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PATHOPHYSIOLOGY OF THE CORTICO-SYMPATHOADRENAL SYSTEM IN THE POSTOPERATIVE PERIOD OF PARTIAL NEPHRECTOMY

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Introduction. Organ-preserving kidney surgeries are widespread in urological practice. Any surgical intervention triggers a cascade of reactions in the body that are characteristic of stressful situations, which adversely affects blood flow volume in the parenchymal organs, worsens microcirculation, and reduces the trophic and reparative abilities of organs. The application of anti-ischemic protection is an essential part of patient rehabilitation to maintain renal function. **Objective.** To investigate the nephroprotective properties of α-tocopherol acetate (a-TA) and its effect on α-tocopherol acetate (a-TA) parameters of the cortico-sympathoadrenal system following organ-preserving kidney surgery. **Material and methods.** An experimental study was performed on 70 white laboratory rats, 10 of which were not subjected to surgical treatment. Sixty rats underwent lower pole left kidney superimposition with Z-joints. Postoperatively, 30 rats were intramuscularly injected with a 10% oil solution of 0.2 mL a-TA twice a day for 5 days. The cortico-sympathoadrenal system parameters were determined on the 7th, 14th, and 28th days. **Results.** Postoperative administration of a-TA resulted in early normalization of the cortico-sympathoadrenal system. **Conclusion.** The studied indices regarding the tissue of the operated kidney are responsible for regulating vascular tone, severity of the inflammatory response, microcirculation, and reparative processes. The use of a-TA accelerates recovery from organ-preserving surgery and biochemical abnormalities.

Keywords: kidney cancer; resection; ischemia; anti-ischemic protection; cortico-sympathoadrenal system; α-tocopherol acetate.

ПАТОФИЗИОЛОГИЯ КОРТИКО-СИМПАТО-АДРЕНАЛОВОЙ СИСТЕМЫ В ПОСЛЕОПЕРАЦИОННОМ ПЕРИОДЕ ПАРЦИАЛЬНОЙ НЕФРЭКТОМИИ

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Введение. Органосохраняющие операции на почке широко распространены в урологической практике. Любое хирургическое вмешательство вызывает в организме каскад реакций, характерных для стрессовой ситуации, которые неблагоприятно влияют на объем кровотока в паренхиматозных органах, ухудшают микроциркуляцию, уменьшая трофические и репаративные возможности органа. Применение средств противоишемической защиты является необходимым звеном реабилитации пациентов с целью сохранения почечной функции. **Цель исследования** — изучить нефропротекторные свойства α-токоферола ацетата (α-ТА), а также его влияние на показатели кортико-симпато-адреналовой системы после органосохраняющей операции на почке. **Материал и методы.** Выполнено экспериментальное исследование на 70 белых лабораторных крысах: 10 животных не подвергались хирургическому лечению, 60 крысам выполнена резекция нижнего полюса левой почки с наложением Z-образных швов. В послеоперационном периоде 30 животным внутримышечно вводили 10 % масляный раствор α-ТА по 0,2 мл 2 раза в день в течение 5 дней. Определение показателей кортико-симпато-адреналовой системы производили на 7, 14 и 28-е сутки. **Результаты.** Послеоперационное введение α-ТА приводит к ран-

ней нормализации состояния кортико-симпато-адреналовой системы. **Вывод.** Изучаемые показатели в ткани оперированной почки отвечают за регуляцию тонуса сосудов, выраженность воспалительного ответа, микроциркуляцию и репаративные процессы. Использование α-ТА ускоряет восстановление возникших вследствие органосохраняющей операции биохимических нарушений.

Ключевые слова: рак почки; резекция; ишемия; противоишемическая защита; кортико-симпато-адреналовая система; α-токоферола ацетат.

INTRODUCTION

Acute renal injury caused by ischemia/reperfusion during organ-preserving surgical treatment of the kidney is an independent risk factor for chronic kidney disease [1]. Kidney disease not only can exacerbate renal dysfunction but can also adversely affect systemic processes, most often in older patients [2]. Because of the urgency of this problem, an active search is under way for various agents that protect the kidneys against intraoperative trauma. At present, there are many ways to prevent ischemia, such as different variants of pharmacological preconditioning and control of the margin of resection [1, 3–7]. Unfortunately, these methods depend not only on the surgeon's experience but also on equipment available. The classical method of organ preservation in surgical treatment of the kidney is the application of "thermal" ischemia, which is considered safe for up to 20 min. Technically, it is not always possible to keep within this time interval or to avoid blood loss [8], which can affect future function of kidney tissue and lead to the development of renal failure [9]. Therefore, the development of methods for postoperative rehabilitation is an urgent task.

