

the kidneys, urinary tract, bladder outlet obstruction (Shilov E.M., et al., 2010). Any of these diseases can cause the development of infectious and inflammatory complications in particular, and urosepsis, where mortality ranges from 20 to 60% (Om P.K. et al., 2009). It is noted as an increase in the number of patients and treatment costs (VS Saveliev et al., 2011). A huge role in preparing patients for kidney transplantation is the elimination of all possible foci of infection, as in post-transplant period used large doses of immunosuppressive drugs, which reduce the reactivity of the body and increase the risk of septic complications, even in the presence of small latent foci of infection (Bernabeu-Wittel M. et al., 2002). The most specific and threatening complication of immunosuppressive therapy after renal transplantation is sepsis, in which mortality reaches 70-76% (Volynchik E.P., 2007). Sepsis has a direct effect on renal graft function (Becker S. et al., 2011). In the appointment of any immunosuppressive therapy, purulent focus in the recipient's body, especially the patient's own kidneys infected with pyelonephritis, are a potential source of bacteremia and hematogenous pyelonephritis of the transplanted kidney (Kabulbaev K.A., 2010). The structure of the causes of urosepsis in this category of patients are of particular importance increased virulence of opportunistic pathogens, activation of the endogenous microflora, and mixed viral infections (Prokopenko E.I. et al., 2010). Attempts to expand the range of used antibiotics do not give the expected results. This is due to the one formed by patients with chronic renal urologic etiology of the disease for many years, tolerance to many classes of antibacterial drugs, the other high frequency stability of community-acquired strains of microorganisms that cause infectious-inflammatory diseases of the urinary tract, to the widely used drugs such as aminoglycosides, aminopenicillins, cephalosporins (including Generation III and IV), (Kozlov R.S., 2010). Resistance of gram-negative bacteria is a significant problem worldwide, especially enterobacteria producing beta-lactamase extended spectrum of action. At the present time in Russia, the prevalence of resistance factor beta-lactamase extended spectrum ranges from 52% to 71%, which is several times greater than in Europe (Grabe M. et al., 2010). Hope to "... the appearance in the near future, new antibiotics that satisfies all the requirements, it is seldom ..." (Paterson D., 2009). Especially in patients with chronic renal failure before and after kidney transplantation. In recent years there have been reports of successful use in the selective adsorption of endotoxin urosepsis Gram-negative bacteria. Published in the literature allows to state the high efficiency and absence of side adverse effects when using selective adsorption in sepsis. (Vatazin A.V. et al. 2011). Analysis of the current domestic and foreign literature, which suggests that the use of complex treatment of selective adsorption of endotoxin can not only compete successfully with emerging septic complications, but also significantly improve the performance of early and late survival in patients with surgical sepsis (Ronco C. et al., 2005; Casella et al., 2006, Yaroustovsky M.B. et al., 2008).

However, the application of the selective adsorption of endotoxin of gram-negative bacteria in patients with chronic renal failure urologic etiology, pre-and post-kidney transplant unit devoted to the study, which was the basis for this study.

FEATURES OF PATIENTS WITH UROLOGICAL DISEASES WITH SEPTIC COMPLICATIONS, RECEIVING RENAL REPLACEMENT THERAPY

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Improvement and implementation of the health system methods of renal replacement therapy provided treatment and prolong life in patients with end-stage chronic renal failure (CRF), but led to other problems. To date, it is obvious that the quality of medical and social rehabilitation, and life expectancy of these patients is mainly determined by the underlying disease and not the choice of method of renal replacement therapy, the addition of many related diseases, such as the special place occupied by an infectious-suppurative processes of various locations. Interestingly, in patients with end-stage renal failure is characterized by certain peculiarities, both in terms of risk factors and the clinical manifestations and therapeutic approaches. Thus, in the Russian Federation according to the Register of renal replacement therapy at the end of 2009 in the treatment of dialysis (hemodialysis and peritoneal dialysis) were almost 19 000 patients (133,6 people per million population), five years earlier, only 11 (77,8 persons per million population) (Bikbov B.T. et al., 2011). Formation of secondary immunodeficiency in patients with chronic renal failure receiving replacement therapy with hemodialysis, explains their easy susceptibility to bacterial infection and the possibility of depression as a result of humoral factors of non-specific protection activate pathogenic microorganisms. Reducing the number of granulocytes in the inflammation, as well as the suppression of the phagocytic function may contribute to the development of systemic infection. In turn, the generalization of the process of bacterial infection, causes more inhibition of the function of all parts of the immune system (Kalantar-Zadeh K. et al., 2003). With the inevitability of empirical antibiotic use is not indicated the use of drugs, rapidly leading to the development of microbial resistance. But even without complying with this principle, the choice of drugs is complex. Thus, isolated from the urine of seven nosocomial *Klebsiella* strains were susceptible only to imipenem (71,4%), polymyxin (100%) and colistin (100%), sensitivity to piperacillin / tazobactam, tsefaperazon / sulbac-

