Urol Res (1986) 14:271–277

Urological Research

Post-Ischemic Renal Function After Kidney Protection With the HTK-Solution of Bretschneider*

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Accepted: February 24, 1986

Summary. The cardioplegic solution HTK of Bretschneider was used for canine kidney protection. The kidneys were perfused with this solution for 6–10 min prior to the induction of ischemia. The kidneys were left in-situ for 60, 90, 120 and 135 min ischemia time at a temperature of 25–34 °C (n = 13). As a control group we used unilateral nephrectomized dogs (n = 9). After unilateral nephrectomy an elevated plasma creatinine in comparison to preoperative values was observed. After 60 and 90 min under HTK-protection the postoperative plasma creatinine was not elevated compared to the control group. After 120 min of ischemia creatinine level was slightly increased to an average of 2.1 mg% on the first and second postoperative day. These experiments indicate the protective effect of the cardioplegic solution for canine kidney preservation in situ.

Key words: Renal ischemia, Renal protection and preservation, Cardioplegic solution HTK.

Introduction

Renal cooling is an essential protective measure against ischemic damage (reviewed in [22, 23, 28, 32]). Either the organ is repeatedly perfused by a cold solution (for example Ringer-lactate [14, 15]) and thus kept below 25 °C, or, for complex manipulations which breach the parenchyma, the organ is cooled from the outside with crushed ice. However, the medulla of the kidney may be insufficiently cooled and thus inadequately protected while the cortex might even be damaged by cooling [13, 30]. For particularly difficult surgical procedures, bench surgery and subsequent autotransplantation into the fossa iliaca [24] may be employed. Despite recently developed methods of treatment, i.e. extracorporeal [8, 9] or percutaneous disintegration of calculi [1], some calculi, a tumor in a solitary kidney, or bilateral stenosis of the renal artery require a method that not only protects the kidney from ischemic damage, but also allows free access to the operative field.

It is thus surprising that so far as we know, no group has applied the widespread experience with myocardial protection, gained from open heart surgery, to in situ kidney preservation.

We have therefore developed in situ protection of the kidney with the original cardioplegic solution HTK [4–7] (*H*istidine-*T*ryptophan-*K*etoglutrate) (Table 1). Following initial perfusion with the cold solution at about 8 °C for 6–10 min, no further cooling is necessary so that the operative field remains exposed. Protection lasts two hours at a median temperature of 32–34 °C [18]. The method has been extensively tested in in vitro experiments involving measurement of intrarenal pH [17] and metabolism [16] as well as in acute reperfusion experiments, which recorded early functional recovery following renal ischemia [18]. The aim of this study was to expand our previous measurements of renal function, 2–3 h immediately after ischemia, by long-term studies in a survival model, prior to clinical use.

Table 1. HTK-solution of Bretschneider

NaCl	15 mmol/l
KCl	9 mmol/l
$MgCl_2$	4 mmol/l
K-α-Ketoglutarate	1 mmol/l
Tryptophan	2 mmol/l
Histidine	180 mmol/l
Histidine-HCl	18 mmol/l
Mannitol	30 mmol/l
pH at 8 °C	7,3
pO_2 at 37 °C	200 mmHg
Osmolarity	310 mosm/l

* Supported by the Deutsche Forschungsgemeinschaft, SFB 89 – Kardiologie Göttingen