Lipid peroxidation processes are involved in the pathogenesis of acute ischemic renal injury during organ-preserving surgical treatment; thus, the use of antioxidants is a reasonable method of correcting the consequences of intraoperative trauma [3]. α-Tocopherol acetate (α-TA) is a natural fat-soluble antioxidant. In the body, it is located mainly in cell membranes. Numerous studies have proved that α-TA influences the redistribution of metabolic reactions in many adaptive processes that prepare cells for oxygen deprivation conditions: for example, it stimulates intracellular increases in the level of cyclic adenosine monophosphate (c-AMP), it supports reserve pathways for the formation of adenosine triphosphate (ATP) during glycolysis, and it activates the synthesis of protein and nucleic acids. α-TA also significantly improves the function of ischemic kidneys, normalizes sodium reabsorption, improves creatinine clearance, reduces the accumulation of malondialdehyde without affecting significantly the activity of antioxidant enzymes, and lowers the oxygen tension in the cortex of the kidney. The use of α-TA as a means of ischemic preconditioning to increase the antioxidant reserve in tissues has increased the rate of survival among experimental animals to 50% [10–23].

MATERIALS AND METHODS

The study was performed with 70 white laboratory rats weighing 200 to 300 g. The work with animals was conducted in accordance with the current Rules for Conducting Works Using Experimental Animals and the Guiding Principles for Biomedical Research Involving Animals. Ten animals were not subjected to surgical treatment and served as an intact group for determining reference values. The other 60 rats underwent organ-preserving surgical treatment of the kidney (resection of the lower pole of the left kidney with the application of Z-shaped sutures to the resection area). In the postoperative period, the 60 animals that underwent surgery were divided into two groups: the control group (n = 30), in which only surgical treatment was performed, and the study group (n = 30), in which 0.2 mL of 10% α-TA oil solution was injected intramuscularly twice a day for 5 days. The levels of creatinine and the hormones of the corticosympathetic adrenal system (CSAS) (adrenaline, noradrenaline, dopamine, serotonin, histamine, and 11-oxycorticosteroid) in the blood and the operated kidney were measured in all laboratory animals on

days 7, 14, and 28. The CSAS indices were studied with the Hitachi MPF-4 spectrophotometer (Hitachi High Technologies, Tokyo). The concentration of test substances in the blood was expressed in micrograms per milliliter, whereas that in the kidney was expressed in micrograms per gram. The levels of adrenaline, noradrenaline, and dopamine were determined by a differential fluorometric method according to Osinskaya (1977), on the basis of their oxidation by iodine with the formation of fluorescent products. The histamine content in the blood was determined by a method based on the measurement of the fluorescence of the condensation products of histamine with ortho-phthaldehyde (the Shore method in the modification of Meshcheryakova, 1987), and that of serotonin was determined with ninhydrin (Proshina, 1981; Menshikova, 1987). The concentration of 11-oxycorticosteroids was determined according to the method of Pankova and Usvatova (1973) with a standard sample.

The rats were sacrificed in compliance with the Guiding Principles for Biomedical Research Involving Animals and the rules set forth in the Declaration of Helsinki.

RESULTS

Changes in the studied indicators of CSAS are presented in Table 1. The level of adrenaline in the animals of the control group increased on day 7 after the surgery in the blood by 26% ($p > 0.05$) and by 40% in the kidneys ($p < 0.05$). By day 14 after surgery, adrenaline levels had decreased sharply by 53% in the blood ($p < 0.05$), which was 41% lower than the preoperative level, and by 59% in the kidneys ($p < 0.05$), which was 43% lower than before surgery. By day 7 after surgery, the level of adrenaline in the blood in the study group had increased by 41% ($p < 0.05$). By day 14, this indicator, in both the study group and the control group, had decreased by 50% and had fallen to 29% below normal values ($p < 0.05$). In the kidneys, on postoperative day 7, in animals that received α-TA, the increase was 26% ($p > 0.05$). By day 14, the adrenaline level in the study group had decreased by 45% ($p < 0.05$), which was 31% ($p < 0.05$) below normal. By day 28, the level of adrenaline had normalized both in the blood and in the kidneys in both experimental groups.

