Barinov E. F., Grigoryan Kh. V., Balykina A. O., Faber T. I. Why a pregnant age can be the risk factor in chronic obstructive pyelonephritis? Journal of Education, Health and Sport. 2017;7(12):644-655. eISSN 2391-8306. DOI http://dx.doi.org/10.5281/zenodo.1295649
http://ojs.ukw.edu.pl/index.php/johs/article/view/5596

The journal has had 7 points in Ministry of Science and Higher Education parametric evaluation. Part B item 1223 (26.01.2017).
1223 Journal of Education, Health and Sport eISSN 2391-8306 7

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 01.12.2017. Revised: 15.12.2017. Accepted: 25.12.2017.

WHY A PREGNANT AGE CAN BE THE RISK FACTOR IN CHRONIC OBSTRUCTIVE PYELONEPHRITIS?

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Abstract

The aim of the study was to identify possible mechanisms that could reproduce the recurrence of CVD in older men against the background of non-steroidal anti-inflammatory drugs and antibiotics, thereby justifying why age and sex may be risk factors for acute pyelonephritis in urolithiasis.

Material and methods. The results of a study of 88 men with chronic obstructive pulmonary disease, including 45 patients over 65 years of age (mean age 74.0 ± 1.3 years) and 43 patients in the age range of 55-65 years (mean age of patients 61.0 ± 0, 8 year). In the phase of remission of CVD, 48 patients were examined and in the phase of relapse-40 patients. The study included patients who took non-steroidal anti-inflammatory drugs (NSAIDs) and antibiotics in a standard dose of at least 5-10 days before hospitalization. From the peripheral blood by centrifugation, plasma-enriched plasma was isolated. Platelet content in 1 μl was 200,000 ± 20,000. To stimulate platelets, adrenaline and ADP (Sigma, USA) were used at an effective concentration (EC50) of 5 μM, which caused platelet aggregation (ATC) in healthy individuals (10 donors) at the level of 50 ± 5%. The aggregation of Tc was evaluated on a Chrono log analyzer (USA). The formation of platelet-leukocyte aggregates (TPA) was modeled in vitro by incubation of stimulated platelets (epinephrine at a concentration of EC50) and intact leukocytes isolated from the peripheral blood of patients

with CVD. The number of intact TL was assessed after the color of blood smears according to the Romanovsky-Giemsa method. **Results.** In the phase of remission of CVD on the background of the appointment of NSAIDs and antibiotics, in patients of the two age groups studied, it was not possible to detect differences in the response of leukocytes. Recurrence of CVD in patients age range 55-65 years was characterized by leukocytosis, neutrophilocytosis, increased ESR ($p < 0.001$), and hypoadrenal reactivity Tc. In men older than 65 years with relapse of CVD, compared with the phase of remission, moderate leukocytosis, neutrophilocytosis ($p < 0.05$) and lymphocytopenia ($p < 0.05$), as well as normo-reactivity of α2-adrenoreceptors Tc. When stimulating Tc with adrenaline in vitro in men over 65 who were in the phase of remission of CVD, the number of formed APs increased significantly ($p < 0.01$); this phenomenon was not reproduced in patients in the age range of 55-65 years.

Conclusion. Despite the use of non-steroidal anti-inflammatory drugs and antibiotics, the age> 65 years and the male sex of the patient may be risk factors for the development of acute pyelonephritis in COPD, which is associated with the maintenance of normal adrenoreactivity of platelets providing recruitment of leukocytes.

Key words: age characteristics of the organism, men, adrenoreactivity of thrombocytes, platelet-leukocyte aggregates.

УДК 616.61–002.3–007.271–036.12–036.87–053.9

ПОЧЕМУ ПРЕКЛОННЫЙ ВОЗРАСТ МОЖЕТ БЫТЬ ФАКТОРОМ РИСКА РЕЦИДИВА ПРИ ХРОНИЧЕСКОМ ОБСТРУКТИВНОМ ПИЕЛОНЕФРИТЕ?