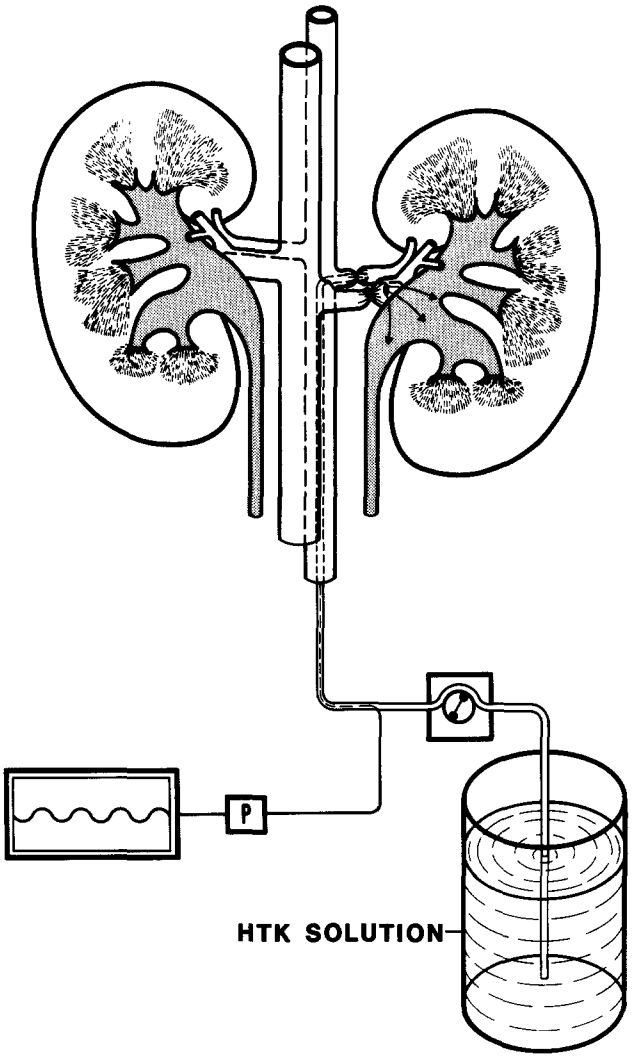

Fig. 1. Operation situs with the perfusion catheter fixed in the renal artery, the renal vein clamped and incised to let the perfusate out. The HTK-solution is delivered by a peristaltic pump and the perfusion pressure is measured at the tip of the catheter [20]

Material and Methods

The experiments were performed on 22 mongrel dogs of both sexes with a median body weight of 32 kg devided in two groups. *Group 1* consisted of 9 unilaterally nephrectomized dogs. *Group 2* consisted of unilaterally nephrectomized dogs together with contralateral renal ischemia of 60 (n = 2), 90 (n = 3), 120 (n = 5) and 135 (n = 3) min at 32–34 °C after perfusion for 6–10 min with HTK-solution of Bretschneider.

After premedication of the animals with 90 mg piritramide[1] and 0,5 mg atropine[2], anesthesia was introduced 30 min later with 7 mg/kg body weight sodium thiopental[3] and was maintained with a combination of fentanyl-dihydrogencitrate[4], isoflurane[5] and N_2/O_2 (4:1). Ventilation was performed with a Dräger respirator type AV1[6] with a continuously recorded endexpiratory CO_2[7] of about 5.5%.

In *group 1*, after a midline laparotomy, one kidney was excised and the other kidney was left completely untouched; the abdomen was then closed.

In *group 2*, one kidney was excised as in group 1 and the other kidney was freed from the peritoneum, and the vessels and the upper part of the ureter were dissected. The uteric blood supply was divided as well as all capsula vessels to exclude any vascular supply to the kidney during experimental ischemia. A kidney perfusion catheter [20] was placed via the aorta abdominalis, distal to the vascular origin of the a. iliaca communis. To avoid any ischemia prior to protective perfusion of the kidney, the catheter was pushed into the renal artery with a perfusion volume of about 100 ml/min already being delivered by a peristaltic pump[8] and was fixed in this position with a tourniquet. Immediately after catheter insertion a perfusion pressure of *about 100 mmHg* was achieved by raising perfusion volume to about *400–500 ml/min* x *100* g_{ww} of the cold (6–10 °C) HTK-solution of Bretschneider[9]. The renal vein was opened and clamped next to the v. cava about 40 s after onset of perfusion (Fig. 1) to allow the perfusate to escape. The perfusion took 6 to 10 min. The temperature of the kidney was below 10 °C at the end of perfusion, but was rewarmed to body temperature (measured by a temperature probe[10] lying in the retroperitoneum) by the surrounding abdomen within one hour of ischemia. Afterwards the venous incision was closed by an atraumatic suture (6–0 silk, BV1 needle)[11], the renal artery was clamped and the perfusion catheter was withdrawn. The kidney was left for the period of ischemia (60, 90, 120 and 135 min) in situ without further cooling. The average renal ischemic temperature therefore was between 25–34 °C.

Following experimental renal ischemia in group 2 reperfusion was started by removing arterial and venous clamps and the abdomen was closed by peritoneal, muscle, subcutaneous and cutaneous sutures.

During the operation standard leads were used to record the ECG. Arterial blood pressure was continuously monitored via a catheter placed in the distal aorta abdominalis and connected to a pressure transducer[12] and an amplifier[13]. Arterial blood samples were taken through this catheter for controlling the acid base[14] and the Na^+/K^+[15] status of the animal.

