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THE EFFECT OF EXOGENOUS PEROXIREDOXIN 6 ON THE MORPHOFUNCTIONAL STATE OF ISOLATED RAT KIDNEY

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Objective: to investigate the role of peroxiredoxin 6 (PRX6) in preserving the morphofunctional state of ischemic isolated kidney during perfusion. **Materials and methods.** The model of an isolated perfused rat kidney was used. Ischemia time was 5 and 20 minutes, perfusion was 50 minutes. To evaluate the effectiveness of PRX6 at different ischemia times, we used the conventional criteria of kidney function and histological methods. **Results.** During short warm ischemia times, exogenous PRX6 improves the morphofunctional state of an isolated kidney during perfusion. During this period, the main criteria for functioning of the isolated ischemic kidney reach acceptable values, renal parenchyma is without severe damage. By the end of perfusion, there was an increase in urine flow rate, glomerular filtration rate, fractional glucose reabsorption, urine urea concentration and proportion of primary urine from 1.5 to 2 times compared with the control lesion. At 20-minute ischemia, the isolated kidney can be recognized as non-viable according to the functioning criteria; the positive effect of PRX6 is leveled. **Conclusion.** The use of recombinant peroxiredoxin 6 for preserving the morphofunctional state of isolated kidneys can be an effective approach in preventing ischemia–reperfusion injury.

Keywords: isolated kidney, ischemia, perfusion, peroxiredoxin.

INTRODUCTION

The popular use of an isolated kidney as a subject of research is down to the convenience of its use for studying renal secretory function, drug metabolism, screening of clinically relevant drug interactions and many aspects of renal metabolism without systemic influences such as blood pressure, hormones or nerve innervation [1–3]. An isolated kidney is an ex vivo model that consists of a whole kidney isolated from the vasculature. Two modifications of the model can be distinguished. Most researchers use the modification described by Nishitsutsuji-Uwo et al. – kidney perfusion through the superior mesenteric artery without ischemia period [4, 5]. The second modification is kidney perfusion retrogradely, through the abdominal aorta without an ischemia period [3, 6]. To interpret the results, it is important that the isolated kidney functions throughout the perfusion period. A number of criteria are used to assess the functioning [1]. In this work, we used a retrograde perfusion model of the kidney; the principal point was the presence of ischemia period of the isolated kidney.

Ischemia and subsequent organ reperfusion activate pathological processes; they trigger an avalanche-like growth of reactive oxygen species and development of oxidative stress, thereby leading to structural and functional tissue damage [7, 8]. Ischemia-reperfusion injury (IRI) is the main cause of primary graft dysfunction and reduced graft viability [9]. In this case, to reduce the concentration of reactive oxygen species and reduce the lesion of isolated organs, the use of antioxidant drugs can be the main therapy direction. In this regard, the use of peroxiredoxin antioxidant enzymes can be a promising solution due to their wide distribution in the body and multifunctionality [10–13]. Among the family members, peroxiredoxin 6 (Prx6) has been the subject of the largest number of studies indicating its protective role in free-radical pathologies [8, 14–16], including in the protection of isolated organs from IRI [17, 18]. Given the protective role of Prx6, the possibility of its application for preserving the morphofunctional state of isolated ischemic kidney should be studied.

The **objective** is to study the role of peroxiredoxin in preserving the morphofunctional state of ischemic isolated kidneys during perfusion.

MATERIALS AND METHODS

Male Wistar rats weighing 230 g were used in the experiments. The animals were kept in a vivarium at the Institute of Cell Biophysics (ICB), Pushchino, Moscow. Experiments with the laboratory animals were conducted in accordance with the provisions of the 1986 European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes. The main document regulating the conduct of this study is the ICB Guidelines for Working with Laboratory Animals, No. 57. dated December 30, 2011.

Recombinant Prx6 was obtained at the Laboratory of Reception Mechanisms, Institute of Cell Biophysics, according to the previously described method [19].

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We used the isolated perfused kidney (IPK) model proposed by J. Czogalla el al. with some modifications [3]. The rats were anesthetized by intravenous injection of 0.5 ml of 3.5% (3 mg/kg) Zoletil 100. Heparin (5000 U/ml) was used to prevent blood clotting. Ischemia was initiated by decapitation. Two time periods of ischemia were chosen: 5 and 20 minutes. The perfusion time was 50 minutes. DMEM culture medium (GIBCO, Invitrogen) with 4.5 g/L glucose content was used as the perfusion solution. The medium included urea (5 mM/liter), creatinine (80 μmM/liter), 6% BSA, and 0.6% BSA. Before perfusion, the solution was oxygenated with an O_2/CO_2 mixture (95%/5%), pH 7.4. Solution temperature was subnormothermic (30–35 °C). The isolated kidney perfusion algorithm is shown in Fig. 1.