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Реферат

Цель исследования - установить возможные механизмы, которые могли бы воспроизвести рецидив ХОПН у мужчин пожилого возраста на фоне применения нестероидных противовоспалительных средств и антибиотиков, тем самым обосновать

почему возраст и пол могут быть факторами риска острого пиелонефрита при уролитиазе.

Материал и методы. В работе представлены результаты исследования 88 мужчин с ХОПН, среди которых было 45 больных старше 65 лет (средний возраст 74,0 ± 1,3 года) и 43- в возрастном диапазоне 55-65 лет (средний возраст больных 61,0 ± 0,8 год). В фазе ремиссии ХОПН обследовано 48 больных и в фазе рецидива- 40 пациентов. В исследование включены пациенты, которые принимали нестероидные противовоспалительные средства (НПВП) и антибиотики в стандартной дозе не менее 5-10 дней до момента госпитализации. Из периферической крови путем центрифугирования выделяли обогащенную тромбоцитами плазму. Содержание тромбоцитов в 1 мкл составило 200 000 ± 20 000. Для стимуляции тромбоцитов использовали адреналин и АДФ (Sigma, США) в эффективной концентрации (EC_{50}) - 5 мкМ, что вызывало у здоровых лиц (10 доноров) агрегацию тромбоцитов (АТц) на уровне 50±5%. Оценку агрегации Тц проводили на агрегометре Chrono-log (США). Формирование тромбоцитарно-лейкоцитарных агрегатов (ТЛА) моделировали in vitro при инкубации стимулированных тромбоцитов (адреналин в концентрации EC_{50}) и интактных лейкоцитов, выделенных из периферической крови пациентов с ХОПН. Количество интактных ТЛА оценивали после окраски мазков крови по методу Романовского-Гимза.

Результаты. В фазу ремиссии ХОПН на фоне назначения НПВП и антибиотиков, у пациентов двух исследованных возрастных категорий не удалось обнаружить различий реакции лейкоцитов. Рецидив ХОПН у пациентов возрастного диапазона 55-65 лет характеризовался лейкоцитозом, нейтрофилоцитозом, повышением СОЭ ($p<0,001$) и гипоадренореактивностью Тц. У мужчин старше 65 лет при рецидиве ХОПН, по сравнению с фазой ремиссии, выявлены умеренный лейкоцитоз, нейтрофилоцитоз ($p <0,05$) и лимфоцитопения ($p <0,05$), а также нормореактивность α2-адренорецепторов Тц; При стимуляции Тц адреналином in vitro у мужчин старше 65 лет, которые находились в фазе ремиссии ХОПН, существенно увеличивалось количество сформированных ТЛА ($p<0,01$); данный феномен не воспроизводился у пациентов в возрастном диапазоне 55-65 лет.

Вывод. Несмотря на применение нестероидных противовоспалительных средств и антибиотиков, возраст >65 лет и мужской пол пациента могут быть факторами риска развития острого пиелонефрита при ХОПН, что связано с сохранением нормальной адренореактивности тромбоцитов, обеспечивающих рекрутирование лейкоцитов.

Ключевые слова: **возрастные особенности организма, мужчины, адренореактивность тромбоцитов, тромбоцитарно-лейкоцитарные агрегаты.**

ЧОМУ ПОХИЛИЙ ВІК МОЖЕ БУТИ ФАКТОРОМ РИЗИКУ РЕЦИДИВУ ХРОНІЧНОГО ОБСТРУКТИВНОГО ПІЄЛОНЕФРИТУ?

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Реферат

Мета дослідження – встановити можливі механізми, які могли б відтворити рецидив ХОПН у чоловіків похилого віку на фоні застосування нестероїдних протизапальних засобів та антибіотиків, тим самим обґрунтувати чому вік і стать можуть бути факторами ризику гострого пієлонефриту при уролітіазі.