The arterial blood pressure was kept around 130/70 mmHg. During the first 1 to 2 h of the operation (normally until ischemia was started) 500 ml glucose 5%[16] and 500–1,000 ml of an isotonic solution[17] was given. The dogs were heparinized by 1.250 I.U.[18]

During the first 12 h postoperatively the dogs had access to water, and from day 2 they received water and food ad libitum. No further therapeutic measures were required. Postoperative recovery ranged from 4 to 16 days. Daily venous blood samples were taken

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1 Dipidolor,; Janssen GmbH, Neuss, FRG
2 Atropinsulfat Drobena; Drobena Arzneimittel GmbH, Berlin, FRG
3 Trapanal; Byk Gulden, Konstanz, FRG
4 Fentanyl-Janssen; Janssen GmbH, Neuss, FRG
5 AErrane-Isofluran (Isofluran); Ohio Medical Pharma-Vertrieb GmbH, Puchheim, FRG
6 Dräger Respirator AV1, Lübeck, FRG
7 Datex Instrumentation OY; Espoo, Finland
8 Doppelpumpe 102000; Stöckert Inst., München, FRG
9 Kardioplegische Lösung HTK nach Bretschneider; Dr. Franz Köhler Chemie GmbH, Alsbach, FRG
10 Temperatur Sonde und Digital Thermometer, Ellab, Kopenhagen, Denmark
11 Nahtmaterial, Ethicon FRG
12 p23ID; Gould Statham Instr., Oxnard, USA
13 Hellige GmbH, Freiburg im Breisgau, FRG
14 Corning Säure-Basen-Analysator 352, Corning GmbH, Gießen, FRG
15 Na/K-Ionenanalyser 914, Corning GmbH, Gießen, FRG
16 Glucose 5% Braun; B. Braun Melsungen AG, Melsungen, FRG
17 Tutofusin; Pfrimmer & Co. GmbH, Erlangen, FRG
18 Heparin-Natrium Braun 2.500 I.E./5 ml; B. Braun Melsungen AG, Melsungen, FRG

Table 2. Group 1: Pre- and postoperative plasma-creatinine (mg/100 ml) before and after unilateral nephrectomy

Experiment No.	op. day	postoperative day						
		1.	2.	3.	4.	5.	6.	7.
125	1.10	1.44	1.44	1.25	1.20	1.39	1.53	–
142	1.05	1.28	1.06	1.13	1.11	1.07	0.99	0.96
143	1.20	1.49	1.40	1.20	1.29	0.94	0.92	1.07
146	1.28	1.80	1.66	1.42	1.40	1.34	1.19	0.83
147	1.49	1.88	1.89	1.53	1.64	1.61	1.61	1.27
151	0.92	1.29	1.32	1.09	1.15	0.97	1.26	1.24
152	1.30	1.59	1.56	1.46	1.28	1.33	1.39	1.49
154	1.09	1.40	1.30	1.35	1.36	1.26	1.14	1.61
155	1.05	1.21	1.35	1.49	1.21	–	1.26	1.21
mean	1.16	1.49	1.44	1.32	1.29	1.24	1.25	1.21
SD	0.17	0.23	0.24	0.17	0.16	0.23	0.23	0.26

for estimation of plasma creatine[19]. Urine was collected when feasible.

At the end of the survival time, the 8 kidneys in group 2, which had been subjected to 120 and 135 min of ischemia, were examined again at laparotomy. Anesthesia was the same as during the first operation. A suitable flow probe[20] was put around the renal artery and connected to an amplifier[21] for measuring renal blood flow. A catheter was placed into the renal vein to take renal blood samples. The renal oxygen consumption was calculated from renal blood flow and arterio-venous oxygen content difference. Urine was collected for 15 min. Afterwards six of the 8 kidneys in this group were perfused for 6 min by cold (6–8 °C) HTK-solution and thereafter for another 6 min by warm (37 °C) 1.5% glutaraldehyde in 0.1 M sodium cacodylate buffer [19] for light and electron microscopy.

From the 2 kidneys, which were not fixed by perfusion, four tissue samples for determination of ATP[22], ADP[23], AMP[23], inorganic phosphate[24], glucose[25] and lactate[26] were taken, whereby each sample consisted of about 2/3 cortex and 1/3 medulla. In these kidneys morphology was studied after fixation by immersion.