tam and moxifloxacin proved to be extremely low. 14,3%, while the rest of the representatives of cephalosporin and fluoroquinolone antibiotics altogether absent (Gabrielian N.I., 2011). With an increasing number of antibiotic-resistant uropathogenic microorganisms in complex treatment of infectious-inflammatory complications in patients with terminal renal failure expedient implementation of specific bacteriophages. Experimental and clinical studies on bacteriophages carried out in recent years have shown their high efficacy in the treatment and prevention of infections caused by multidrug-resistant strains of bacteria (Kutateladze M., 2010). An important principle of antibiotic therapy of infectious-inflammatory complications in dialysis patients is also a strict individualization of its schemes and non-standard assignments, regulated by existing regulations, reducing the development of side effects of drugs. Ideally, a modification of antibiotic therapy should take into account the dynamic determination of pharmacokinetic parameters, but since this approach is not feasible in clinical practice, when selecting the dose of antibiotic should take into account patient age, residual renal function, the ways of elimination and the degree of dialyzable drug. Thus, a certain portion of patients with chronic renal failure receiving dialysis replacement therapy, puts a high risk for the development of infectious and inflammatory complications. The peculiarity of the risk factors, etiology and pathogenesis of infection-purulent process in terminal renal failure results in features of its clinical course, a complex of antibiotic therapy and prevention.

РАЗНОЕ

ВОЗМОЖНОСТЬ РЕГУЛИРОВАНИЯ АКТИВНОСТИ ЦИТОХРОМА P450 3A4 ВИТАМИНАМИ-АНТИОКСИДАНТАМИ

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В ряде экспериментальных и клинических исследований продемонстрирована возможность витаминов выступать в качестве средств регуляции биотрансформации и фармакологического действия лекарственных веществ, путем изменения активности ферментов метаболизма ксенобиотиков, в том числе системы цитохрома P450.

Для исследования каталитической активности цитохромов P450 были применены электрохимические системы.

Электрохимический анализ каталитической активности цитохрома P450 3A4 показал, что витамины С, А и Е влияют на восстановление цитохрома P450

3A4. Эти данные позволяют предположить возможность взаимного влияния витаминов и лекарственных препаратов, метаболизируемых цитохромом P450 3A4, при проведении комплексной терапии. Этот класс витаминов проявляет антиоксидантные свойства, что приводит к повышению катодного тока, соответствующего восстановлению гема этого функционально значимого гемопroteина. Аскорбиновая кислота в концентрации 0,028-0,56 мМ стимулирует катодный восстановительный пик (электрохимический сигнал) цитохрома P450 3A4. В присутствии диклофенака - типичного субстрата цитохрома P450 3A4 - наблюдается рост каталитического тока, свидетельствующий об электрокатализе и стимулирующем действии аскорбиновой кислоты. В присутствии витаминов А и Е также регистрируется дозозависимое (в диапазоне 10-100 мкМ) увеличение каталитического тока цитохрома P450 3A4: максимальное увеличение составляет $229 \pm 20\%$ для 100 мкМ витамина А, и $162 \pm 10\%$ для 100 мкМ витамина Е. Витамин Е в присутствии ингибитора итраконазола не дает существенного увеличения каталитического тока, в отличие от витамина А, что может указывать на проявление субстратных свойств витамином Е. Электрохимический подход для анализа каталитической активности цитохрома P450 3A4 и исследования влияния биологически активных соединений на электрокатализ является чувствительным и эффективным сенсорным подходом, позволяющим использовать низкие концентрации белка на электроде (до 10^{-15} моль/электрод), проводить анализ без участия белков-партнеров и выявлять взаимодействие лекарственных препаратов в доклинических экспериментах.

Выводы. Проведенное электрохимическое исследование в опытах *in vitro* продемонстрировало возможный механизм взаимодействия витаминов-антиоксидантов с лекарственными препаратами на уровне метаболизма. Полученные данные так же доказывают проявление субстратных свойств витамина Е по отношению к цитохрому P450 3A4.

ИСПОЛЬЗОВАНИЕ ИНДЕКСА ЦИТИРОВАНИЯ В ОПРЕДЕЛЕНИИ НАУЧНОГО КАЧЕСТВА

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Обычно качество научных наблюдений, исследований определялось просто оценкой, даваемой коллегами, которые получали информацию. Определение качества научного вклада является весьма не простой задачей. Со времени начала цифровой революции, с развитием международных баз данных опубликованных статей, ситуация изменилась. Начи-