Ischemia period. With the onset of ischemia, within 5 minutes, the right kidney was isolated from the common vascular system by consecutive application of ligatures on the vessels and catheterization of the renal artery through the abdominal aorta. Additionally, the inferior vena cava was dissected and then catheterized. The right ureter was isolated, catheterized and placed in a urine collection tank [3, 20]. After 5 minutes of ischemia, blood was removed from the vascular bed of the isolated kidney by flushing it with a perfusion buffer for 5 minutes. To determine the effects of exogenous peroxiredoxin 6, 0.2 mg/ml Prx6 was added to the perfusion buffer and perfused in the isolated kidney during blood removal from the vascular bed. Perfusion rate at this stage was 3 ml/min. The exogenous Prx6 concentration in the perfusion solution was chosen based on previously obtained data on effective reduction of IRI of the small intestine and kidneys using Prx6 [8, 14].

Perfusion period. At the end of ischemia, the isolated kidney was perfused for 50 minutes with a perfusion buffer. There was no Prx6 in the perfusion buffer at this stage. The first 20 minutes of perfusion was the stabilization period. Throughout the perfusion period, urine was collected from the ureter every 10 minutes. At the end of perfusion, the renal tissue was fixed for further examination. All rats were divided into 10 groups (N = 5) (Table 1).

To assess the effectiveness of Prx6 as a means of preserving the morphofunctional characteristics of the isolated kidney throughout the perfusion period, several generally accepted functioning criteria were analyzed [1]. The magnitude of these criteria was determined every 10 minutes in the studied urine samples.

– Perfusion pressure, mmHg. (PP) was maintained at 90–100 mmHg and regulated by changing perfusion flow rate (PFR). PFR was considered satisfactory if it corresponded to normal renal blood flow rate – 4–5.3 ml/min·g of the kidney [21].
– Urine flow rate (UFR), μl/min, was calculated by dividing the collected volume of urine from the ureter by the time. The first urine collection was initiated 20 minutes after perfusion had started, since the first 15 minutes of urination was irregular. UFR values below 30 μl/min are unsatisfactory and indicate the absence of ultrafiltration processes [1].
– Glomerular filtration rate (GFR), ml/min·g, was determined by creatinine clearance using the equation [5]:

$$GFR = \frac{M_{Cr} \times UFR}{P_{Cr}},$$

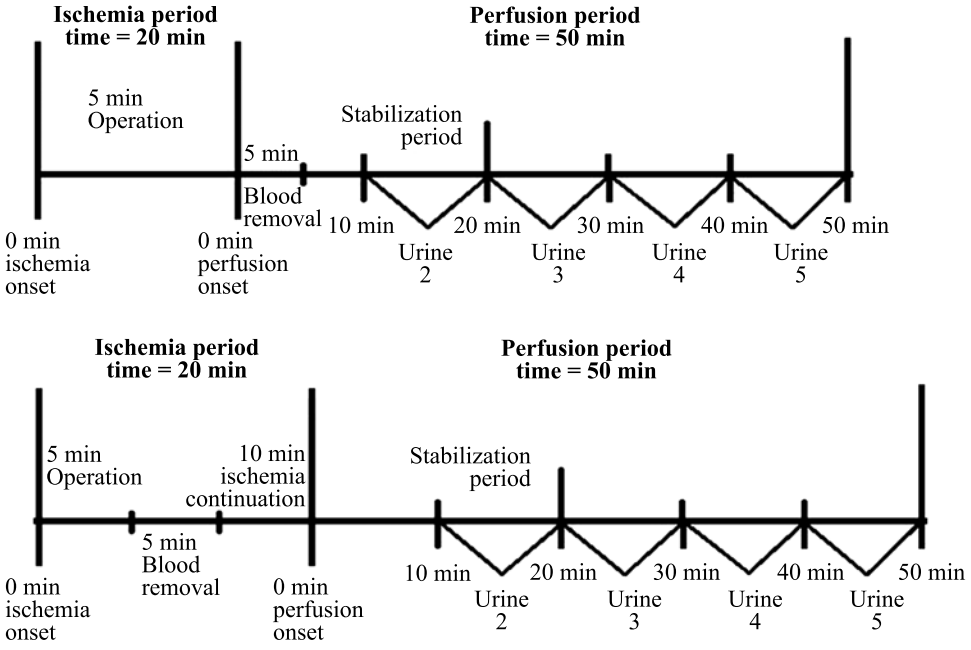

Fig. 1. Isolated kidney perfusion algorithm: а – ischemia time 5 min; б – ischemia time 20 min. Prx6 (0,2 mg/ml) was added to perfusion buffer at the stage blood removal. There is no Prx6 in the perfusion buffer during the perfusion period

M_{Cr} is urine creatinine level (mg/ml), UFR is urine flow rate (ml/min), and P_{Cr} is perfusate creatinine concentration (mg/ml). The minimum allowable value for GFR is >0.5 mL/min [6]. Creatinine levels in the investigated urine and perfusate samples were determined on Reflotron Plus device (Roche Diagnostics, Switzerland) every 10 minutes.