Матеріал і методи. В роботі представлені результати дослідження 88 чоловіків з ХОПН, серед яких було 45 хворих старше 65 років (середній вік 74,0±1,3 роки) і 43 у віковому діапазоні 55-65 років (середній вік хворих 61,0±0,8 рік). У фазі ремісії ХОПН обстежено 48 хворих і у фазі рецидиву– 40 пацієнтів. В дослідження включені пацієнти, які приймали нестероїдні протизапальні засоби (НПВЗ) і антибіотики в стандартній дозі не менше 5-10 днів до моменту госпіталізації. З периферичної крові шляхом центрифугування виділяли збагачену тромбоцитами плазму. Зміст тромбоцитів в 1 мкл становив 200 000 ± 20 000. Для стимуляції тромбоцитів використовували адреналін і АДФ (Sigma, США) в ефективній концентрації (EC_{50}) - 5мкМ, що викликала у здорових осіб (10 донорів) агрегацію тромбоцитів (АТц) на рівні 50 ± 5%. Оцінку агрегації Тц проводили на агрегометрі Chrono-log (США). Формування тромбоцитарно-лейкоцитарних агрегатів (ТЛА) моделювали in vitro в умовах інкубації стимульованих тромбоцитів (адреналін в концентрації EC_{50}) і інтактних лейкоцитів, виділених із периферичної крові пацієнтів з ХОПН. Кількість інтактних ТЛА оцінювали після забарвлення мазків крові за методом Романовського-Гімза.

Результати. В фазу ремісії ХОПН на тлі призначення НПЗП і антибіотиків, у пацієнтів двох досліджених вікових категорій не вдалося виявити розбіжностей реакції лейкоцитів. Рецидив ХОПН у пацієнтів вікового діапазону 55-65 років

характеризувався лейкоцитозом, нейтрофілоцитозом, підвищенням ШОЕ (p<0,001) і гіпоадренореактивністю Тц. У чоловіків старіше 65 років при рецидиві ХОПН, в порівнянні з фазою ремісії, виявлені помірний лейкоцитоз, нейтрофілоцитоз (p <0,05) і лімфоцитопенія (p <0,05), а також нормореактивность α2-адренорецепторів Тц. При стимуляції Тц адреналіном in vitro у чоловіків старіше 65 років, які знаходились в фазу ремісії ХОПН, суттєво збільшувалась кількість сформованих ТЛА (p <0,01), даний феномен не відтворювався у пацієнтів вікового діапазону 55-65 років.

Висновок. Незважаючи на застосування нестероїдних протизапальних засобів і антибіотиків, вік > 65 років і чоловіча стать пацієнта можуть бути факторами ризику розвитку гострого пієлонефриту при ХОПН, що пов'язано із збереженням нормальної адренореактивності тромбоцитів? які забезпечують рекрутування лейкоцитів.

Ключові слова: **вікові особливості організму, чоловіча стать, адренореактивність тромбоцитів, тромбоцит-лейкоцитарні агрегати.**

To date, the problem of initiation of acute inflammatory reaction in the urinary tract (UHF) with urolithiasis has not been adequately covered in the literature; there is no clarity in the mechanisms that trigger the interaction of blood cells in the transition from chronic to acute inflammation with urolithiasis, which holds back the development of informative diagnostic methods and remedies for pyelonephritis. In this regard, the analysis of possible risk factors for acute pyelonephritis with urolithiasis continues, which is due not only to the need for prevention of sepsis, but also - the establishment of predictors of recurrence of chronic obstructive pyelonephritis (CPR) [1]. As a rule, the search for risk factors is related to mathematical modeling, that is, with the calculation of relative risk for each indicator used by the same or other nephrologist to verify the etiology and pathogenesis of urolithiasis, assess the effectiveness of treatment and predict the development of complications [2]. The range of possible risk factors for pyelonephritis develops widely, however, there is no meta-analysis of publications regarding informativity and specificity of indicators of acute and chronic inflammation. The task of determining the risk factors is even more complicated if the patient receives nonsteroidal anti-inflammatory drugs (NSAIDs) and antibiotics, since the clinical and laboratory diagnosis is not enough informative to differentiate the phase of remission and relapse of the disease [3]. According to literature [4], the most important risk factors for acute pyelonephritis with urolithiasis are age and gender of patients, and the reactivity of blood cells. One feature is paying attention to it - risk factors that are discovered by some researchers are not always reproduced in other nephrology centers, which leads to the search

for new informative indicators. From our point of view, the causes of this phenomenon are associated with a lack of knowledge that would explain why these or other risk factors can initiate the development of acute pyelonephritis with urolithiasis.

