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DIFFERENTIAL TREATMENT APPROACH LESIONS OF THE GASTROINTESTINAL TRACT PATIENTS WITH CHRONIC KIDNEY DISEASE

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This paper presents thecurrent state of problems concerning the mechanisms of gastric lesions in patients with chronic kidney disease (CKD). Presents the current views of scientists Nephrology and Gastroenterology attherelationship between Helicobacterpylori (HP)-mediated diseases of the stomach and duodenum and progression of chronic kidney disease. The paper studied the dynamics of systemic and local content of prostaglandin E_2 in patients with chronic kidney disease stage II and III, determined by the long course of chronic or recurrent pyelonephritis with the presence of erosive and ulcerative lesions of the stomach and duodenum.
Keywords: chronic kidney disease, chronic pyelonephritis, prostaglandin E_2, erosive and ulcerative lesions of the stomach and duodenum, mukogen.

Formulation of the problem. PgE2, PgI2 are generally recognized be able to contribute to the restoration of the mucous membrane of the stomach (MMS), positively affecting morphological changes, status of peroxide oxidation of lipids, proliferative activity of epithelial cells and depth of Hp. Now this concept is universally recognized [1; 6; 7; 12; 13].

Hp has a systemic effect on all processes in the stomach. This processes have a direct pathogenic effect on the kidneys in patients with chronic kidney disease (CKD). The damaging influence of aggressive factors of systemic action increases with the growth of the degree of CKD. It leads to an acceleration of the progress of the CKD [4; 13].

Patiens with CKD and erosive-ulcerative lesions of the stomach and duodenum have an increase in the allocation of inflammatory mediators such as renal prostanoids (prostaglandins and thromboxanes),derivates of arachidonic acid, histamine and bradykinin etc. Some of them, especially PgE2, contribute to increased mucus secretion in MMS and some other effects. They are widely discussed in the literature and cause controversial conclusions [1; 3; 7; 8; 16].

Pathogenic microorganisms cause same changes in the mucous membrane of the kidney pelvis and cavity as Hp causes in MMS. Macrophages, lymphocytes, neutrophils and monocytes are activated, which causes the formation of inflammatory mediators such as renal prostanoids (prostaglandin E_2 and thromboxanes), derivatives of arachidonic acid [9; 14; 15].

Renal prostanoids (prostaglandins and thromboxanes) are involved in the regulation of renal hemodynamics, tubular transport of ions, as well as renin secretion. Besides they can be active participants, inflammatory mediators under the influence of damaging factors (inflammatory substances, toxic changes in CKD) [2; 3; 4; 9]. Two forms of cyclooxygenases (COG) are expressed in the kidneys:

1) Structural (COX 1)
2) Induced (COX 2)

COX-1 is synthesized in the body constantly under normal conditions and provides products of prostaglandins PgE2, PgI2. It improving the protective properties of the mucous membrane of the stomach [7; 9]. PgE2 increases the secretion of mucus and bicarbonates and suppresses the secretion of hydrochloric acid. PgE2 increases the secretion of mucus and bicarbonates, suppresses the secretion of hydrochloric acid. PgI2 maintains the optimal level of hemodynamics in the microcirculatory system, normalizes the state of the membranes of the labrocytes and lysosomes, regulates the function of the blood vessel epithelium, activates cell proliferation in the regeneration processes and suppresses the production of free radicals and enzymes by neutrophils.

COX-2 is synthesized in inflammation. It provides the synthesis of proinflammatory prostaglandins. Causes characteristic signs of inflammation such as spasm vessels of the microcirculation system, exudation to the inflammatory site, pain and fever [5; 8; 9; 10].

Unresolved tasks. The questions to the pathogenetic justification of differentiated treatment of patients with the combined diseases of the kidney and the gastrointestinal tract are relevant. Because polyorganic pathology has its own pathways and changes the overall clinical picture of the patient.

The purpose. To study the dynamics of systemic and local content of prostaglandin E_2 in patients with chronic kidney disease II and III stages, due to the long course of chronic recurrent pyelonephritis with the presence of erosive-ulcerative stomach lesions under the influence of mucogens.

Materials and methods. 105 patients with CKD II-III stages were examined, due to prolonged course of chronic pyelonephritis with the presence of Hp-negative (and with the previous eradication of this pathogen) erosive-ulcerative lesions of the stomach (EULS) with preserved secretory function and patients with CKD without EULS. The survey includes 56 men and 49 women aged 17 to 70 years.