– Reabsorbed glucose fraction (RGF), %, is expressed as the fraction of glucose from ultrafiltrate reabsorbed by the kidneys [1, 5]:

$$RGF = 1 - \frac{UFR \times M_{Gl}}{GFR \times P_{Gl}},$$

M_{Gl} is urine glucose level, P_{Gl} is perfusate glucose level, GFR is glomerular filtration rate. Glucose levels in tested urine samples were determined on Accu-Chek glucometer (Roche, Germany) every 10 minutes. RGF reflects the functionality of proximal channels and should be at least 90% in IPK model [1, 2].

– Terminal urine percentage (TUP), %, is expressed as a ratio of terminal urine amount in the sample to GFR. This criterion reflects the % of ultrafiltrate that is excreted as terminal urine [22].

– The urine urea level (UUL), μmol/10 min, was measured as urea concentration in urine sample multiplied by the amount of secondary urine in the sample. Urea concentration in the tested urine samples was determined on a Reflotron Plus device (Roche Diagnostics, Switzerland) every 10 minutes. Urea concentration in perfusate was 5 mM.

Renal tissue was subjected to histological examination, including H&E staining of paraffin sections of renal tissue (VITROSTAIN Biovitrum, Russia). Slice thickness was 3 microns. Microscopic analysis of sections was performed on a Leica DM 6000 microscope with a Leica DFC 490 digital camera.

Statistical analysis and plotting were performed using SigmaPlot 11.0 software (Systat Software Inc.). Results were expressed as mean value ± standard deviation. A P value <0.05 was considered statistically significant.

RESULTS

Assessment of the functional state of isolated ischemic kidney

Groups 1–4 were subjected to a 5-minute ischemia and 50-minute perfusion. The design of the experiment is shown in Fig. 1.

No urine formation was observed when 6% BSA was injected into the perfusion buffer (group 1), although PP and PFR were consistent with normal values throughout the perfusion period. The absence of urine made it impossible to assess the functional criteria under study. In group 2 (0.6% BSA), by the end of perfusion, of all criteria, only PFR and UFR corresponded to minimally permissible values (5.7 ± 0.5 ml/min·g and 49 ± 2.5 μL/min, respectively).

The dynamics of the functioning criteria of the isolated ischemic kidney during perfusion in groups 3–4 is shown in Fig. 2. PP and PFR were constant during perfusion in both groups and had acceptable values. Prx6 had no effect on the dynamics of these criteria (Fig. 2, a). For UFR, there was an increase during perfusion and criterion values were above the minimum acceptable values throughout the perfusion period in both groups. With Prx6, there was a significant 1.5-fold increase in UFR by the end of perfusion relative to group 3 (115 ± 23 μL/min and 178 ± 28 μL/min, respectively) (Fig. 2, b, Table 2). In group 3, GFR did not change during the perfusion period and did not reach minimum permissible values (0.2 ± 0.04 mL/min·g) by the end of perfusion (Fig. 2, b); RGF, although increasing during perfusion, also did not reach minimum tolerated values at 71% by the end of perfusion (Fig. 2, d, Table 2). Using Prx6 brings these criteria to values above the minimum. The data revealed a statistically significant difference between groups 3 and 4 in these criteria by the end of per-

Table 1

Experimental groups

Experimental group	Ischemia time (min)	Additive/stage of adding additive to the perfusion buffer
1	5	6% bovine serum albumin (BSA) / perfusion period
2		0.6% BSA / perfusion period
3		No additive
4		Prx6 / blood removal stage
5	20	6% BSA / perfusion period
6		0.6% BSA / perfusion period
7		No additive
8		Prx6 / blood removal stage
9	0	No perfusion
10	90	No perfusion

Note. BSA was in the perfusate at the perfusion stage. Prx6 was in perfusate at the blood removal stage. Group 9 – kidneys of intact animals, group 10 – kidneys without perfusion period.

fusion (Table 2). TUP is higher in group 3, here 63% of the primary ultrafiltrate was excreted as terminal urine; in contrast, in the Prx6 group, this figure was 1.5-fold lower ($p < 0.05$) (Fig. 2, g). Both groups showed an increase in UUL toward the end of perfusion; however, this criterion was significantly (2-fold) higher in the Prx6 group (7.3 ± 1.8 μmol/10 min and 13 ± 1.7 μmol/10 min, respectively) (Fig. 2, e). Table 2 summarizes the values of the renal function criteria in groups 1–4 at the end of perfusion.

Groups 5–8 were subjected to a 20-minute ischemia period, with a 50-minute perfusion period. The design of the experiment is shown in Fig. 1.