The purpose of the study was to establish possible mechanisms that could reproduce the recurrence of CPR in elderly men against the background of the use of NSAIDs and antibiotics, thereby justifying why age and sex can be a risk factor for acute pyelonephritis with urolithiasis.

To exclude the influence of gender characteristics of patients with leukopoies in urolithiasis, studies were conducted only on men. The paper presents the results of a study of 88 patients with CPR, including 45 patients over 65 years of age (mean age 74.0 ± 1.3 years) and 43 in the age range of 55-65 years (mean age 61.0 ± 0.8 year). In the remission phase (1st group), 48 patients were examined for HOF and in the relapse phase (2 nd group) - 40. All patients at the stage of hospitalization in the urology department performed a comprehensive clinical examination according to the traditional scheme adopted for the diagnosis of urolithiasis (complaints, collection anamnesis, physical examination, clinical and laboratory studies, excretory urography, ultrasound and radiological examination, bacteriological examination of urine), which allowed to diagnose the remission phase and recurrence of CPR. The study included patients taking NSAIDs and antibiotics in a standard dose of at least 5-10 days prior to hospitalization. In the analysis of the hemogram (ABX Pentra XL 80-HORIBA, France), the number of formed elements, the leukocyte formula and the absolute number of different types of leukocytes were determined. In analyzing the reaction of the organism to the development of inflammation, the rate of erythrocytes shedding (SLE) and the level of C-reactive protein were estimated. From the peripheral blood by centrifugation, plasma-enriched platelets were isolated; platelet content (Tc) in 1 μl was 200,000 ± 20,000. To stimulate Tc, adrenaline and ADP (Sigma, USA) were used at an effective concentration (EC50) of 5 μM, resulting in 50 ± 5% platelet aggregation (ATC) in healthy individuals (10 donors). The estimation of aggregation Tc was carried out on an aggregometer Chrono-log (USA). The formation of platelet-leukocyte aggregates (TLCs) was modeled in vitro under conditions of incubation of stimulated platelets (adrenaline in the concentration of EC50) and intact leukocytes isolated from the peripheral blood of patients with CPR. The number of intact TBWs was evaluated after staining of blood smears using the Romanovsky-Gimza method. Statistical processing of the results was carried out in MedStat and MedCalc packages. The difference was statistically significant at $p < 0.05$.

Results and discussion

Achievement of the set goal is possible by solving the following research questions. Is leukocyte reactivity in the remission phase and recurrence of CKD in men over 65? In men aged 55-65, the average diameter of a concrete is 16.0 ± 2.6 mm. The content of leukocytes (95% CI 5.2 x 109 - 7.5 x 109 / l) and ESR (95% CI 7-24 mm / hr) corresponded to the reference range in the remission phase of the CKD (group 1, n = 20) (p> 0.05). Leukocytosis in the recurrence phase of CPR (2nd group; n = 23) was 14.5 ± 0.7 x 109 / l, indicating the presence of acute inflammation in the CSF. The magnitude of the SSEE (37.0 ± 2.0 mm / yr; 95% DI 16-58 mm / yr) increased in comparison with the 1st group by 4.6 times (p <0.001). The neutrophil content (NF) in the blood of patients in the 1st group (95% CI 56% - 60%) was lower than the upper limit of the "norm"; In the 2nd group, their number increased by 37.9% (p <0.001). The number of lymphocytes (LF) in the 1st group was within the "norm"; In the 2nd group, their low content was determined. The number of eosinophils did not differ in both groups, the basophils in the recurrence phase of CPR increased more (p <0.05). In the 1st group, the content of monocytes (M) was at the level of the upper limit of the "norm" (95% CI 6% - 10%), with relapse their number decreased to 2,0 ± 0,2% (p □0,001). Thus, for men aged 55-65 years, leukocytosis, neutrophilocytosis and elevated ESRD are characteristic of recurrent HPLC.