After the surgical intervention in the animals of the control group, the concentration of noradrenaline in the blood had increased significantly (42%) by day 14 and subsequently normalized. In the study group, similar dynamics of the indicator were evident: namely, an increase to 51% ($p < 0.05$) by day 14, followed by a decrease. At the end of the experiment, the level of noradrenaline remained 39% higher than preoperative values ($p < 0.05$). In the kidneys in the control group, the level of noradrenaline had increased by 18% on day 7 ($p < 0.05$) and by 30% on day 14 ($p < 0.05$), and the levels subsequently normalized by the end of the experiment ($p > 0.05$). Changes in noradrenaline in the kidneys in the study group were not significant.

The level of dopamine in the control group decreased progressively in the blood until day 14 (by 39% by day 7 and by 50% by day 14). By the end of the experiment, its content tended to increase (26%) but did not reach the baseline level. In the kidneys, the maximum (to one third of normal levels) decrease in dopamine ($p < 0.05$) was observed on day 7, and then dopamine content gradually increased; however, by day 28, it remained below the preoperative level by 37% ($p < 0.05$). On day 7 after the surgery, in the study group, levels of dopamine had decreased by 46% in the blood ($p < 0.05$) and by 56% in the kidneys ($p < 0.05$). After α-TA was administered, the concentration of dopamine increased from day 14 and exceeded the baseline level by 49% in the blood by the end of the experiment ($p < 0.05$); in the kidneys, in contrast, it exceeded the baseline level by only 32% ($p < 0.05$). In the study group, there was a significant increase by 55% in the level of dopamine by day 14 of the experiment and a significant increase by 101% by the end of the experiment. There were no statistically significant changes in the kidneys in the control group.

Glucocorticoid activity in the blood of control group animals was 51% higher on day 7 ($p < 0.05$) and decreased by 12% on day 14; values remained higher (by 32%) in relation to the reference level ($p < 0.05$) and again increased by the end of the experiment to 82% of the baseline level ($p < 0.05$). In the study group, the indices on days 7 and 14 were identical to those in the control group, and on day 28, there was a decrease in

Table 1

Changes in the indices of the cortico–sympathetic–adrenal system in white rats with a resected kidney in the study and control groups.

Indicator	Group	Before the surgery (n = 10)	Day 7 (n = 60)	Day 14 (n = 60)	Day 28 (n = 60)
Adrenaline	Blood (μg/mL)				
	Control group	0.094 ± 0.007	0.118 ± 0.015	0.055 ± 0.009*	0.080 ± 0.006
	Study group	0.094 ± 0.007	0.133 ± 0.016*	0.067 ± 0.008*	0.100 ± 0.009
	Kidney (μg/g)				
	Control group	0.562 ± 0.052	0.788 ± 0.084*	0.321 ± 0.039*	0.540 ± 0.033
	Study group	0.562 ± 0.052	0.706 ± 0.066	0.388 ± 0.042*	0.525 ± 0.040
Noradrenaline	Blood (μg/mL)				
	Control group	0.114 ± 0.008	0.135 ± 0.010	0.162 ± 0.011*	0.122 ± 0.014
	Study group	0.114 ± 0.008	0.144 ± 0.013	0.172 ± 0.016*	0.158 ± 0.013*
	Kidney (μg/g)				
	Control group	3.186 ± 0.198	3.764 ± 0.194*	4.077 ± 0.232*	3.433 ± 0.230
	Study group	3.186 ± 0.198	3.705 ± 0.172	3.865 ± 0.288	3.222 ± 0.221
Dopamine	Blood (μg/mL)				
	Control group	0.111 ± 0.007	0.068 ± 0.011*	0.055 ± 0.008*	0.082 ± 0.006*
	Study group	0.111 ± 0.007	0.060 ± 0.010*	0.085 ± 0.007*/**	0.165 ± 0.020 */**
	Kidney (μg/g)				
	Control group	1.230 ± 0.126	0.408 ± 0.049*	0.653 ± 0.075*	0.780 ± 0.099*
	Study group	1.230 ± 0.126	0.544 ± 0.077*	0.690 ± 0.098*	0.842 ± 0.087*
11-oxycorticosteroid	Blood (μg/mL)				
	Control group	0.65 ± 0.06	0.98 ± 0.11*	0.86 ± 0.10	1.18 ± 0.12*
	Study group	0.65 ± 0.06	0.98 ± 0.11*	0.86 ± 0.10	0.48 ± 0.10**
Histamine	Blood (μg/mL)				
	Control group	0.102 ± 0.003	0.137 ± 0.011*	0.184 ± 0.013*	0.109 ± 0.004
	Study group	0.102 ± 0.003	0.112 ± 0.014	0.155 ± 0.015*	0.104 ± 0.007
	Kidney (μg/g)				
	Control group	0.502 ± 0.045	0.901 ± 0.088*	1.100 ± 0.132*	0.736 ± 0.077*
	Study group	0.502 ± 0.045	0.728 ± 0.084*	0.789 ± 0.100*	0.461 ± 0.033**
Serotonin	Blood (μg/mL)				
	Control group	0.068 ± 0.003	0.137 ± 0.010*	0.184 ± 0.013*	0.109 ± 0.004*
	Study group	0.068 ± 0.005	0.096 ± 0.008*/**	0.101 ± 0.010*/**	0.077 ± 0.011**
	Kidney (μg/g)				
	Control group	0.418 ± 0.032	0.633 ± 0.055*	0.750 ± 0.061*	0.580 ± 0.052*
	Study group	0.418 ± 0.032	0.580 ± 0.039*	0.660 ± 0.060*	0.404 ± 0.030**