[19] Beckman, Creatinine Analyzer 2, Beckman Instruments GmbH, München, FRG

[20] Blood flow transducer, Gould-Statham Instruments Inc., Puerto Rico 00919

[21] Hellige Blutströmungsmesser, System Hillers, Hellige GmbH, Freiburg, FRG

[22] Testkombination ATP, Boehringer Mannheim GmbH, Mannheim, FRG

[23] Testkombination ADP/AMP, Boehringer Mannheim GmbH, Mannheim, FRG

[24] Anorganisches Phosphat, Merckotest, E. Merck Diagnostica, Darmstadt, FRG

[25] D-Glucose, Bestimmung mit Hexokinase und Glucose-6-phosphat-Dehydrogenase nach H. U. Bergmeyer et al. In: Bergmeyer HU (ed) Methoden der enzymatischen Analyse, 3. Auflage, Bd II. Verlag Chemie, Weinheim 1974, 1241

[26] L-(+)Lactat, Bestimmung mit Lactat-Dehydrogenase und NAD. In: Bergmeyer HU (ed) Methoden der enzymatischen Analyse, 3. Auflage, Bd II. Verlag Chemie, Weinheim 1974, 1510

Results

After unilateral nephrectomy (*group 1*, $n = 9$) the mean plasma creatinine was elevated from the 1st to the 5th postoperative day in comparison with preoperative values. After 6 days the plasma creatinine fell to preoperative values (Table 2).

In *group 2* (unilateral nephrectomy and contralateral ischemia of 60, 90 and 120 min at 32–34 °C after HTK-protection) the plasma creatinine was not elevated after *60 min of ischemia* in comparison to group 1 (no ischemia). After *90 min of ischemia* the plasma creatinine was slightly increased in comparison to the control group, especially in experiment 131. The plasma creatinine fell to the normal range beyond the 6th or 7th postoperative day in comparison to the control group with unilateral nephrectomy (Table 2). After *120 min of ischemia* we found increased plasma creatinine on the first postoperative day in comparison to the control group. From the 3rd postoperative day the mean plasma creatinine was below 2 mg/100 ml with one exception (Table 3).

The osmolarity in the urine decreased from preoperative values of about 1,200 mosmol/kg H_2O to about 400 mosmol/kg H_2O on postoperative day 1. However, during the observation period we were able to measure values of up to 900 mosmol/kg H_2O. The fractional Na^+-excretion was elevated to about 4% at the first postoperative day, but was on the upper limit of the normal range from the second day on (Fig. 2).

The five kidneys with 120 min of ischemia were examined again after 3 to 7 days (mean 6 days). The renal oxygen consumption was on the average 5.7 ± 0.6 ml/min x 100 g_{ww}, the renal blood flow was 418 ± 58 ml/min x 100 g_{ww}, the glomerular filtration rate was 43 ± 7 ml/min x 100 g_{ww} and the filtration fraction was $15 \pm 1\%$ (Table 4).

The morphology from two of these experiments (120 min of ischemia at 32–34 °C under HTK-protection) is shown in Fig. 3. In Exp. 335 under low magnification mostly

Table 3. Group 2: Pre- and postoperative plasma-creatinine (mg/100 ml) before and after unilateral nephrectomy and contralateral ischemia* after HTK-protection

renal* ischemia (min)	Experiment No.	op. day	postoperative day												
			1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	13.	15.	16.
60	126	0.94	1.38	1.37	1.24	1.06	0.97	1.07	1.02	–	–	–	–	–	–
	129	1.22	1.71	1.49	1.42	1.25	1.39	1.26	1.19	–	–	–	–	–	–
90	130	0.94	1.71	1.90	1.48	1.36	1.10	1.04	1.14	–	–	–	–	–	–
	131	1.01	2.35	2.13	1.85	1.67	1.55	1.52	1.49	–	–	–	–	–	–
	137	1.11	1.44	1.46	1.69	1.67	1.48	1.32	1.31	–	–	–	–	–	–
120	335	0.99	1.92	1.94	1.59	1.50	1.35	1.75	1.67	–	–	–	–	–	–
	342	0.75	2.00	1.80	1.65	1.65	1.50	1.75	1.67	–	–	–	–	–	–
	352	1.07	2.23	2.28	1.75	1.67	1.49	1.54	1.54	–	–	–	–	–	–
	354	0.83	2.51	2.60	2.58	2.39	2.08	2.08	1.84	–	–	–	–	–	–
	355	1.21	1.82	1.61	1.44	1.25	–	–	–	–	–	–	–	–	–
135	371	1.47	2.47	3.17	2.40	2.44	2.41	2.11	1.88	1.77	1.70	–	–	–	–
	373	1.23	3.17	3.70	3.37	2.95	2.98	2.78	–	–	–	–	–	–	–
	374	1.04	2.92	3.68	3.23	2.67	2.53	2.53	2.20	2.24	2.11	2.00	1.83	1.68	1.65