In men older than 65 years, the diameter of the concrete was 30.0 ± 5.5 mm, that is, it was approximately 2 times larger. The level of leukocytes in the 1st group (n = 25) was in the reference range, and in the 1 st and 3 rd quartiles, the value of the indicator did not go beyond the lower and upper limits (95% CI 5.1 x 109 - 7.5 x 109 / l). In the 2 nd group (n = 20) there was leukocytosis, and the increase in the total number of leukocytes in the blood compared to the 1st group was 59.1% (p <0.05; 95% CI 6.1 x 109 - 23 , 2 x 109 / l). Moreover, in patients older than 65 years, the number of leukocytes in the peripheral blood was 27.6% lower (p <0.05) than in the age of 55-65 years. Thus, age reduction of leukocytosis takes place and this despite the fact that in this age group of patients recorded the largest concrements. If we judge from the magnitude of the upper limit of the "norm" of SSEE (15 mm / h.) And the level of C-reactive protein (5.2 mg / l), then in patients in the remission phase of CTCN, there is no inflammatory reaction. However, the median of indicators is higher than that of patients aged 55-65. In patients of the 1st group, SLE is higher by 36.5% compared with the 2nd group (p <0.05; 95% DI 16-48 mm / h). Interestingly, in patients older than 65 years, SLE was less than 40.6% (p <0.05) than in patients aged 55-65. Thus, in patients older than 65 years, there is a tendency to decrease the incidence of SLE in comparison with patients aged 55-65 years.

The higher numbers of segmental NF in the blood of patients in group 1, in comparison with those in the range of 55-65 years (20% on average, p <0,05), are noticed. In the 2nd group, the number of segment-nuclear NFs was similar in the age group of patients and reached 80%, but the interpretation of the results varies, if we analyze the degree of increase in the number of these granulocytes: in patients 55-65 years it was 37.9%, and older 65 years - 10.6%. Thus, with age, the reserve capacity of the organism to produce differentiated (mature) NF significantly decreases. It is important to find out - is an effective maximal neutrophilopoiesis in persons over 65 years old? To answer this question, we analyzed the number of bat-nuke NFs in both groups. In the 1st group, their content was at the level of the lower limit of the "norm", but was significantly less than that in patients aged 55-65 years (p <0,05). In the 2nd group, the number of young forms of NF significantly increased and even went beyond the upper limit of the norm (p <0,05). Moreover, the content of these forms of NF in circulating blood exceeds the value of such in men aged 55-65 years (p <0,05). Thus, in persons older than 65 years in the phase of recurrence of CPR, despite the greater number of segmental (mature forms) NF, a tendency to increase the formation of young forms of data of leukocytes appears.

The dynamics of eosinophils and basophils is interesting for its asymmetry, if the number of eosinophils was greater in the remission phase, then the basophils are in the phase of recurrence of CPR. The absolute number of LF in the 1st and 2nd groups was 1.0 ± 0.4 x 109 / l and 0.65 ± 0.22 x 109 / l respectively. The content of LF in the 1st group corresponded to the lower limit of the "norm", however, with respect to the age group of 55-65 years, the content of these leukocytes is approximately 35% lower (p <0,05). Thus, lymphopenia occurred in men older than 65 years old. The situation is unexpected, since it is believed that the presence of long-term CPR in patients is accompanied by lymphocytosis. Is this phenomenon associated with the presence of the underlying disease - SLE, is unknown. In the 2nd group there was a decrease in the number of LF by 33.6% (p <0.001) compared with group 1. For comparison, in patients aged 55-65, the number of LF in the phase of recurrence of CPR was approximately 2 times lower than in the remission phase (p <0.001). Consequently, the age-old feature of lymphocytopoies in the elderly (aged 65 years) is manifested by the restriction of LF products during the recurrence of COPD, although such a hemopoietic reaction is less pronounced compared with patients aged 55-65. With low LF content, the M reaction to the development of acute inflammation in the CSF, which can regulate lymphopoies during the transition from chronic inflammation to acute, is of interest. Absolute amount of monocytes is 0.40 ± 0.07 · x 109 / l and 0.38 ± 0.05 · x 109 / l,