*Significant difference ($p < 0.05$) between experimental and intact animals. **Significant difference ($p < 0.05$) between groups of control animals and groups of animals treated.

the level of glucocorticoid activity by 44%; this index reached the preoperative level ($p > 0.05$) and was 2.5 times lower than the reference values.

The level of histamine in the blood and in the kidneys of control animals were significantly higher on day 7 (43% and 79%, respectively) and on day 14 (80% and 119%, respectively) and then decreased (became normalized in the blood but remained 47% above the norm [$p < 0.05$] in the kidneys). With the administration of α-TA, in the blood a significant increase in the index (52%) occurred only on day 14. In the kidneys of study group animals, the histamine level significantly increased on days 7 and 14 after the surgery by 45% and 57%, respectively, with the normalization of the index

by day 28 ($p > 0.05$) and was 37% lower than the level of histamine in the kidneys of the control group animals ($p < 0.05$).

The level of serotonin in the blood of control group animals doubled by the end of the first week ($p < 0.05$) and increased by 2.7 times by the end of the second week ($p < 0.05$). By the last day of the experiment, the level of serotonin had decreased but remained 1.6 times ($p < 0.05$) higher than the preoperational level. In the study group, a significant increase in serotonin concentration was observed only on days 7 and 14 of the experiment (by 41% and 49%, respectively, in blood and by 39% and 59%, respectively, in the kidneys). On day 28 of the experiment, serotonin levels in the study group had returned to normal ($p > 0.05$). In comparison with the control group, the use of α-TA produced a significant decrease in serotonin levels in the blood throughout the postoperative period (by 43%, 82%, and 42%, respectively). In comparison with control group indices, the changes produced by α-TA in the kidneys remained statistically insignificant on days 7 and 14, and at the end of the experiment, the serotonin level was below the control level by 30% ($p < 0.05$).

Fluctuations in the level of blood creatinine throughout the experiment in both groups were within the normal range and were statistically insignificant.

