PROSTAGLANDIN DYNAMICS IN PATIENTS WITH CHRONIC KIDNEY DISEASE AND LESIONS OF THE STOMACH MUCOSA

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Introduction. Today it is known that prostaglandins (PG), including PgE2,PgI2, are able to contribute to the rehabilitation of damaged gastric mucosa (GM) that positively influence on the morphological changes, regression of rebuilding changes, the proliferative activity of epithelial cells and the depth of occurrence of Helicobacter pylori (HP)-simultaneously affect several elements of pathogenesis [1,6,7,12,13].

All processes in the stomach ,which are under the influence of Hp ,are systemic in nature and show a direct pathogenic effect on the kidneys in patients with chronic kidney disease (CKD).

The damaging effects of aggressive systemic factors increase and cause acceleration of progression of CKD with the increasing degree of it. [4.13].

The increase of the excretion of inflammatory mediators is observed in patients with CKD with the presence of erosive and ulcerative lesions of the stomach (EULS)- renal prostanoids (prostaglandins and thromboxanes), arachidonic acid, histamine, bradykinin and others. Some of them, especially PgE2, enhances mucus in GM and some other effects that are widely discussed in the literature and cause conflicting conclusions [1,3,7,8,16].

A respond of mucous membrane of renal pelvises and cups on pathogenic properties of microorganisms, as during colonization of gastric mucosa with Hp, are characterized by activation of proinflammatory cytokines of blood (precursor of arachidonic acid), macrophages (mast cells or labrocytes), lymphocytes, neutrophils and monocytes, which promotes the expression of inflammatory mediators - renal prostanoids (prostaglandins including prostaglandin E2 and thromboxane), arachidonic acid [9,14,15].

Renal prostanoids (prostaglandins and thromboxanes) are involved in regulating renal hemodynamics, tubular transport of ions and renin secretion. In addition, they can be active participants as mediators of inflammation by the action of damaging factors (inflammatory substances, toxic changes at CKD) [2,3,4,9].

Two forms of cyclooxygenase(COG)are expressed in the kidneys:

1. Structural (COG - 1).

2. Induced (COG - 2).

COG - 1 is synthesized in the body constantly under normal conditions and provides production of prostoglandin PgE2, PgI2 that are improving the protective properties of gastric mucosa [7,9]. PgE2 increases the secretion of mucous helium and bicarbonates, inhibits secretion of hydrochloric acid. PgI2 supports optimal level of hemodynamics in the microcirculation, normalizes the state of labrocytes and lysosomes membranes, regulates the function of vascular epithelium, activates cell proliferation in normal processes of regeneration and inhibits the production of free radicals and enzymes by neutrophils.

COG - 2 is produced during the inflammation in the large quantities. It provides a synthesis of proinflammatory prostaglandins, causing its characteristic features - vasospasm of microcirculation, exudation in the inflammatory focus, pain and fever [5,8,9,10].

Consequently, there is a close relationship between the development of erosive and ulcerative gastroduodenal lesions and progression of CKD. It should be noted that the progression of both pathological processes are interrelated, Hp infection causes a number of systemic effects (activation of proinflammatory cytokines, apoptosis, selection of biologically active substances that enhance ischemia, hypoxia of the affected tissue, activation of the hemostatic platelet level) that detect pathogenic effects on kidneys and progression of CKD. On the other hand, kidney disease, especially in reducing their function, are reduced the processes of COX-1 activation, resulting in reduced production of prostaglandins, which are important to support both local and systemic hemodynamics in normal and, in particular, take part in protecting the stomach from aggression factors (increased mucus, bicarbonate excretion, etc.). [5,10,13,16].

The aim was to study the dynamics of the systemic and local content of prostaglandin E2 in patients with chronic kidney disease stage II and III, due to a long course of chronic recurrent pyelonephritis with the presence erosive and ulcerative lesions of the stomach under the influence of mukohen.

Materials and Methods

The study has involved 105 patients with CKD Stage II-III, due to a long course of chronic pyelonephritis with the presence Hp-negative (and with the previous eradication of the pathogen) erosive and ulcerative lesions of the stomach with preserved secretory function and patients with EULS without CKD. Among the examined patients,there were 56 men and 49 women with the age from 27 to 60 years. There were also examined 20 healthy individuals of the similar age. The control group was consisted of patients with the presence of CKD II-III without EULS (29 people). Patients were divided into 2 groups: the first group was consisted of 39 patients with EUKS and without CKD; II group - 37 patients with CKD stage II-III with the presence EULS before treatment. Patients were examined before the treatment and after 3 weeks of treatment with mukohen. Mucohen was taken by one tablet 3 times a day 30 minutes before the meal.

The clinical picture, radiological and endoscopic data, results histopathological study of biopsies of the gastric mucosa were taken into concideration during the verification of diagnosis EULS. Patients with CKD were conducted examination and treatment according to clinical protocols of renal patients, were examined glomerular filtration rate (GFR) and daily level of proteinuria.

The level of indicators PG E 2 was performed in serum, urine, gastric juice of patients and assessed by immunoenzymatic method using commercial test - kits (Kit) company "Assay Designs, Inc.", USA. The serum samples were centrifuged at 1500 rev. / min. for 10-15 minutes. Separated serum was taken and used in immunoferment analyzer ("Picon" number 01391409).