When 6% BSA was injected into the perfusion buffer (group 5), no urine formation was observed, PFR did not meet the minimum acceptable values. Absence of urine made it impossible to assess the function parameters under study. In group 6 (0.6% BSA), by the end of perfusion, of all the criteria, only UFR corresponded to

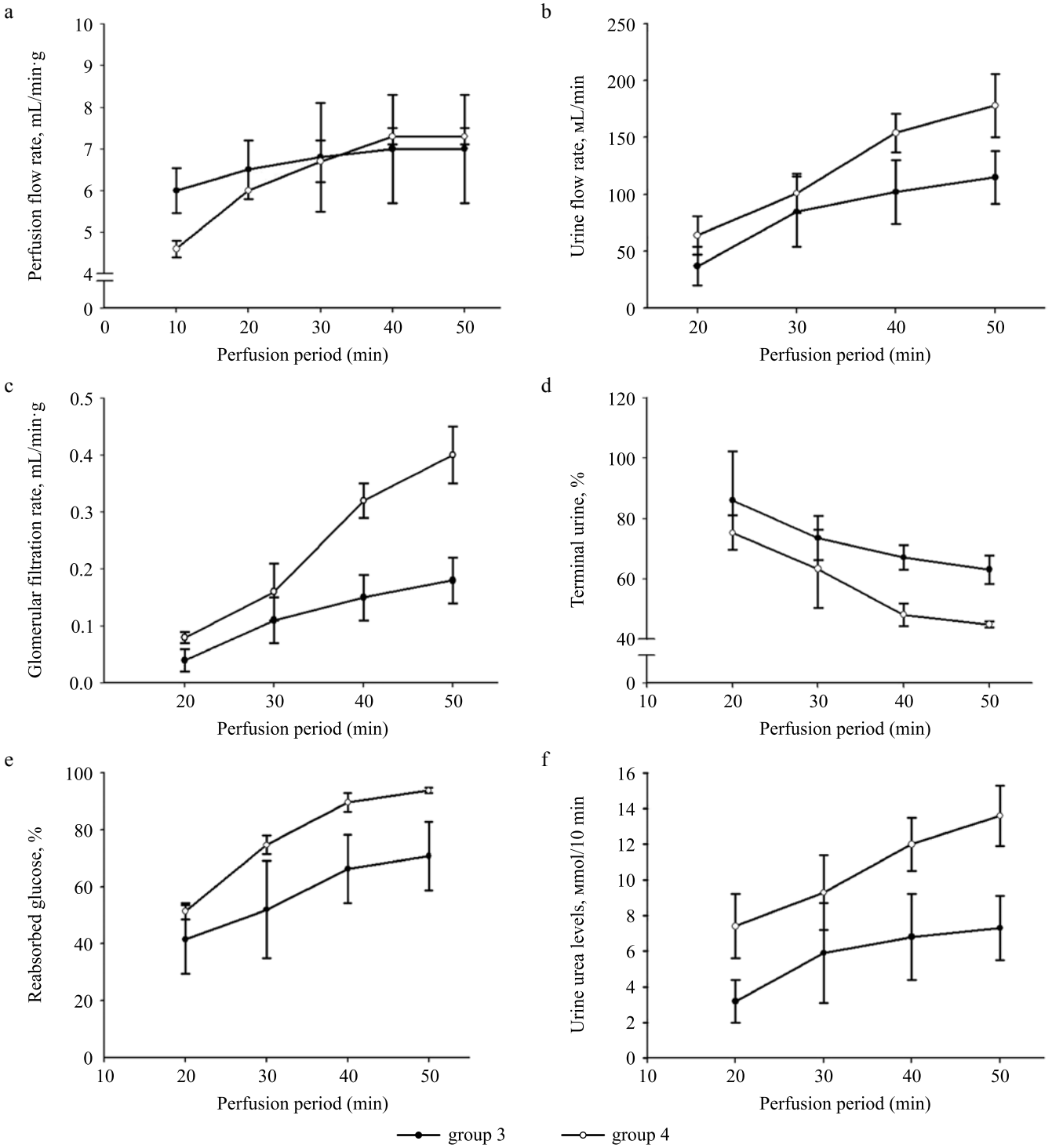

Fig. 2. The dynamic of the criteria of the functioning of an isolated ischemic kidney during perfusion (ischemia 5 minutes / perfusion 50 minutes). The first 20 minutes of perfusion is the stabilization period

the minimum acceptable values (44 ± 4.6 μl/min). There was increased pressure in both groups, with reduced perfusion flow rate.

The dynamics of the functioning criteria of the isolated ischemic kidney during perfusion in groups 7–8 is shown in Fig. 3. Perfusion pressure and perfusion flow rate were constant during perfusion in both groups and had acceptable values. Prx6 had no effect on the dynamics of these parameters (Fig. 3, a). In both groups, UFR was above the minimum acceptable values throughout the perfusion period. With Prx6, there was no significant increase in UFR by the end of perfusion relative to group 3 (137 ± 40 μL/min and 146 ± 41 μL/min, respectively) (Fig. 3, b, Table 2). The GFR and RGF values were below the minimum tolerated values throughout the perfusion period in both groups. The use of Prx6 did not take GFR and RGF above the minimum values even by the end of perfusion (0.16 ± 0.05 mL/min and 44%, respectively) (Fig. 3, c, E). In groups 7–8, TUP and UUL did not change significantly during perfusion. By the end of perfusion, the values of these criteria did not differ significantly between the groups (Fig. 3, d, f, Table 2). Table 2 shows the values of renal function criteria in groups 7–8 at the end of perfusion.

Table 2 shows the values of the kidney function criteria in the experimental groups at the last 10-minute perfusion interval.

