ORIGINAL ARTICLE

CHANGES IN PROSTAGLANDIN LEVELS IN BLOOD SERUM OF PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE ON THE BACKGROUND OF THE OSTEOCHONDROSIS OF THE SPINE AND OBESITY

DOI: 10.36740/WLek202210134

Yelyzaveta S. Sirchak, Oleksandr O. Boldizhar, Yaroslav F. Filak, Olena V. Ustych, Velentina Yu. Koval, Vasyl Ye. Barani, Inna S. Borisova
UZHHOROD NATIONAL UNIVERSITY, UZHHOROD, UKRAINE

ABSTRACT

The aim: To study the features of changes in the level of prostaglandins (I_2 and $F_{2\alpha}$) in blood serum of patients GERD on the background of OH of the cervical and thoracic spine and obesity.

Materials and methods: The examined patients included 56 patients with GERD and OH of the cervical and thoracic spine. All patients had their blood serum prostaglandin (Pg) $F_{2\alpha}$ and 6-keto prostaglandin $F_{1\alpha}$ (blood prostacyclin – Pg I_2) levels examined using the method of immunoassay analysis.

Results: In all patients with GERD and OH an excessive body weight or obesity of varying degrees was found while analyzing anthropometric study results. The determination of prostaglandin $F_{2\alpha}$ and prostacyclin (Pg I_2) levels in blood serum in patients with GERD and OH and healthy individuals was performed. A more pronounced increase of Pg I_2 and Pg $F_{2\alpha}$ in blood serum in patients with GERD and OH with III degree obese was found and the smallest concentration of prostaglandines in blood serum was diagnosed in patients with excessive weight ($p<0.05$).

Conclusions: 1. In patients with GERD and OH, an increase in levels of prostaglandins $F_{2\alpha}$ and I_2 in blood serum has been established. 2. The relationship between the duration of excess body weigh, obesity and the dynamics of the level of prostaglandin Pg I_2 and $F_{2\alpha}$ in blood serum in patients with GERD on the background of OH has been established.

KEY WORDS: gastroesophageal reflux disease, osteochondrosis, prostaglandin(I_2, prostaglandin $F_{2\alpha}$

Wiad Lek. 2022;75(10):2497-2500

INTRODUCTION

The increased interest towards gastro-esophageal reflux disease (GERD) is caused by the high prevalence of this disease with a permanent upward trend (~5% annual increase). Moreover, in some cases, extra-esophageal manifestations may come to the foreground in clinical findings. In addition, in 25% of cases, GERD occurs along with extra-esophageal symptoms: bronchopulmonary, cardiac, otorhinolaryngopharyngeal, and dental [1-4].

As it is known, the etiopathogenesis of GERD is based on the imbalance between the protection factors (barrier function of the lower esophageal sphincter, effective esophageal clearance, normal resistance of the esophagus mucosa) and aggression (hydrochloric acid, pepsin, bile, pancreatic enzymes, etc.) [5-7]. Many hormones and biologically active substances (BAS) in the body (estrogen, progesterone, prostaglandins, somatostatin, cholecystokinin, etc.) affect the tension of the lower esophageal sphincter [8].

The search for new factors that play a role in the formation of GERD is especially relevant in patients with polymorbid pathology, the treatment of which requires medications that may adversely affect the condition of the mucous membrane of the upper gastrointestinal tract, as well as its functional activity.

Osteochondrosis (OH) of spine is also one of the most common diseases among the adult population, which affects from 40 to 80% of the world's inhabitants. Manifestations of OH are back pain, headaches, which are seen in 25-30% of patients after 30 years old [9, 10]. According to modern recommendations, patients are prescribed non-steroidal anti-inflammatory drugs (NSAIDs) to reduce pain and improve the quality of life in case of the musculoskeletal system damage. Side effects of NSAIDs are very often observed during treatment with this group of drugs. The main negative property of all NSAIDs is a high risk of digestive tract disorders. Thus, dyspepsia is observed in 30-40% of patients receiving NSAIDs, in 10-20% – erosions and ulcers of the stomach and duodenum, in 2-5% – bleeding and perforation. Dyspepsia is the main reason for discontinuation of NSAIDs in more than 50% of cases. Most often, this symptom is noted in patients with a history of digestive tract pathology [11].

