypertension, but without concomitant pathology. Non-rational eating behavior in the form of external and emotional types is likely to lead to energy saving in the body and to favor the occurrence and progression of hypertension[19-20]. On the other hand, an insufficient amount of fiber, vegetables, and fruits in the diet leads to IBS-C[21-23].

Repeated food consumption in such patients usually includes sweet desserts, animal proteins, and does not include any fruit or vegetables, promoting both constipation and alteration of lipid metabolism[24,25]. The established domination of external and emotional types of eating behavior in patients with comorbid pathology is caused by the higher postprandial ghrelin level, which regulates and stimulates the appetite[26].

Buss et al[27] put forward the hypothesis of the association between general plasma ghrelin, types of eating behavior, stress and metabolic processes in cardiovascular system. This is proved by the fact that in women with excess body weight, ghrelin level is positively correlated with the consumption of calories, increasing the craving for high-caloric food, as well as with systolic blood pressure, insulin resistance, and heart rate[28-29].

Conclusions

The combination of irritable bowel syndrome and arterial hypertension with different degrees of obesity leads to a significant systolic and diastolic blood pressure rise and higher risk for the non-dipper BP profile compared to patients with arterial hypertension and obesity.

Our study revealed an inverse proportional relationship between basal ghrelin level and blood pressure values. Postprandial ghrelin level rise is accompanied by eating behavior disorders (higher number of patients with emotional and external types) and is likely to maintain the excess body weight and contribute to elevated blood pressure.

Compliance with Ethics Requirements:

„The authors declare no conflict of interest regarding this article"

„The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study"

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