respectively, in groups 1 and 2 ($p > 0.05$). In Group 1, the content of M corresponds both to the reference range and to the value of the indicator in patients aged 55-65 years, and therefore, age-specific features of the reaction M in the phase of remission of CHOPN are not observed. In the 2nd group, in the presence of acute inflammation, the number of M does not undergo significant changes and is within the reference range, that is, their "irradiance" is preserved. Thus, in men of two age groups (55-65 years and over 65 years), the remission phase of CKD in the background of the appointment of NSAIDs and antibiotics failed to detect differences in the response of leukocytes. In men older than 65 years of age, the prevalence of recurrence of CPR, in relation to the remission phase, is moderate leukocytosis and neutrophil cytosis ($p < 0.05$) and lymphocytopenia ($p < 0.05$).

Given the severity of the reaction scant leukocytes during HOPN conditions for the appointment of NSAIDs and antibiotics, it makes sense to turn to assess reactivity, which makes blood cells specifics response in inflammation. From our point of view, as an indicator of reactivity of an organism it would be possible to use the magnitude of cellular response to the effect of adrenaline, that is, to evaluate their adrenoactivity. This methodological approach is based on the fact that (a) sympatho-adrenal system is involved in maintaining the homeostasis of an organism; (b) evaluation of adrenoreceptor activity of cells is readily reproducible in an in vitro test on blood cells, in particular, platelets that have adrenoreceptors; (c) platelets are participants in the inflammatory response, since they provide recruiting leukocytes from the blood into the inflammation zone and modulate immune responses [5]. It can be assumed that in elderly men, the reactivity of leukocytes depends on the adrenoactivity of the organism. In this case, the transition from the phase of remission to the recurrence of chronic obstructive pulmonary disease is due to increased adrenoactivity of the platelets.

The research question - is the adreno-reactivity of the organism older than 65 years old in the phase of remission and recurrence of CKD in the context of the use of NSAIDs and antibiotics? In the remission phase, the hypoadrenoreceptor Tc was observed in both groups of patients. In the phase of recurrence of CKD in men older than 65 years, the normacreactivity of α2-adrenergic receptors in response to EC50 adrenalin (47.0 ± 4.0%) was detected, whereas in the age group of 55-65 years the hyoid adrenal reactivity Tc (18.0 ± 4 , 2%; $p = 0.013$). At the same time, the difference between the ADP-induced ATS was not found: in patients older than 65 years, aggregation was recorded at 47.0 ± 2.4% (95% left GER and 43.4% RH, and 55.4% right DI), in the age group 55 -65 years - at the level of 43,0 ± 2,0% (95% left CI 32,3% and right CI - 61,1%); Differences in mean values of ATS are not

statistically significant. Thus, in men older than 65 years of implementation of acute inflammatory reaction (relapse of CPR) occurs against the background of normal functioning α2-adrenoreceptors Thc; in patients aged 55-65 years, adrenaline is not the leading cause of inflammation.

It has been established that Tc modulates the inflammatory reaction by interacting with leukocytes by forming TPA [6]. In turn, Tz are under the influence of humoral stimuli, primarily adrenaline and cytokines, capable of potentiating the effects of paracrine agonists such as ADP and the platelet activation factor (FAT). It can be assumed that the presence of concrement in the bowel or the ureter periodically provokes the obstruction of the ESS, or directly stimulates afferent links in the autonomic nervous system, which leads to the activation of the sympathetic adrenal system (SAS) [7]. As a result, the level of adrenaline and glucocorticoids in the circulating blood increases, which could stimulate the corresponding receptors and cause a change in the functional activity of Tc and leukocytes. It has been established that adrenaline affects the development of inflammatory response, and it can be seen that it is a direct stimulating effect on leukocytes, and indirectly - through the activation of Tc. The research question - can adrenaline initiate the development of acute inflammatory response in men older than 65 years in the remission phase of CKD in the context of the use of NSAIDs and antibiotics?