Assessment of the morphological state of the isolated ischemic kidney

Fig. 4 shows the morphology of renal tissue from different experimental groups. The kidneys of intact animals had distinguishable sections of the nephron in the cortical layer: renal corpuscle and renal convoluted tubules: proximal (canal cells have a pronounced brush border) and distal (Fig. 4, a). An hour and a half of ischemia and absence of perfusion led to development of foci of necrobiosis and necrosis in the renal parenchyma, desquamative changes in the ducts, and focal capillary-venous full-blooded cortical substance with erythrostasis (Fig. 4, b). During short periods of ischemia in the isolated kidney after perfusion, the general morphofunctional structure of the nephron was preserved (Fig. 4, c, d). For groups 3–4, a general morphological pattern was observed: hydropic dystrophy in the juxtamedullary zone, foci of canal lesions, and absence of cellular debris. When Prx6 was used, there was decreased lesion of the tubular epithelium; the proximal tubular nephrocytes had a pronounced brush border. The distal tubules were unchanged (Fig. 4, d). With an increase in the isolated kidney ischemia time to 20 minutes in groups 7–8, a similar morphological picture was observed by the end of perfusion, particularly disorder in the morphofunctional structure of the nephron. The presence of granular masses in capsule lumen and focal spasm of capillary loops were noted. Foci of hydropic dystrophy of canal epithelium appeared, absence of brush border of proximal canal nephrocytes, necrosis of individual epitheliocytes and cell groups. There was a depletion in the tubules due to decreased epithelial height and lumen dilatation. Homogeneous masses and desquamated epithelial cells were noted in the lumen of canals. The lesion was zoned and pronounced in the cortical layer. The degree of lesion decreased towards the lateral margin. The use of Prx6 did not cause a change in the morphological state of the renal tissue and did not reduce the lesion.

DISCUSSION

The IPK model is recognized for the study of renal function [1, 23], and is also of practical importance for assessment of preservation methods [22, 24]. In the IPK model, three interrelated renal transport processes – filtration, secretion and reabsorption – are close to their in vivo functioning criteria; in addition, the glomeruli and proximal tubule functions are preserved. The disadvantages of the model include impaired renal hemodynamics

Table 2

Functioning criteria at the end of the perfusion period

Criteria			PFR, ml/min·g	UFR, μl/min	GFR ml/min	RGF, %	UUL, μmol/10 min	TUR, %
Min values			4–5.3	>30	>0.5	>90		
5 min ischemia	No. 1	6% BSA	7.5 ± 2.8	–	–	–	–	–
	No. 2	0.6% BSA	5.7 ± 0.5	49 ± 2.5	0.01 ± 0.01	50	4.2 ± 0.5	61 ± 0.5
	No. 3	No additive	6.9 ± 1.3	115 ± 23	0.18 ± 0.04	71 ± 12	7 ± 1.8	64 ± 4.7
	No. 4	Prx 6	7.3 ± 0.2	178 ± 28	0.4 ± 0.05	94 ± 1	13 ± 1.7	45 ± 1
20 min ischemia	No. 5	6% BSA	2 ± 0.7	–	–	–	–	–
	No. 6	0.6% BSA	3.4 ± 1	44 ± 4.6	0.05 ± 0.01	21 ± 6	2.8 ± 3.6	92 ± 6.5
	No. 7	No additive	5.6 ± 1	137 ± 40	0.16 ± 0.05	46 ± 13	9.6 ± 3	85 ± 3.2
	No. 8	Prx 6	5.1 ± 0.3	146 ± 41	0.16 ± 0.04	44 ± 13	9.6 ± 1	91 ± 2.3

due to high perfusion flow rate and impaired functions of the distal tubules [1].

In this study, we used a model of retrogradely perfused mouse isolated kidney [3]. Perfusion was performed with DMEM synthetic medium. In our IPK model, the principal point was having a thermal ischemia period of 5 and 20 minutes. The period of 5 minutes was chosen as the minimal period of blood flow interruption. The 20-minute thermal ischemia period is described as the most optimal for subsequent recovery of isolated kidney function during transplantation [26]. Ischemia is known to trigger a number of pathological reactions that lead to disruption in the functions of vital cell structures. Subsequent reperfusion leads to progression of pathological processes. Studies in recent years have repeatedly pointed to the key role of oxidative stress in the pathogenesis of renal IRI. The main participants in the chain of events leading to oxidative stress are reactive oxygen and nitrogen species: there is a sharp increase in the generation of these free radicals in kidney cells [7]. In this