DISCUSSION

The kidney is the most important excretory and endocrine organ [24]. Any surgical intervention involving the kidneys affects the activity of the sympathoadrenal and renin–angiotensin–aldosterone systems and the metabolism of catecholamines in the body, which are closely related [25, 26]. Catecholamines, serotonin, histamine, and kinins from the source of ischemic injury play an important role in the occurrence of primary microcirculatory and rheological disorders in the renal parenchyma and trigger disorders of systemic hemodynamics [27, 28]. To assess the severity of biochemical abnormalities in the parenchyma of the operated kidney, we monitored the levels of CSAS indices responsible for the regulation of vascular tone, the severity of the inflammatory response, the microcirculation, and reparative processes. Resection of the lower pole of the left kidney with preservation of the contralateral organ led to a hormonal-mediator imbalance, which was manifested by an increase in vasoconstrictive monoamines (adrenaline, noradrenaline, and serotonin) and in 11-oxycorticosteroid, which potentiated them, and by a decrease in vasodilatory monoamines (dopamine). The blood creatinine indices in both groups were not much affected by the surgery performed and did not differ from the similar blood values of the intact rats, which, in our opinion, reflected sufficient total renal function. The mechanism of the protective effect of α-TA as a natural antioxidant is based not only on its antioxidant properties but also on its membrane-stabilizing action: the ability to influence the adaptation of cellular metabolism to the conditions of ischemia. Its use in the postoperative period led to an early recovery of the CSAS indices in the experiment.

CONCLUSION

The dynamics of the levels of adrenaline, noradrenaline, dopamine, serotonin, histamine, and 11-oxycorticosteroid in the blood and tissue of the kidneys of laboratory animals were affected by the use of α-TA in the postoperative period. These changes are a prerequisite for improving microcirculation, reducing the intensity of inflammatory reactions, and increasing reparative processes in the surgical site; these findings confirm the nephroprotective properties of α-TA.

REFERENCES

1. Индароков Т.Р., Серегин А.В., Лоран О.Б., и др. Превентивный гемостатический шов при открытой резекции почки как один из способов сохранения почечной функции // Онкоурология. – 2017. – Т. 13. – № 3. – С. 39–45. [Indarokov TR, Seregin AV, Loran OB, et al. Preventive hemostatic suture during open kidney resection as an option to preserve the renal function. *Onkourologiya*. 2013;9(1):17-23. (In Russ.)]. doi:10.17650/1726-9776-2017-13-3-39-45.
2. Дряженков И.Г., Комлев Д.Л., Лось М.С. Факторы ишемического повреждения почки при ее резекции // Клиническая медицина. – 2013. – Т. 91. – № 6. – С. 21–25. [Dryazhenkov IG, Komlev DL, Los MS. Factors of ischemic injury of the kidney when