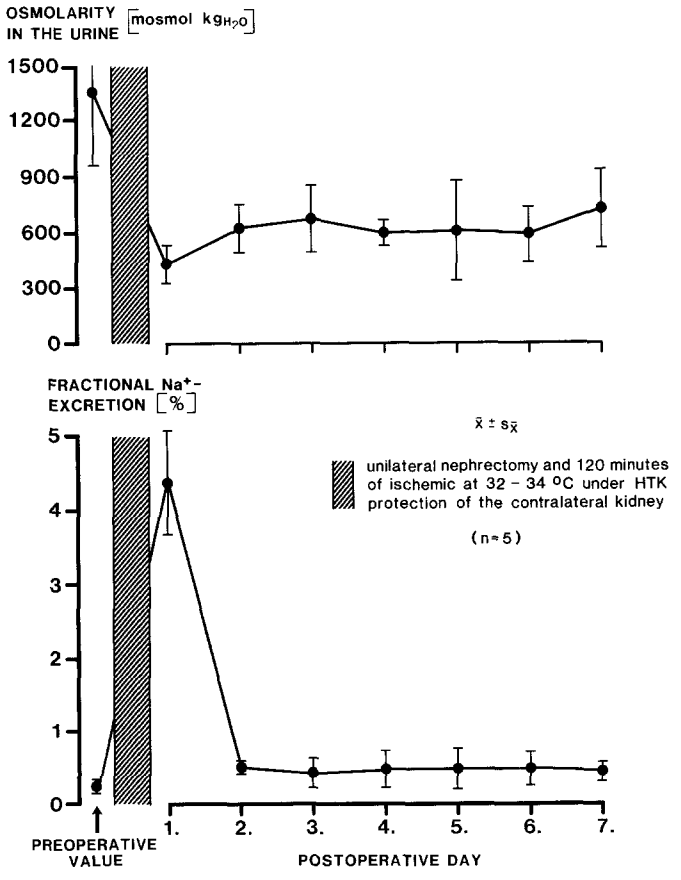


Fig. 2. Pre- and postoperative mean values ± S.E.M. of the osmolarity in the urine and the fractional sodium excretion

Table 4. Final examination after 4 to 7 days (mean after 6 days) after 120 min of ischemia under HTK-protection (n = 5)

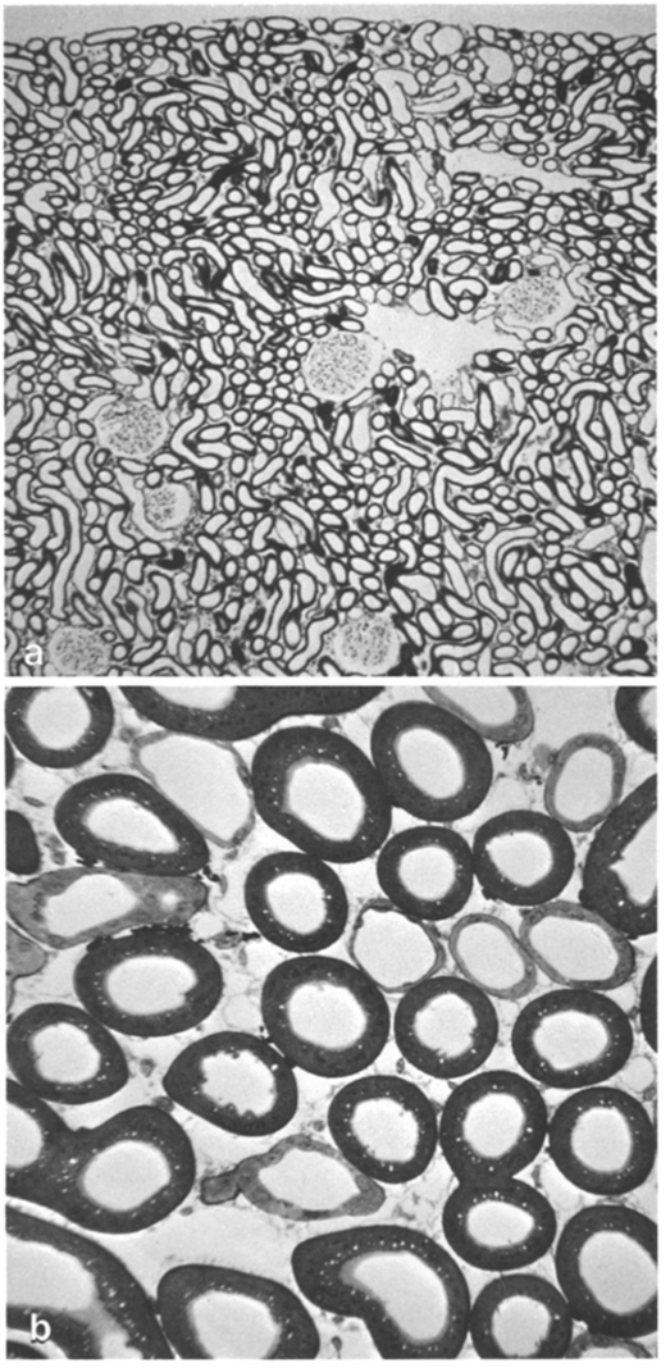
	mean	±	S.E.M.
Renal oxygen consumption[a]	5.7		0.6
Renal blood flow[a]	418.0		58.0
Glomerular filtration rate[a]	43.0		7.0
Filtration-fraction[b]	14.5		1.0