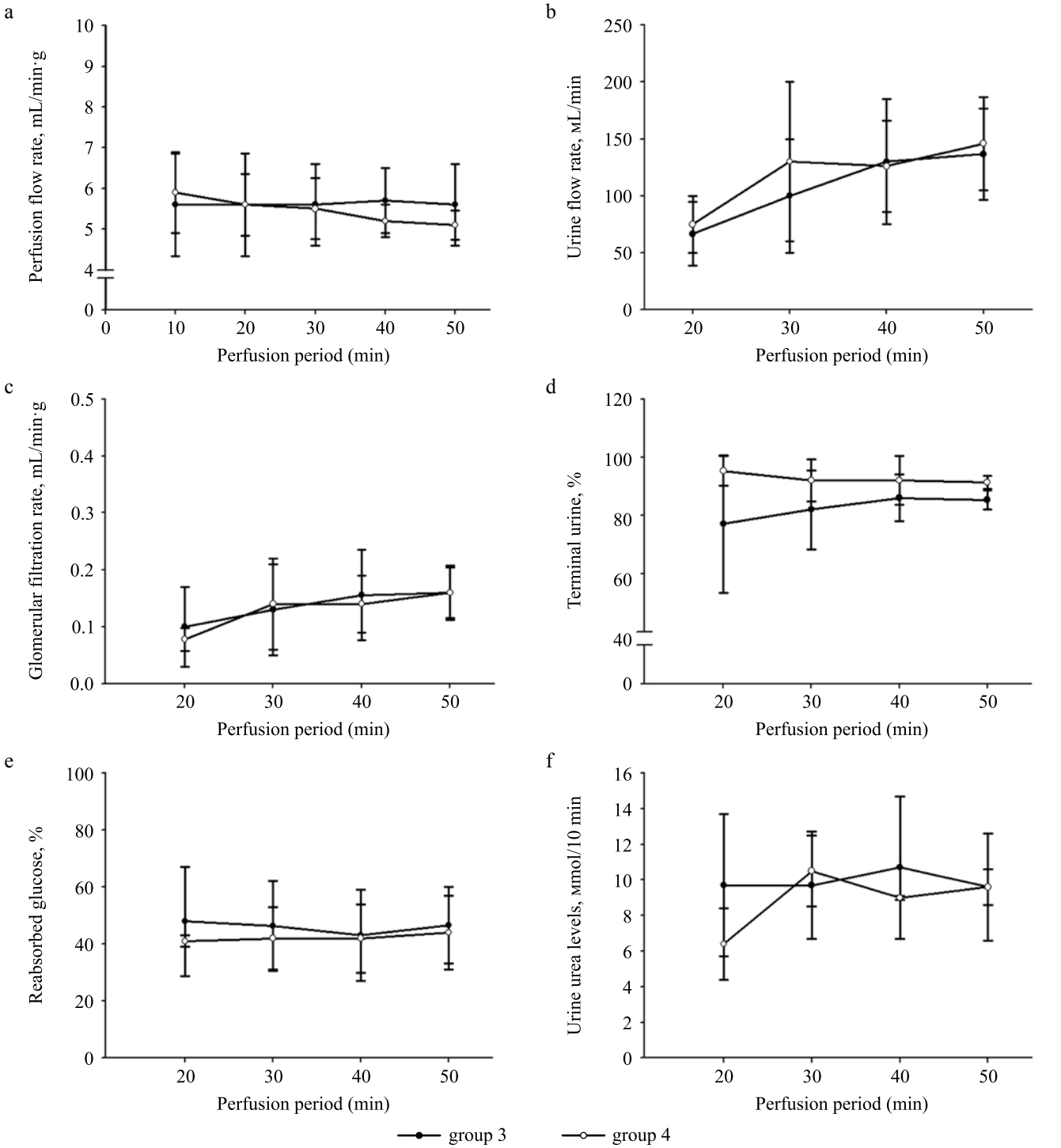

Fig. 3. The dynamic of the criteria of the functioning of an isolated ischemic kidney during perfusion (ischemia 5 minutes / perfusion 50 minutes). The first 20 minutes of perfusion is the stabilization period

work, exogenous antioxidant enzyme Prx6 was used to protect the isolated organ from the damaging effects of IRI and to improve the morphofunctional characteristics of the isolated ischemic kidney. As part of the perfusion solution, Prx6 was injected locally into the isolated kidney at the onset of ischemia. Thus, Prx6 was in the kidney tissue throughout the ischemia period and at the beginning of perfusion. It has been previously shown that when an isolated kidney is perfused with exogenous Prx6, the protein is distributed through the vessels of the renal glomeruli and the vessels accompanying the thin tubule [20]. Besides, the renal tissue has its own pool