itisresected. *Klinicheskaya meditsina.* 2013;91(6):21-25. (In Russ.)]
3. Гребенчиков О.А., Лихванцев В.В., Плотников Е.Ю., и др. Молекулярные механизмы развития и адресная терапия синдрома ишемии-реперфузии // Анестезиология и реаниматология. – 2014. – № 3. – С. 59–67. [Grebenchikov OA, Likhvantsev VV, Plotnikov EYu, et al. Molecular mechanisms of ischemic-reperfusion syndrome and its therapy. *Anesthesiology and Reanimatology.* 2014;(3):59-67. (In Russ.)].
4. Ивахно К.Ю., Карнаух П.А. Совершенствование открытой резекции почки с использованием интраоперационного УЗИ // Медицинская наука и образование Урала. – 2012. – № 2. – С. 102–103. [Ivakhno KYu, Karnaukh PA. Perfection of open resection of the kidney with the use of intraoperative ultrasound. *Medical science and education of the Ural.* 2012;(2):102-103. (In Russ.)]
5. Носов А.К., Лушина П.А., Петров С.Б. Лапароскопическая резекция почки без ишемии и без наложения гемостатического шва на зону резекции у пациентов с раком почки // Урологические ведомости. – 2016. – Т. 6 (спецвыпуск). – С. 76–77. [Nosov AK, Lushina PA, Petrov SB. Laparoscopic resection of the kidney without ischemia and without the application of the haemostatic suture to the resection area in patients with kidney cancer. *Urologicheskie vedomosti.* 2016;6(Suppl):76-77. (In Russ.)]
6. Сафронова Е.Ю., Нюшко К.М., Алексеев Б.Я., и др. Способы осуществления гемостаза при выполнении резекции почки // Исследования и практика в медицине. – 2016. – Т. 3. – № 1. – С. 58–65. [Safronova EYu, Nyushko KM, Alekseev BYa, et al. Methods of carrying out hemostasis while performing a resection of the kidney. *Research and practice in medicine.* 2016;3(1):58-65. (In Russ.)]
7. Чернышев И.В., Ханакаев Р.А. Анализ собственной и индуцированной флуоресценции злокачественных новообразований и интактных тканей почек // Экспериментальная и клиническая урология. – 2014. – № 4. – С. 32–37. [Chernishev IV, Khanakaev RA. Analysis of own and induced fluorescence of the malignant kidney tumors and healthy tissue. *Experimental and Clinical Urology.* 2014;(4):32-37. (In Russ.)]
8. Зырянов А.В., Пономарев А.В. Время тепловой ишемии и кривая обучения при малоинвазивной резекции почки // Урология. – 2013. – № 9. – С. 26–30. [Zyryanov AV, Ponomarev AV. Warm ischemia time and learning curve in minimally invasive partial Nephrectomy. *Urology*. 2013;(9):26-30. (In Russ.)]
9. Евсеев С.В., Гусев А.А. Значение оценки почечной функции при почечно-клеточном раке // Вестник урологии. – 2013. – № 3. – С. 39–53. [Evseev SV, Gusev AA. Value assessment of renal function in renal cell carcinoma. *Herald of Urology.* 2013;(3):39-53. (In Russ.)]
10. Aryamanesh S, Ebrahimi SM, Abotaleb N, et al. Role of endogenous vitamin E in renal ischemic preconditioning process: differences between male and female rats. *Iran Biomed J.* 2012;16(1):44-51.
11. Shokeir AA, Barakat N, Hussein AA, et al. Role of combination of L-arginine and α-tocopherol in renal transplantation ischaemia/reperfusion injury: a randomized controlled experimental study in a rat model. *BJU Int.* 2011;108(4):612-618. doi: 10.1111/j.1464-410X.2010.09943.x.
12. Yurdakul T, Kulaksizoglu H, Pişkin MM, et al. Combination antioxidant effect of α-tocoferol and erdosteine in ischemia-reperfusion injury in rat model. *Int Urol Nephrol.* 2010;42(3):647-655. doi: 10.1007/s11255-009-9641-y.
13. Кирпатовский В.И., Голод Е.А., Надточий О.Н., Обухова Т.В. Влияние α-Токоферола на парциальные функции ишемизированной почки // Урология. – 2006. – № 5. – С. 80–84. [Kirpatovskiy VI, Golod EA, Nadtochiy ON, Obukhova TV. Effects of alpha-tocopherol on partial functions of the ischemic kidney. *Urologiia.* 2006;(5):80-84. (In Russ.)]
14. Gurel A, Armutcu F, Sahin S, et al. Protective role of alpha-tocopherol and caffeic acid phenethyl ester on ischemia-reperfusion injury via nitric oxide and myeloperoxidase in rat kidneys. *Clin Chim Acta.* 2004;339(1-2):33-41.
15. Avunduk MC, Yurdakul T, Erdemli E, Yavuz A. Prevention of renal damage by alpha tocopherol in ischemia and reperfusion models of rats. *Urol Res.* 2003;31(4):280-285. doi: 10.1007/s00240-003-0329-y.
16. Attia DM, Verhagen AM, Stroes ES, et al. Vitamin E alleviates renal injury, but not hypertension, during chronic nitric oxide synthase inhibition in rats. *J Am Soc Nephrol.* 2001;12(12):2585-93.
17. Rhoden EL, Pereira-Lima L, Telöken C, et al. Beneficial effect of alpha-tocopherol in renal ischemia-reperfusion in rats. *Jpn J Pharmacol.* 2001;87(2):164-166.
18. Nagel E, Meyer zu Vilsendorf A, Bartels M, Pichlmayr R. Antioxidative vitamins in prevention of ischemia/reperfusion injury. *Int J Vitam Nutr Res.* 1997;67(5):298-306.
19. Кирпатовский В.И., Никифорова Н.В., Кудрявцев Ю.В., Надточий О.Н. Использование эмульсии альфа-токоферола для антиоксидантной защиты ишемизированных и консервированных почек // Бюллетень экспериментальной биологии и медицины. – 1996. – Т. 121. – № 5. – С. 499–503. [Kirpatovskiy VI, Nikiforova NV, Kudriavtsev IuV, Nadtochii ON. Use of an alpha-tocopherol emulsion for antioxidant protection of ischemic and conserved kidneys. *Bjulleten eksperimentalnoj biologii i mediciny.* 1996;121(5):499-502. (In Russ.)]
20. Aktoz T, Aydogdu N, Alagol B, et al. The protective effects of melatonin and vitamin E against renal ischemia-reperfusion injury in rats. *Ren Fail*. 2007;29(5);535-542.
21. Федорук А.С., Гоженко А.И., Роговый Ю.Е. Защитное воздействие α-токоферола на функцию почек и перекисное окисление липидов при острой гемической гипоксии // Патологическая физиология и экспериментальная терапия. – 1998. – № 4. – С. 35–38. [Fedoruk AS, Gozhenko AI, Rogovy YuE. Protective effect of a-to-caffeine on kidney function and lipid peroxidation in acute hemic hypoxia. *Pathological physiology and experimental therapy*. 1998;(4):35-38 (In Russ.)]