The data processed statistically using Student criterion. All indicators were presented as mean values from their mean error (M ± m). Significant was considered difference at $p < 0.05$.

Results and Discussion

As a result of the study it was revealed that in patients of the first group, decreased the levels of PgE2 in serum (720,02 ± 14,23 pg / ml), which was credible compared with corresponding indicators in a group of healthy individuals (12.01 pg 1050.10 + / ml) ($p < 0.05$) and control group (1028.33 + 11.04 pg / ml). Dynamics of indicators of second group was similar and during its assessment it was discovered a credible reduction of PgE2 in serum (respectively 625.44 + 13.21 pg / mL) compared with healthy indicators data ($p < 0.05$) and control group ($p < 0.05$) and patients of the first group ($p < 0.05$). PgE2 content in blood of patients of the control group did not differ from the norm ($p > 0.05$). Due to the conducted treatment with inclusion of mkohen in patients of groups I and II, levels of PgE2 in blood significantly increased in comparison with the corresponding data before treatment (I group - 839.47 + 12.34 pg / ml and group II - 10.32 pg 898.04 + / ml), where in both cases ($p < 0.05$).

In evaluating the indicators of PgE2 in gastric juice was found it's probable decline in patients of I and II groups before treatment (respectively 7506.13 and 8927.41 + 13.21 + 13.26 pg / ml) ($p < 0.05$) compared with norm and control (respectively 13400,14+ 13,411.17 + 3.12 and 12.35 pg / ml). This indicates that the local deficit of PgE2 accompanies EULS can't be corrected without the use mukohen. As a result of a treatment was noted a significant increase of PgE2 in gastric juice in I and II groups after 3 weeks of treatment (11,256.44 + 12,55ph / ml and 11134,05 ± 12,15 pg / ml), which was credible compared with indicators of patients before treatment ($p < 0.05$), but still far from the norm.

Results of the study of PgE2 content in the urine of patients showed a possible decline of this indicator in patients of all groups (I group - 480.19 + 12.38; group II - 13.51 and 501.16; control group - 643.41 + 13.22 pg / mL) versus healthy (814,02+ 13.18 pg / ml) ($p < 0.05$). But it should be noted that after treatment with the inclusion of mukohen, PgE2 content in the urine of patients increased (respectively in the above mentioned groups - 698.14 + 12,11ph / ml; 585,79 ± 9,87 pg / ml and 732,34 ± 10,99 pg / ml), which was credible compared to the relevant data of these groups of patients studied before adding mukohen treatment ($p < 0.05$). In the studied patients of II group after 3 weeks of treatment were determined positive changes in the gastro-intestinal tract (from 56, 8 + 3.12 ml / min. 69,1+ 4 to 87 ml / min.) as well as reducing the daily proteinuria (from 1.59 + 0.12 to 0.83 + 0.10 ml / min.) ($p < 0.05$). This demonstrates absence of negative impact of mukohen on renal function.

When conducting the study of linear correlations between the studied parameters was revealed a direct correlation dependence between the content of PgE2 in blood and GFR ($r = 0,58$) ($p < 0.05$), which proves that with decreasing og GFR due to progression of CKD, reduces production of local PgE2 by kidneys, which reduces its admission to the general bloodstream. In addition, we found a direct correlation between the level of PgE2 of gastric juice and PgE2 of blood ($r = 0, 67$) ($p < 0.05$). We revealed a strong inverse correlation dependence between indicators of PgE2 of urine and daily proteinuria levels ($r = -0, 78$) ($p < 0.05$). This proves that progressive kidney damage is accompanied by a shortage of general and local PgE2.

Therefore, the study of dynamics of PgE2 content in blood, gastric juice and urine of patients showed that with the presence of EULS, content of local (in gastric juice) and general PgE2 is significantly reduced. Lack of its content in the organism helps to maintain inflammation and worsens local regeneration. In patients with CKD stage II-III in our study was observed an expressed shortage of content of PgE2 of urine and blood serum which also indicates the suppression of local recovery processes in kidneys and in the whole organism. In patients with chronic kidney disease II-III degree due to the presence of morphological (sclerosis) and functional disorders decreases a production of PgE2 by kidneys. Consequently are compounded ischemic changes of kidney vessels, are supported the processes of inflammation, as described above, that is causing the progression of CKD.

In this way, pathological changes with combined CKD stage II-III and EULS have interdependent progressive character and contribute to deepening of

pathological lesions in the stomach and in kidneys. Due to a strong positive effect of mukohen, as shown in our study, which appears on the local (stomach, kidneys) and on a general (blood) levels, due to entering of unchanged drug in into the bloodstream, it can be successfully used in treatment of patients with CKD, combined with erosive lesions of the stomach.

Conclusions

1. In case of EVUSH, a content of local (in gastric juice) and general PgE2 is significantly reduced.
2. In CKD patients stages II-III, is marked an expressed shortage of PgE2 content in urine and blood serum.
3. Pathological changes in combination of CKD stage II-III and EVUSH have interdependent progressive character.
4. The positive effect of mukohen, which manifests itself on the local (stomach, kidneys) and on a general (blood) levels can be successfully used in treatment of patients with CKD, combined with erosive lesions of the stomach.

Literature

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