The patients were divided into 4 groups: first group was consisted of 37 patients with CKD II-III stages without stomach lesions; second group − 68 patients with CKD II-III stages with the presence of EULS before treatment; third group − 31 patients of the CKD of II-III stages with the presence of EULS after 3 weeks of treatment without the use of mucogen; fourth group − 37 patients with CKD II-III stages with the presence of EULS after 3 weeks of treatment with the use of mucogens in complex therapy for 1 tab. 3 times a day in 30 min. before meals.

The clinical picture, X-ray and endoscopic data, histological findings (staining with hematoxylin and eosin) examination of the gastric mucosal biopsies for diagnosis verification were taken into account. The glomerular filtration rate and the level of daily proteinuria in the studied patients were also investigated

The level of prostaglandin E_2 (PGE2) was measured in serum of blood, urine and gastric juice in patients and assessed using the immune enzyme method using commercial test kits (Kit) from "Assay Designs Inc.", USA. Serum samples were centrifuged at 1500 r/pm during 10-15 minutes. Separated serum was taken and used in the immuno-enzyme analyzer ("Picon" № 01391409). The obtained data are processed statistically using Student's criteria. All indicators are presented as average values with the average errors (M ± m). Reliable considered the difference at $p < 0,05$.

Results and discussion. As a result of the study, it was found that in patients with Group I, the level of PGE2 was slightly lower in serum (920.02 ± 4.23 pg/ml). But these changes were not probable with the corresponding indices of a group of healthy individuals (1050.10 + 2.01 pg/ml) ($p > 0.05$). The dynamics of the indices of the II and the III groups was the same. The probable reduction in serum PGE2 serum levels (520.44 + 3.37 and 632.21 + 2.78 pg/ml, respectively) compared to those in healthy and Group I patients ($p < 0.05$) was found. In patients of IV group, the level of PGE2 blood was increased in comparison with the corresponding data of groups II and III of patients (839,47 + 2,34 pg/ml) ($p < 0,05$).

Inassessing the parameters of PGE2 in gastric juice, they were found to decrease in patients of groups II and III (correspondingly, 7506,13 + 3,21 and 8927,41 + 3,26 pg/ml) ($p < 0,05$) incomparison with the norm and their content in patients without lesion of the stomach (Group I) (13400,04 + 3,12 and 13411,17 + 2,35 pg/ml, respectively). This indicates that the local deficit of PGE2 accompanies the EULS and is not adjusted without the use of mucogens. Then, asinpatients takingmucogens (IV group), a significant increase PGE2 leveling astricjuice was observed after 3 week soft reatment (11256.44 + 2.55 pg/ml) ($p < 0.05$) compared with II and III groups. Results of the study of the content of PGE2 in the urine of patients showed a decrease in this index in patients of all groups (Group I − 480.19 + 2.38; Group II − 501.16 + 3.51 and Group III − 643.41 + 3.22 pg/ml) versus healthy (814.02 + 3.18 pg/ml) ($p < 0.05$). After treatment with the inclusion of mucogens (group IV), the content of PGE2 in urine was increased (698.14 + 2.11 pg/ml) and was significantly different from those of the rest of the patients being studied ($p < 0.05$). In the studied patients, after 3 weeks of treatment, positive changes were detected from the glomerular filtration rate (GFR) (from 48.8 + 5.12 ml/min to 59.1 + 4.87 ml/min), as well as a decrease in the level of daily proteinuria (from 2,1 + 0.12 to 0.99 + 0.10 ml/min) ($p < 0.05$). This proves the absence of negative influence of Mucogene on the function of the kidneys.

In the course of studying the linear correlation between the investigated parameters, there was a direct correlation between the content of PGE2 blood and GFR ($r = 0.58$) ($p < 0.05$). With a decrease in GFR due to the progression of CKD, production by the kidneys of the local PGE2 decreases, which also reduces its incidence in the common bloodstream. Direct correlation was found between the level of PGE2 gastric juice and PGE2 blood ($r = 0.67$) ($p < 0.05$), which can also be explained accordingly. A strong correlation between the parameters of PGE2 of urine and the level of daily proteinuria ($r = -0.78$) was found ($p < 0.05$), which proves the progressive nature of kidney damage. It is accompanied by a deficit of local and general PGE2.