[a] (ml/min x 100 g_{ww})
[b] (%)

intact tubuli are seen with some regeneration of epithelium with a normal interstitial space. In Exp. 352, under higher magnification, only some cytoplasmic vacuoles within the proximal epithelial cells and a slight focal interstitial edema are shown (Fig. 3).

After 135 min of ischemia the plasma creatinine was elevated to about 3 and to nearly 4 mg% on postoperative days one and two respectively and the time course of decrease was prolonged (Table 3).

The kidneys subjected to 135 min of ischemia were also finally examined after 6, 9 and 16 days. The oxygen consumption was between 3.7 and 7.3 ml/min x 100 g_{ww}. The glomerular filtration rate was between 27 and 57 ml/min x 100 g_{ww}. In experiment 371 and 373 we did not carry out perfusion fixation of the kidneys and therefore obtained biochemical analysis. The ATP was about 12 μmol/g_{dw} and the TAN was about 16 μmol/g_{dw} (Table 5).



Discussion

Although intrarenal acidosis [17], energy consumption [11, 16] and morphological features [2, 3, 10, 19, 26, 29] provide useful indicators of kidney preservation, postischemic function is the critical test of the protective ability of a preservation technique. From this view point we examined dog kidneys under two conditions. As a control group we used unilateral nephrectomized dogs and found that the creatinine level increased to between 1.2 to 1.9 mg% on the first postoperative day. After clinical nephrectomy a raised creatinine value would not be expected, but in a clinical situation non functionning renal tissue is often removed. The creatinine value stayed above normal up to the 5th postoperative day. In our experimental situation nephrectomy is analagous to a loss of 50% of the glomerular filtration surface. The plasma creatinine found is very close to the value obtained by a 50% reduction of creatinine clearance [12].

After protection with the HTK-solution of Bretschneider kidneys tolerate ischemic intervals of 60 and 90 min with a slight increase of the creatine level. After 120 min of ischemia the creatinine value was 2.10 and 2.05 mg% on average on the first and second postoperative days. From day three onwards, the plasma creatinine was below 2 mg% and then further decreased.

To obtain further information about the composition of the urine, we attempted to take samples every day in the 120 min ischemia group. The osmolarity (mosmol/kg H_2O) in the urine and the fractional Na-excretion (%) [21] was reduced to 420 mosmol/kg H_2O and to 4,4% on average on the first postoperative day. From the second postopera-

Fig. 3. a Exp. 335, right kidney, perfusion fixation (Goldner) 120 min of ischemia under HTK-protection at 32–34 °C, 7 days postoperative: Overview of the cortex: mostly intact tubuli with only here and there (*above*) regenerating epithelia, interstitial space normal, x 106. b Exp. 352, right kidney, silver impregnation (MOVAT) after perfusion fixation, 120 min ischemia under HTK-protection at 32–34 °C, 4 days postoperative, *detail:* mostly intact cortex with few vacuoles in proximal epithelial cells and with a slight focal interstitial edema, x 264

Table 5. Renal metabolite content ($\mu mol/g_{dw}$)

	ATP	ADP	AMP	TAN	P_i	Glucose	Lactate
Control[a]	9.8	4.0	1.5	15.3	28.4	60.4	11.5
($n = 9$)	0.4	0.2	0.1	0.5	2.2	11.3	1.9
Exp. 371[b] (after 9 days)	12.2	3.1	1.2	16.5	36.4	24.4	9.5
Exp. 373[b] (after 6 days)	11.2	3.7	1.2	16.1	30.6	27.8	3.9

[a] mean ± S.E.M.

[b] 135 min of ischemia, HTK-protection

tive day the osmolarity was above 600 mosmol/kg H_2O and reached values of 900–1,000 mosmol/kg H_2O and the fractional Na-excretion was below 0.5%. These values are comparable with preischemic values.

At the end of the observation period we made final measurements. The results are given in Table 4. Even though a slightly increased plasma creatinine was noted (see Table 3) in comparison to the control croup (see Table 2), the renal oxygen consumption, the blood flow, the glomerular filtration and the filtration fraction were within the normal range.