22. Надточий О.Н. Профилактика постишемических функциональных расстройств почки при операциях с временным прекращением почечного кровотока (экспериментальное исследование): дис. … канд. мед.наук. – М., 2000. [Nadtochiy ON. Prophylaxis of postischemic functional disorders of the kidney during operations with temporary discontinuance of renal blood flow (experimental study). [dissertation] Moscow; 2000. (In Russ.)]
23. Кирпатовский В.И., Надточий О.Н., Сыромятникова Е.В. Возможности пролонгации допустимых сроков ишемии почки при использовании разных вариантов противоишемической защиты // Урология. – 2003. – № 3. – С. 7–10. [Kirpatovskiy VI, Nadtochy ON, Syromyatnikova EV. Possibilities of prolonging the permissible periods of kidney ischemia when using different variants of anti-ischemic protection. *Urologiia.* 2003;(3):7-10. (In Russ.)]
24. Nishimura M, Takahashi H, Yoshimura M. Upregulation of the brain renin-angiotensin system in rats with chronic renal failure. *Acta Physiol.* 2007;189:369-377.
25. Фатеев Д.М. Влияние нефрэктомии и резекции почки на адаптивные возможности системы кровообращения (клинико-экспериментальное исследование): Дис. … канд. мед. наук. –СПб., 2013. [Fateev DM. Influence of nephrectomy and kidney resection on the adaptive possibilities of the circulatory system (clinical and experimental research). [dissertation] St. Petersburg; 2013. (In Russ.)]. Доступно по: www.infran.ru/Diss-Sovet/Fateev-text-autoref.pdf. Ссылка активна на 20.04.18 г.
26. Иванов А.П. Клинико-экспериментальные обоснования органосохраняющих операций при раке почки: Дисс. … д-ра мед. наук. – М., 2012. [Ivanov AP. Clinical and experimental substantiations of organ-saving operations in kidney cancer. [dissertation] Moscow; 2012. (In Russ.)]. Доступно по: http://muctudde.ucoz.ru/news/kliniko_ehksperimentalnye_obosnovanija_organoso/2013-04-12-101. Ссылка активна на 20.04.18 г.
27. Boero R, Pignataro A, Ferro M, Quarello F. Symparhetic nervous system and chronic renal failure. *Clin and Exper Hypertension.* 2001;23(1-2):69-75.
28. Pilote L, Abrahamowicz M, Eisenberg M, et al. Effect of different angiotensin-converting-enzyme inhibitors on mortality among elderly patients with congestive heart failure. *CMAJ.* 2008;178:1303-1311.
29. Николаева А.А., Королева С.В., Ашмарин И.П. Дофамин–серотонин–соматостатин: изучение взаимодействий в этой системе обещает новые перспективы в теории и практике // Экспериментальная и клиническая фармакология. – 2009. – № 2. – С. 60–64. [Nikolaeva AA, Koroleva SV, Ashmarin IP. Research of interactions in the dopamine-serotonin-somatostatin system promises new outlook in fundamental and practical respects. *Experimental and Clinical Pharmacology*. 2009;(2):60-64.(In Russ.)]
30. Бизунок Н.А. Биогенные амины — эндогенные модуляторы клеточной генерации активных форм кислорода // Белорусский медицинский журнал. – 2004. – № 4(10). – С. 11–8. [Bizunok NA. Biogenic amines – endogenous modulators of the cellular reactive oxygen species generation. *Belorusian Medical Journal.* 2004;4(10):11-18. (In Russ.)]

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