Consequently, the results of the study of the dynamics of the content of PGE2 in blood, gastric juice and urine of patients showed that in the presence of EULS the content of local (in gastric juice) and total PGE2 is significantly reduced. It gives a deficite of local protective factors (mucous helium and bicarbonate) and contributes to the deterioration of local and systemic microcirculation processes, which indicates a decrease in total PGE2. Insufficient content in the body contributes to maintaining inflammation, worsening local processes of regeneration. Patients in the CKD II stage II in our study noted a marked deficiency in the content of PGE2 urine and serum, which also indicates the inhibition of local renal rehabilitation processes in the kidney and in the body as a whole. In patients with CKD II-III degree due to the presence of sclerosis and functional disorders, the production of prostaglandin E_2 is reduced by the kidneys. As a result, ischemic changes in the kidney vessels and inflammatory processes are progressing. This causes the progression of the CKD.

Summing up the above, it can be confirmed that pathological changes in combination of CKD II-III stage and ELUS have interdependent progressive character and contribute to the deepening of pathological lesions of both the stomach and the kidneys. Shows the expressed positive effect of mucogens, which manifests itself at the local level (stomach, kidneys) and in general (blood) due to falling part of the drug intact in the bloodstream. That's why we can successfully use this drug in the treatment of patients with CKD, combined with erosive lesions of the stomach. It has no negative influence on the functional state of the kidneys.

Thus, the problem of studying the mechanisms of the progression of interdependent pathological changes in patients with CKD with the presence of erosive-ulcerative lesions of the stomach and duodenum is extremely interesting, insufficiently studied and requires the continuation of active scientific research in this direction.

Conclusions:

1) In the presence of ELUS the content of local (in gastric juice) and total PGE2 is significantly reduced.

2) Patients with CKD II-III stages in our study noted a marked deficiency of the content of PGE2 urine and serum.

3) Pathological changes in the combination of CKN II-III stage and EWSH are interdependent progressive character.

4) Positive action of mucogens, which manifests itself at the local level (stomach, kidneys) and in general (blood), can successfully use this drug in the treatment of patients with CKD, combined with erosive lesions of the stomach.

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МЕДИЧНІ НАУКИ

ПАТОГЕНЕТИЧНІ ОСОБЛИВОСТІ ТА ДИФЕРЕНЦІЙОВАНИЙ ПІДХІД ДО ЛІКУВАННЯ УРАЖЕННЬ ШЛУНКОВО-КИШКОВОГО ТРАКТУ У ПАЦІЄНТІВ З ХРОНІЧНОЮ ХВОРОБОЮ НИРОК

Анотація
В даній роботі представлений сучасний стан проблеми механізмів ураження шлунково-кишкового тракту у хворих на хронічну хворобу нирок (ХХН). Викладені сучасні погляди вчених-нефрологів та гастроентерологів на взаємозв'язок між Helicobacter pylori (HP) – опосередкованими ураженнями шлунка та дванадцятипалої кишки та прогресуванням хронічної хвороби нирок. В дослідженні вивчена динаміка системного і локального вмісту простагландина E_2 у хворих хронічною хворобою нирок II і III стадії, зумовлена тривалим перебігом хронічного рецидивуючого пієлонефриту з наявністю ерозивно-виразкових уражень шлунку та дванадцятипалої кишки.

Ключові слова: хронічна хвороба нирок, хронічний пієлонефрит, простагландин E_2, ерозивно-виразкові ураження шлунка та дванадцятипалої кишки, мукоген.

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ДИФФЕРЕНЦИРОВАННЫЙ ПОДХОД К ЛЕЧЕНИЮ ПОРАЖЕНИЯ ЖЕЛУДОЧНО-КИШЕЧНОГО ТРАКТА У ПАЦИЕНТОВ С ХРОНИЧЕСКОЙ БОЛЕЗНЬЮ ПОЧЕК

Аннотация
В данной работе представлены современное состояние проблемы относительно механизмов поражения желудка у больных хронической болезнью почек (ХБП). Изложены современные взгляды ученых нефрологов и гастроэнтерологов на взаимосвязь между Helicobacter pylori (HP)-опосредованными поражениями желудка и двенадцатиперстной кишки и прогрессированием хронической болезни почек. В работе изучена динамика системного и локального содержания простагландина E_2 у больных хронической болезнью почек II и III стадии, обусловленную длительным течением хронического рецидивирующего пиелонефрита с наличием эрозивно-язвенных поражений желудка и двенадцатиперстной кишки.
Ключевые слова: хроническая болезнь почек, хронический пиелонефрит, простагландин E_2, эрозивно-язвенные поражения желудка и двенадцатиперстной кишки, мукоген.