As these experiments were carried out with the catheter used experimentally [20], which allowed exact perfusion pressure measurements, but which is traumatic to the renal artery, we carried out 3 further experiments with an angiography catheter of diameter Charrière 7, which can be placed in the aorta by the Seldinger technique. This type of catheter is not as traumatic as the type used experimentally. To check how close we were to the limits of the ischemic tolerance, we carried out these experiments with an ischemic duration of 135 min. All dogs survived, but with a higher plasma creatine value (see Table 3).

The basis of the protective effect of the HTK-solution may be seen by inspecting the electrolyte composition: Sodium is, in comparison with the extracellular space, reduced by a factor of 10, potassium and magnesium are slightly increased and the solution is calcium-free; this reduces the energy turnover during ischemia [4–7] and is reversible within 15 min if blood reperfusion takes place. The low sodium in the HTK-solution is similiar to that in the Euro-Collins- or UCLA II solutions [25, 27], for sodium resorption is the main energy-consuming process in the kidney [31], which can effectively be reduced by lowering the Na^+-concentration. To wash out the sodium completely from the extracellular space, the kidney has to be perfused for at least 6 min, but normally we perfused our kidneys for 8–10 min to reach a complete "equilibration" of the extracellular space [18]. As the HTK-solution is Ca^{++}-free and Mg^{++}-enriched (4 mmol/l) the Ca^{++} is rapidly washed out of the vascular system of the kidney. By this mechanism a low perfusion resistance of less than 0.2 (mmHg/ml/min x 100 g_{ww} x cP) was reached.

The low electrolyte content of this solution allows a high buffer concentration of nearly 200 mosmol/l at isoosmolarity. Tryptophane and α-Ketoglutarate are present in the solution, as they have been shown to be necessary for "membrane protection" [7].

The kidney protective solutions used clinically are either of an extracellular type (Ringer-lactate) [14] or of a so-called intracellular type [2, 3, 10, 11, 27]. With the latter solution the potassium concentration of about 115 mmol/l (Collins) [11] or 126 mmol/l (UCLA II) [27] in our opinion prevents its routine use for in-situ renal preservation and for live related donor kidney transplant. As the potassium in the HTK-solution is slightly elevated in comparison with the extracellular space, care must be exercised in the clinical situation, but we have not recorded cardiac signs such as arrhythmia, although we have allowed up to approximately 500 ml to flow via the renal vein into the circulation.

In conclusion this solution prolongs the ischemic interval tolerated (in comparison with unprotected kidneys at body temperature) from 15–30 min to 120–135 min, that is about fivefold.

Acknowledgements. The authors wish to thank Mrs. R. Dohrmann for her excellent technical and operative assistance during the experiments for many years. We thank Mrs. G. Dallmeyer, Mrs. H. Haacke andMrs. B. Riekhoff for biochemical analyses, Mrs. U. Kneissler and Mrs. W. Gebauer for morphological preparation of the kidneys, Mrs. E. Neumeyer, Mrs. R. Ecke and Mrs. A. Dawe for preparation of the figures and for typing the manuscript.

References

1. Alken P, Hutschenreiter G, Guenther R, Marberger M (1981) Percutaneous stone manipulation. J Urol 125:463–466
2. Andrews PM, Coffey AK (1982) Factors that improve the preservation of nephron morphology during cold storage. Lab Invest 46:100–120
3. Andrews PM, Coffey AK (1983) Protection of kidneys from acute renal failure resulting from normothermic ischemia. Lab Invest 49:87–98
4. Bretschneider HJ (1964) Überlebenszeit und Wiederbelebungszeit des Herzens bei Normo- und Hypothermie. Verh Dtsch Ges Kreislaufforsch 30:11–34
5. Bretschneider HJ, Hübner G, Knoll D, Lohr B, Nordbeck H, Spieckermann PG (1975) Myocardial resistance and tolerance to ischemia: Physiological and biochemical basis. J Cardiovasc Surg 16:241–260
6. Bretschneider HJ (1980) Myocardial protection. Thorac Cardiovasc Surg 28:295–302
7. Bretschneider HJ, Gebhard MM, Preusse CJ (1984) Cardioplegia, principles and problems. Physiology and pathophysiology of the heart. Martinus Nijhoff. Boston, pp 605–616
8. Chaussy Ch, Brendel W, Schmiedt E (1980) Extracorporeally induced destruction of kidney stones by shock waves. Lancet 13:1265–1268
9. Chaussy Ch, Eisenberger F, Wanner K, Forssman B, Hepp W, Schmiedt E, Brendel W (1976) The use of shock waves for the destruction of renal calculi without direct contact. Urol Res 1:175
10. Coffey AK, Andrews PM (1983) Ultrastructure of kidney preservation: varying the amount of an effective osmotic agent in isotonic and hypertonic preservation solutions. Transplantation 35–136
11. Collins GM, Green RD, Carter JM, Halasz NA (1981) Adenine nucleotide levels and recovery of function after renal ischemic injury. Transplantation 31:295–296
12. Doolan PD, Alpen FL, Theil GB (1962) A clinical appraisal of the plasma concentration and endogenous clearance of creatinine. Am J Med 32:65–79
13. Dreikorn K, Horsch R (1984) Aktueller Stand renoprotektiver Maßnahmen bei Operationen an der insuffizienten Niere. Urologe A 23:3–8
14. Eadie GDA, Tilney NL, Najafi H, Economou SG, Beattie CJ Jr (1965) Renal hypothermia. In vivo transaortic perfusion with Ringer's lactate. Arch Surg 90:554
15. Eisenberger F, Chaussy Ch, Hofstetter A, Marx FJ (1977) Langzeituntersuchungen nach hypothermer Perfusion der Niere. Aktuel Urol 8:239
16. Kallerhoff M, Hölscher M, Kläß G, Helmchen U, Bretschneider