Therefore, the study of the clinical course, as well as factors and levels of various biologically active substances that may play an important role in the pathogenetic mechanism of

GERD in patients with combined pathology, including OH, is an extremely relevant problem of modern clinical medicine.

THE AIM

To study the features of changes in the level of prostaglandins (I_2 and $F_{2\alpha}$) in blood serum of patients GERD on the background of OH of the cervical and thoracic spine and obesity.

MATERIALS AND METHODS

At the clinical base of the Department of Internal Diseases Propaedeutics of the Medical Faculty of the SHEI "Uzh-NU" (gastroenterological, endocrinological, neurological department of the KNP "ZOKL named after A. Novak" TRC and patients who were under outpatient observation by a family doctor at their residence place) during 2019-2022 years, 56 patients with GERD and OH of the cervical and thoracic spine were examined. Among the examined patients, there were 32 (57.1%) men, 24 (42.9%) women. The average age was 43.6±4.2 years. The control group included 20 practically healthy people (12 men (60.0%), 8 women (40.0%)). The average age was 44.1±5.2 years.

All studies were performed with the consent of the subjects, and the methodology of their conduct was in accordance with the Helsinki Declaration of Human Rights of 1975 and its revision of 1983, the Convention of the Council of Europe on Human Rights and Biomedicine, and the legislation of Ukraine. All examined patients were subjected to anthropometric, general clinical, laboratory and instrumental methods of examination. 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. According to the obtained data, in compliance to WHO recommendations, patients were distributed according to their BMI in the following way: BMI 16.0 and less corresponded to the expressed deficient body weight; 16.0-18.5 – insufficient body weight; 18.0-24.9 – normal weight; 25.0-29.9 – excessive weight; 30.0-34.9 – I degree obesity; 35,0-39,9 – II degree obesity; 40.0 and more – III degree obesity (morbid obesity).

Osteochondrosis of the cervical and thoracic spine was diagnosed based on physical, general clinical examination methods, as well as the results of computed tomography of the spine.

The diagnosis of GERD was established according to the criteria of the unified clinical protocol (order of the Ministry of Health of Ukraine dated 31.10.2013 № 943) taking into account complaints, endoscopic examination data, etc. To confirm the diagnosis, the examined patients underwent fibroesophagogastroduodenoscopy (FEGDS) using endoscopy equipment Pentax ERM-3300 video processor and flexible fiber endoscopes Pentax E-2430, GIF-K20. Also, 24-hour pH monitoring according to Prof. V.N .Chernobrovy's method was performed.

The Los Angeles (LA) classification (1998) was used for endoscopic assessment of the degree of damage to the esophagus: grade A – single erosion ≤5 mm; grade B – ≥1 erosion> 5 mm long that does not occupy the entire space between 2 adjacent folds of the esophagus; grade C – ≥1 erosion that occupies the entire space between ≥2 folds of the esophagus and ≤75% of the perimeter of the esophagus; grade D – erosions or ulcers occupying ≥75% of the esophageal perimeter [10].

In the examined patients, HP-infection was diagnosed using a rapid urease test (CLO-test) before the comprehensive treatment. The effectiveness of eradication therapy was assessed 4 weeks after treatment using the ^{13}C-urea breath test (^{13}C-UBT) (IZINTA, Hungary).

All patients had their blood serum prostaglandin (Pg) $F_{2\alpha}$ and 6-keto prostaglandin $F_{1\alpha}$ (blood prostacyclin – Pg I_2) levels examined using the method of immunoassay analysis with the help of the test system Enzo Life Sciences, "BCM Diagnostics" (USA).

The analysis and processing of the results of the examination of patients was carried out using the Statistics for Windows v.10.0 computer program (StatSoft Inc, USA) using parametric and non-parametric methods of evaluating the obtained results.

RESULTS

In all patients with GERD and OH an excessive body weight or obesity of varying degrees was found while analyzing anthropometric study results – Table I.

The determination of prostaglandin $F_{2\alpha}$ and prostacyclin (Pg I_2) levels in blood serum in patients with GERD and OH and healthy individuals was performed. The results are presented in Table II.

Increased levels of prostaglandins of examined patients with GERD and OH were established. Attention is called to a more significant increase in Pg I_2 concentration compared with Pg $F_{2\alpha}$, in blood serum.