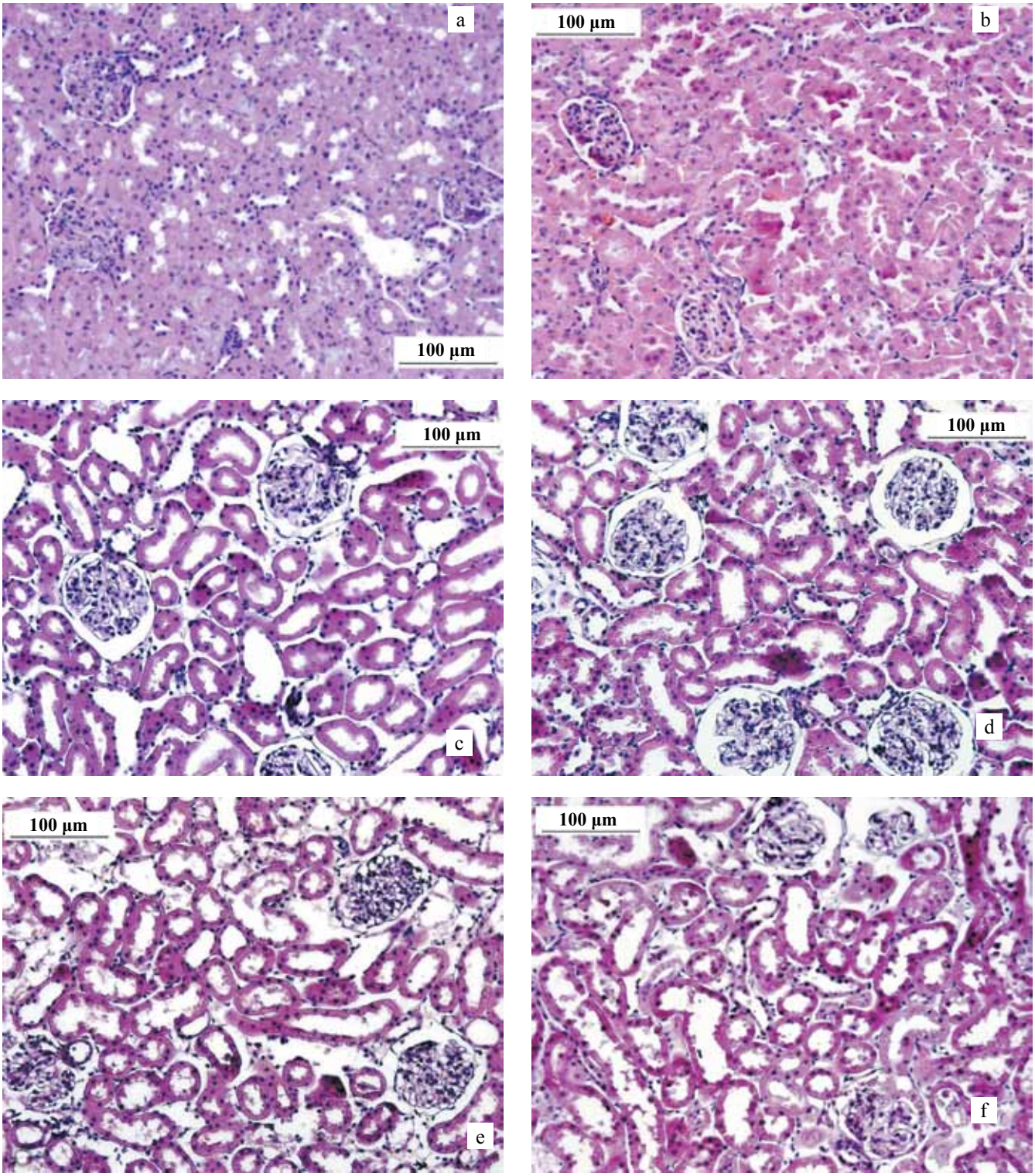

Fig. 4. Morphology of renal tissue: а – native control; б – kidney, no perfusion, ischemia 90 minutes; в – group 3 (ischemia period 5 min / perfusion period 50 min, no Prx6); г – group 4 (ischemia period 5 min / perfusion period 50 min, + Prx6); д – group 7 (ischemia period 20 min / perfusion period 50 min, no Prx6); е – group 8 (ischemia period 20 min / perfusion period 50 min, + Prx6). Eosin-hematoxylin, ×200

of Prx6 in the tubular segments of the nephron, and it is at these sites that increased Prx6 expression is observed during IRI [27]. To assess the effectiveness of Prx6 as a means to preserve the morphofunctional characteristics of the isolated ischemic kidney, several generally accepted functioning criteria were analyzed: PP, PFR, UFR, GFR, RGF, TUP [1, 22] and UUL.

PP was maintained at 90–110 mmHg by changing the PFR from 2 to 7.5 ml/g/min·g in different groups (Table 2). By the end of perfusion, maximal PFR was observed at 5-minute ischemia amidst a 6% BSA background; minimal PFR was observed at 20-minute ischemia on a 6% BSA background. Despite high PFR in group 1 (6% BSA), there was no urine formation. It is noted that adding high BSA doses to the buffer decreases GFR; on the contrary, isolated kidneys perfused with synthetic medium without BSA addition tend to increase GFR and RGF [22]. Macroscopically, there was an about 1.5-fold increase in the size of isolated kidneys during perfusion. This is a natural process, as there are factors contributing to fluid accumulation in the tubules – lack of nerve control of afferent arterioles and blockage of lymphatic vessels [4].

Monitoring of the main criteria of isolated kidney functioning began after hemodynamic equilibrium was established, when PFR and PP held constant values (stabilization period (20 minutes)).