HJ (1981) Influence of different kidney-protective-solutions (HTK-solution by Bretschneider, Euro-Collins-solution) on metabolism and energetics of ischemic kidneys. Pflügers Arch 392:R15
17. Kallerhoff M, Hölscher M, Kehrer G, Kläß G, Bretschneider HJ (1985) Effects of preservation conditions and temperature on tissue acidification in canine kidneys. Transplantation 39: 485–489
18. Kallerhoff M, Kehrer G, Siekmann W, Blech M, Gebhard MM, Helmchen U, Bretschneider HJ (1985) Experimentelle Anwendung der kardioplegischen Lösung HTK nach Bretschneider für eine in-situ-Protektion von Nieren. Experimentelle Urologie. Springer, Berlin Heidelberg New York Tokyo, pp 180–188
19. Kallerhoff M, Blech M, Kehrer G, Kleinert H, Schnabel PhA, Siekmann W, Helmchen U, Bretschneider HJ (1985) A new method for perfusion fixation of dog kidneys. Pflügers Arch 405: R33
20. Kehrer G, Kallerhoff M, Siekmann W, Blech M, Bretschneider HJ (1985) Construction and experimental application of a catheter for selective arterial kidney perfusion in situ. Urol Res 13:85–89
21. Kehrer G, Kallerhoff M, Gebhard MM, Gersing E, Siekmann W, Blech M, Helmchen U, Bretschneider HJ (1984) Renal excretion regulation during recovery from the impacts of an ischemic stress under HTK-protection. Pflügers Arch 402:R23
22. Marberger M (1978) Ischämie und regionale Hypothermie bei Operationen am Nierenparenchym. Steinkopff, Darmstadt
23. Marberger M, Dreikorn K (1983) Renal Preservation. Williams and Wilkins, Baltimore
24. Ota K, Mori S, Awane Y, Ueno A (1967) Ex situ repair of renal artery for renovascular hypertension. Arch Surg 94:370–377
25. Petritsch PH (1976) Pathophysiologie der Nierenschädigung nach temporärer Ischämie. Urol Int 31:428–443
26. Pfaller W (1982) Structure function correlation on rat kidney. Quantitative correlation of structure and function in the normal and injured rat kidney. Springer, Berlin Heidelberg New York
27. Sacks SA, Petritsch PH, Kaufmann JJ (1973) Canine kidney preservation using a new perfusate. Lancet 1024–1028
28. Schilling A (1984) Acute ischemic renal failure, renal preservation and intrarenal surgery. Zuckschwerdt, München
29. Siekmann W, Blech M, Kallerhoff M, Kehrer G, Bretschneider HJ, Helmchen U (1985) Morphologische Befunde nach zweistündiger kompletter Nierenischämie unter Anwendung verschiedener Protektionsverfahren. Verh Dtsch Ges Pathol 69: 612
30. Sturm W, Marx FJ, Chaussy Ch, Eisenberger F (1984) Zum Stellenwert der Unterkühlungsmethoden zur operativen Steinentfernung. Urologe A 23:9–12
31. Thurau K (1961) Renal Na reabsorption and O_2 uptake in dogs during hypoxia and hydrochlorothiazide infusion. Proc Exp Biol Med 106:714–717
32. Wickham JEA (1984) Intrarenal surgery. Churchill Livingstone, London New York

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