An estimation of change in prostaglandin levels in the examined patients was performed depending on the violation of BMI (Table III).

A more pronounced increase of Pg I_2 and Pg $F_{2\alpha}$ in blood serum in patients with GERD and OH with III degree obese was found and the smallest concentration of prostaglandines in blood serum was diagnosed in patients with excessive weight ($p<0.05$).

The obtained data indicate that in case of the combination of several pathological states (GERD, OH, increased BMI), a more pronounced increase in the concentration of prostacyclin is observed.

DISCUSSION

We have not found any scientific works that discuss the role of prostaglandins in patients with the combination of GERD, OH and obesity. Takeuchi K. (2010) highlights the role of prostaglandins, predominantly type E, in GERD and chronic gastritis. At the same time, the authors have proven that Pg E_2 protects the esophagus from acid reflux and provides cytoprotection of the stomach [12].

Table I. Distribution of examined patients according to their BMI

Indicator	Examined patients with GERD and OH (n=56)
BMI, kg/m^2	38.96 ± 4.61
Excessive body weight	30. 3 %
I degree obesity	42.9 %
II degree obesity	21.4 %
III degree obesity	5.4 %

Table II. Levels of prostaglandins in blood serum in the examined patients

Examined patients	Indicator	
	Pg I_2 (pg/ml)	Pg $F_{2\alpha}$ (pg/ml)
Control group (n=20)	51.14 ± 3.23	72.25 ± 2.31
Patients with GERD and OH (n=56)	141.22 ± 5.64*	136.22 ± 4.71*

Note: the difference in indicators between the control group and groups of patients with GERD and OH - * $p<0.01$.

Table III. Change in prostaglandin levels in the examined patients depending on nutrition status

Indicator	Examined patients with with GERD and OH I group (n=56)	
	Pg I_2 (pg/ml)	Pg $F_{2\alpha}$ (pg/ml)
Excessive weight	116.23 ± 8.98	104.12 ± 6.15
I degree obesity	132.14 ± 4.16	128.15 ± 4.12
II degree obesity	148.20 ± 7.75^	141.17 ± 8.91^
III degree obesity	152.23 ± 10.15*	162.00 ± 5.11*

Note: ^ $p<0.05$ – the difference in the indicators in patients with excessive weight and II degree obesity is reliable; * $p<0.05$ – the difference in the indicators in patients with excessive weight and III degree obesity is reliable.

We have studied the levels of class I_2 and $F_{2\alpha}$ prostaglandins, which have a divergent effect on the body, namely: Pg I_2 exhibits a relaxing effect, while prostaglandin $F_{2\alpha}$, on the contrary, has constrictive properties. According to the results of our study, increased levels of blood serum prostaglandins $F_{2\alpha}$ and I_2 in patients with GERD and OH of spine were determined. When characterizing the change in prostaglandins by classes, a predominant increase in prostacyclin in the blood serum was detected. Prevalence of prostaglandin, which has a relaxing effect on smooth muscles, including the digestive system, suggests its effect on the formation of GERD, especially on the background of OH. It is plausible that the loss of the physiological balance between prostaglandins, which have opposite effects on the internal organs on the background of metabolic disorders in obesity, may be considered as one of the components affecting the lower esophageal sphincter, leading to its relaxation and the formation of GERD manifestations. The obtained data require further investigation and analysis of changes in prostaglandins in OH of spine and their probable effect on the formation of GERD in these patients.

CONCLUSIONS

1. In patients with GERD and OH, an increase in levels of prostaglandins F2α and I2 in blood serum has been established.
2. The relationship between the duration of excess body weigh, obesity and the dynamics of the level of prostaglandin Pg I_2 and $F_{2\alpha}$ in blood serum in patients with GERD on the background of OH has been established.