The studies were conducted on the model of in vitro formation of platelet-leukocyte aggregates (TLCs) that provide co-operation, activation of blood cells and participate in the initiation of inflammation. In the phase of remission of CPR in the basal conditions (without stimulation of blood cells by adrenaline), the number of CABD in individuals over 65 years old was 2.67 ± 0.31%, in patients aged 55-65 years - 2.93 ± 1.51%. Consequently, in the elderly and middle age, the initial possibilities of interaction of Tc and leukocytes, aimed at the implementation of inflammatory response, did not differ statistically significantly ($p > 0.1$). When added to the adrenal stimulated thrombocytopenic leukocyte (ES50), in individuals aged 65 years, the number of TBWs exceeded the basal level by 40% ($p < 0.01$), whereas in patients in the range of 55-65 years - by 7-8% ($p > 0.1$). The obtained results confirm the participation of adrenalin in the development of acute inflammation in CKD in the elderly, and this is possible due to the preservation of normal adrenoactivity Tc. In patients aged 55-65 years, with low sensitivity of α2-adrenoreceptors Thc, adrenaline (EC50) does not reproduce the stimulating effect on the formation of TPA.

The prediction of the transition from chronic inflammation to acute urolithiasis, in essence, to determine the risk factors for recurrence of CPR, remains an urgent problem of

nephrology and clinical pathophysiology, since it opens up the possibility of timely prophylactic treatment of patients. However, the effectiveness of such treatment depends on whether - mechanisms have been established that trigger acute inflammation in relation to each precursor recurrence of CPR. Often, nephrologists are limited to the statement of the presence of risk factors of a disease, without trying to understand the essence of the participation of a factor in the pathogenesis of the disease. A typical example can be the statement in the publications of the fact that age and sex is a risk factor for diseases, and quite different: acute pyelonephritis, heart failure, stroke, hepatitis, etc. But why is this possible? The most common presentation is related to age-related changes in the tissues and organs of a person and the gender characteristics of endocrine regulation of inflammatory response, which is interpreted as the reactivity of the organism. Just the lack of knowledge regarding the assessment of reactivity of the organism is lacking to explain the contradiction in the significance of those or other risk factors, or the presence of laws of age properties with completely different diseases associated with inflammation. The results of the study did not reveal significant differences in the response of leukocytes to CKD in men of two age groups (55-65 years and over 65 years of age). Interpretation of the results of the analysis changes, taking into account the reactivity of the organism, in particular, the adrenoreceaction of Tc, which initiate the recruitment of leukocytes from the blood by forming TPA. Thus, in vitro studies have shown that in patients older than 65 years of age in the remission phase of CKD, even against the background of the use of NSAIDs and antibiotics (blockade COX-1 and decrease in the synthesis of ThA2), the normal tetracycline reactivity was maintained, whereas in the age range of 55-65 years Hyodoadrenoractivity was taking place TC. As a consequence, incubation with adrenaline-activated Tc with leukocytes was accompanied by the formation of TPO, more pronounced in patients older than 65 years. Reproduction of blood cell interaction in vitro explains the possible mechanisms of initiation of acute inflammation in elderly men in the remission phase of COPD, which provides a theoretical substantiation of the validity of the use of age and sex indicators of the patient as risk factors for the development of pyelonephritis in urolithiasis.

Conclusion

Old age and male patient's gender may be risk factors for acute pyelonephritis in the remission phase of CKD, despite the use of nonsteroidal anti-inflammatory drugs and antibiotics, due to the preservation of normal platelet adrenoactivity. Under conditions of activation of the sympatho-adrenal system in urolithiasis, platelet stimulation with adrenaline is accompanied by the formation of platelet-leukocyte aggregates, which provide recruiting of

leukocytes from the blood into the center of inflammation of the urinary tract.

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