At 5-minute ischemia, the isolated kidney function criteria in all groups had values above the minimum (Table 2). For group 2 (0.6% BSA) and 3 (No additive), these parameters can include PP, PFR, and UFR. For GFR and RGF, the values are below the minimum acceptable values. Histological evaluation of renal tissue in these groups revealed foci of internal canal lesions. Damage of proximal canals already in the early stages of ischemia was due to their high level of metabolic activity [25]. The use of Prx6 extends the list of criteria of isolated kidney functioning with admissible values: PP, PFR, UFR, GFR and RGF. When Prx6 was used, there was increased UFR, GFR, and RGF and decreased TUP, compared with group 3. This pattern indicates improved filtration, secretion and reabsorption of ultrafiltrate when using Prx6 during perfusion of ischemic isolated kidneys. Any value above 90% using Prx6 indicates preservation of the functionality of the tubular structures of isolated ischemic kidney by the end of perfusion. This is confirmed by histological analysis results. A decrease in the lesions of tubular structures using Prx6 is also confirmed by the almost 2-fold increase in the amount of urea in terminal urine, compared to group 3. Since the main sites responsible for urea transport are the proximal tubule and the thin segment of the ascending part of the loop of Henle [25], we cannot say whether these very tubular structures are preserved. Increase in UUL levels may not be directly related to preservation of tubular structures; however, morphological evidence obtained suggests that this very process significantly contributes to the urea transport process. Thus, by functional criteria, exogenous Prx6 significantly improves the functional state of the isolated kidney during perfusion after short thermal ischemia periods.

Evaluation of the isolated kidney after 20 minutes of ischemia showed that with increasing duration of ischemia, among the functioning criteria, only UFR has acceptable values. The other criteria have values below the minimum (Table 3). The use of Prx6 does not raise these criteria to higher values. Within the time group, absence of BSA in the perfusate increases GFR and RGF, but does not take them to the required level. Low RGF indicates impaired glucose reabsorption processes in proximal channels [28]. A similar situation is observed with UUL, there are increased levels in the absence of BSA in the solution. Thus, after 20 minutes of ischemia, the kidney can be considered non-viable. Lack of kidney function is most likely due to the fact that ischemia duration is of fundamental importance for the survival of the isolated organ. In the ischemic kidney, with the beginning of perfusion, hypo- and hyperperfusion foci appear. Against the background of acute tubular necrosis, there is spasm of arterioles supplying the glomerulus, which can lead to intraorgan blood flow disruption and no-reflow [26]. The presence of tubule lesions was confirmed by histological analysis. Previously, it was shown that increasing ischemia duration to 45 minutes leads to critical parenchymal injury and decrease in UFR to less than 30 μl/min. The use of Prx6 at these times leads to decreased lesion of the isolated kidney, compared to the control lesion. However, despite the protective effect of Prx6 at the critical stages of ischemia, renal parenchyma injury remains high [20].

Thus, the use of synthetic media in the IPK model is appropriate only in the early stages of ischemia. During this period, some criteria of isolated kidney functioning reach acceptable values. Renal tissue structure is preserved, but there are foci of dystrophic changes in the juxtamedullary zone and proximal canals. With increasing ischemia duration, renal tissue damage intensifies, tubular necrosis develops, which manifests as a decrease in functionality criteria and cessation of functioning of the isolated ischemic organ. The use of exogenous Prx6 positively influences the morphofunctional state of isolated kidneys only in the early stages of ischemia. In this case, the criterion values are higher than the minimum allowable, which may indicate the functioning of the isolated ischemic kidney for a certain period when it is perfused with a synthetic medium. Morphologically, the morphostructural integrity of nephrons was noted in the early stages of ischemia.

Prx6 is a polyfunctional antioxidant enzyme with peroxidase activity, low phospholipase activity, and participates in many processes in the cell [10–13]. The fact that Prx6 protects the isolated kidney at short ische-

mia periods indicates that in this case the peroxidase activity of Prx6 makes the main contribution to organ protection. The experience of using recombinant Prx6 for protection of isolated organs has been reported. The protective effect of Prx6 has been shown in a perfusion model of isolated rat heart. It was noted that Prx6 normalizes heart rate, maintains myocardial contractile activity, and prevents lipid peroxidation [17]. Exogenous Prx6 has shown its protective effect for preconditioning of rat heart transplant. Prx6 has been shown to reduce the severity of cardiac IRI and promote normalization of its morphofunctional state during heterotopic transplantation [18].

CONCLUSION

In a model of an isolated perfused kidney, exogenous recombinant Prx6, locally injected before ischemia, was shown to have a renoprotective effect. When interpreting obtained evidence, a fundamental factor was taken into account: response of the isolated kidney differs from the natural one due to suppression of humoral regulation and absence of innervation [4]. In this regard, the effect of Prx6 in the isolated kidney may probably differ from its protective effects in the kidney in vivo [8].

Based on the data obtained, it is reasonable to suggest that the use of exogenous recombinant Prx6 may be an effective approach to preserving the isolated kidney during transplantation, since the inclusion of Prx6 in the composition of known perfusion solutions as a powerful antioxidant agent will help to reduce free-radical oxidation processes. In this regard, further experimental studies are required.

We used equipment provided by the Optical Microscopy and Spectrophotometry Department at Pushchino Scientific Center for Biological Research, Moscow, to obtain the microphotographs presented in this paper.

The authors declare no conflict of interest.

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