REFERENCES

1. Konykova L.A., Konykov A.V. Gastroesophagealnaya refluxnaya bolezny: vnepischevodniye proyavleniya [Gastroesophageal reflux disease: extra-esophageal manifestations]. Medical Bulletin of the MIA. 2016;1 (80): 47-51. (in Russian).
2. Ivashkin V.T., Truhmanov A.S. Evolyucia predstavlenij o roli naruseniy dvigatelnoy funkcii pichevoda v pathogeneze gastroesophagealnoy refluxnoy bolezni [The evolution of ideas about the role of disorders of the motor function of the esophagus in the pathogenesis of gastroesophageal reflux disease]. Russian Journal of Gastroenterology, Hepatology, Coloproctology 2010;20 (2): 13-19. (in Russian).
3. Tkach S.M. Diagnostika, I lechenije kislotozavisimoj patologii u bolnich sacharnim diabetom [Diagnosis and treatment of acid-dependent pathology in patients with diabetes mellitus]. Clinical endocrinology and endocrine surgery. 2017:3 (59): 21-27. (in Russian)
4. Kliaritskaia I.L., Moshko Y.A., Iskova I.A., Kryvoy V.V. GERB i ozhirenije, osobennosti klinicheskogo techenija [GERD and obesity, clinical features]. Crimean therapeutic journal. 2017; 2: 45-49. (in Russian)
5. 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. doi: 10.1038/ajg.2012.444.

6. Frazzoni M., Manta R., Mirante V.G. et al. Esophageal chemical clearance is impaired in gastro-esophageal reflux disease – A 24 h impedance-pH monitoring assessment. Neurogastroenterol. Motil. 2013;25: 399-406. e295. doi: 10.1111/nmo.12080.
7. Dragomiretskaya N.V. Ways to improve GERD therapy. Health of Ukraine. Thematic number. Gastroenterology. Hepatology. Coloproctology 2016;4(42):21. (in Russian)
8. Kusnir I.E. GERD in obese patients: pathophysiological mechanisms of development, features of the course and approaches to therapy. Health of Ukraine. Thematic number. Gastroenterology. Hepatology. Coloproctology. 2013; 3 (29): 70-71. (in Russian)
9. Keenan O.J., Turner P.G., Yeates D., Goldacre M.J. Epidemiology of hospitalized osteochondritis dissecans in young people: incidence, geographical variation and trends over time in England from 2002 to 2010. Knee. 2014;21 (2): 497-500.
10. Marchenko O.K., Manzhulovskij V.N., Deshovij Ye.G. Kompleksnaya fizicheskaya reabilitatsiya pri osteokhondroze grudnogo otdela pozvonochnika s narusheniyem osanki [Complex physical rehabilitation for osteochondrosis of the thoracic spine with impaired posture]. Sportivna meditsina – Sports medicine 2. 2013, 126p. (in Russian).
11. Babinets L.S., Halabitska I.M. Evaluation of pancreatotropic and joint efficiency of intracellular systemic enzyme in osteoarthritis. Family medicine, 5-6. 2020;(91-92): 66-69. (in Ukrainian).
12. Takeuchi K. Prostaglandin EP receptors and their roles in mucosal protection and ulcer healing in the gastrointestinal tract. Adv. Clin. Chem. 2010;51: 121-44.

The study was performed within the framework of the scientific topics "Polymorbid Pathology of Digestive System Diseases, Features of Pathogenesis and the Possibility of Correction" (state registration number 0118U004365) researched by the Department of Propedeutics of Internal Diseases of State University "Uzhhorod National University" and "Clinical and Pathogenetic Features of Polymorbid Diseases in the Digestive System and Development of Differentiated Therapy Scheme in the Conditions of the COVID-19 Pandemic" (state registration number 0121U110177).

ORCID and contributionship:
Yelyzaveta S. Sirchak: 0000-0001-6738-0843 [A, F]
Oleksandr O. Boldizhar: 0000-0002-9553-5782 [B]
Yaroslav F. Filak: 0000-0002-7510-263X [B, D, E]
Olena V. Ustych: 0000-0002-4360-8601X [B]
Velentina Yu. Koval: 0000-0001-8423-9534 [B, C]
Vasyl Ye. Barani: 0000-0002-2616-2230 [C, E]
Inna S. Borisova: 0000-0003-4254-6004 [E]

Conflict of interest:
The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Yelyzaveta S. Sirchak
Uzhhorod national university
1 Narodna sqr., 88000 Uzhhorod, Ukraine
tel: +380509761794
e-mail: sirchakliza777@gmail.com

Received: 17.04.2022
Accepted: 08.09.2022

A – Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article