CHANGES IN LOCAL BLOOD FLOWS OF THE SOLITARY KIDNEY IN PARTIAL DISTURBANCES OF THE AUTONOMIC INNERVATION

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KEY WORDS: kidney; compensatory hypertrophy; desympathization; deparasympathization; local blood flow.

The problem of denervation injury of a transplanted organ still remains unsolved even though neurodystrophic changes are regarded as one of the foremost causes of early loss of function and development of late rejection crises, even of directly tissue-typed transplants [3, 5]. After transplantation of the kidney, the blood flow within the organ remains the sole factor for realization of trophic influences on its tissues, which are known to survive chronic denervation damage [3, 4]. In the quest for pathogenetic methods of reinnervation and pharmacological correction of neurotrophic disturbances in the trasnplatned kidney, explanation of the relative contribution of disturbances of neurotransmitter function in different parts of the autonomic nervous system to hemodynamic disturbances in different layers of the renal parenchyma is particularly interesting.

Since selective blocking of one type of efferent innervation of an organ chosen for investigation is virtually impossible to achieve surgically, in the present investigation changes in local blood flows of the solitary kidney, as the model of a transplant, were studied after chronic pharmacological desympathization and blockade of the parasympathetic nerves.

EXPERIMENTAL METHOD

Male Wistar rats weighing initially 160 g were used. Under hexobarbital anesthesia (40 mg/kg) a right-sided nephrecotomy was performed on the experimental animals, and a mock operation on the controls. The nephrectomized animals of series I received daily injections of guanethidine sulfate (Ismelin, from "Pliva," Yugoslavia) in a dose of 50 mg/kg, animals of series II received two injections (30 mg/kg each) of atropine sulfate; rats of series III and those undergoing the mock operation received injections of the corresponding volumes of isotonic solution. Local blood flow was recorded in the renal cortex and medulla under standardized pentobarbital anesthesia strictly in a dose of 50 mg/kg on the 4th, 7th, 15th, 30th, 60th, 90th, and 120th days after setting up the model, five or six animals being used at each time. The local blood flow was measured by the method of clearance of inhaled hydrogen, using a transducer with a pair of platinum-tipped electrodes 1 and 4 mm long, ensuring accurate localization of their tips in the renal cortical and medullary layers [1]. The blood flows were calculated by means of recorded exponential curves of clearance of three or four inhalations of hydrogen, by the equation LRBF = $0.693/T_{1/2} \times 100$ (ml/min/g tissue), where $T_{1/2}$ denotes the half-elimination time of hydrogen [6]. Pairs of clearance curves for each animal were recorded after the background trace twice or three times, with a change in position of the transducer in the kidney. The systemic BP was monitored during the experiment by the transducer of an EM 2-01 electromanometer, connected to catheter introduced into the femoral artery. The location of the electrodes was verified macroscopically after electrolytic destruction of the tissue in the region of the electrode tips at the end of the experiments. The results were analyzed by Student's test.

EXPERIMENTAL RESULTS

Recording local blood flows in the renal cortex and medulla of the control animals showed that their values were 1.8 ± 0.23 and 0.45 ± 0.11 ml/min/g tissue, respectively, in

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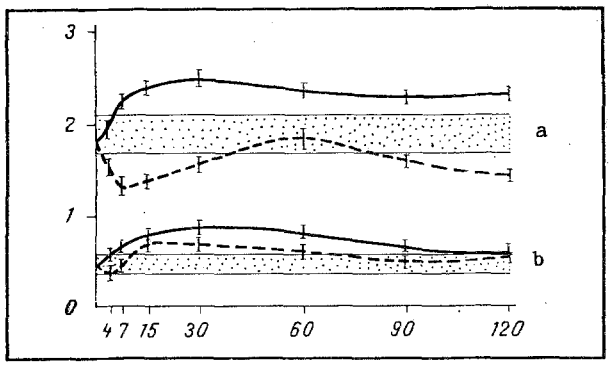

Fig. 1

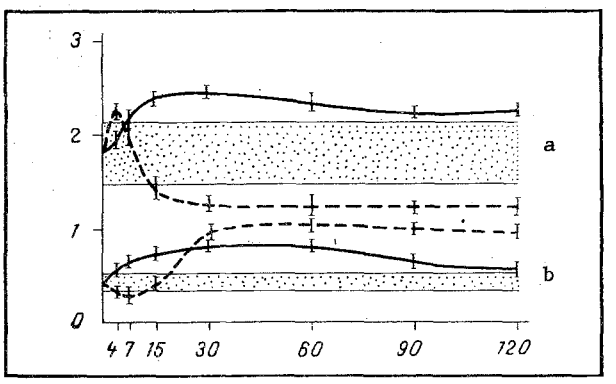

Fig. 2

Fig. 1. Time course of changes in cortical (above) and medullary (below) blood flows of the solitary residual kidney during compensatory hypertrophy (continuous line) and with chronic blockade of the parasympathetic innervation (broken line). Here and in Fig. 2: abscissa, time of experiment (in days); ordinate, LRBF (in ml/min/g tissue); a and b) range of control parameters.

Fig. 2. Time course of changes in local cortical and medullary blood flows in residual kidney after chronic desympathization (broken line).

agreement with known data [1]. These parameters reflect the intensity of the "nutritive" peritubular circulation and give an indirect idea of the glomerular blood flow, i.e., parameters of the local cortical blood flow reflect the degree of blood supply mainly of the convoluted tubules and the cortical segments of the collecting tubules, whereas those of the medullary blood flow reflect the blood supply to Henle's loops and the medullary collecting tubules.

The high level of blood supply of the residual kidney after nephrectomy is an adaptive mechanism of compensatory hypertrophy, in full agreement with the results our dynamic investigations of local blood flows in the compensatorily hypertrophied kidney (CHK) [2]. Thus the progressive increase in hemoperfusion of the cortex lasted up to 30 days, 35% longer than in the control, and was followed by a decrease to 2.3 ± 0.07 ml/min/g tissue, i.e., to values above the control levels. The intramedullary blood flow also underwent similar phasic changes, maximal values being recorded on the 30th and 60th days.

Continuous atropinization of the nephrectomized animals led to a biphasic reduction of the cortical blood flow, with a maximum on the 7th-15th day after the experiment began (Fig. 1). Depression of this parameter in the early stages was due to an increase in the myogenic tone of the juxtaglomerular arterioles, of sympathetic origin, against the background of inhibition of cholinergic mediation, i.e., the "unmasking" of the high initial sympathogenic tone of the renal vessels, leading to cortical vasoconstriction. Against this background the extraglomerular blood flow increased, causing an increase in the marginally reduced medullary blood flow, and indicating activation of the phenomenon of shunting of the blood flow into the medullary zone. Equalization of the cortical tissue blood flow by the 60th day was followed by a repeated tendency for it to be reduced, possibly due to inhibiton, now direct, of the trophic influences of acetylcholine and the guanylate-cyclase system as triggers of cell division and hyperplasia on plastic processes, especially in blood vessels, at a time of increasing mass of cortical tubules. There is no doubt that chronic relative insufficiency of the blood supply of the cortical segments of the tubular system of the solitary kidney is one of the leading causes of inhibition of compensatory hypertrophy after deparasympathization [7].

The pathogenesis of the local changes in the renal hemodynamics recorded after desympathization was more complex and was explained not only by the intrarenal adrenergic effect, but also by the systemic hypotensive effect of the sympatholytic, leading to a significant reduction of BP by 18% throughout the experiment. Thus in this series, during the first week an increase in the peritubular cortical and a decrease in the intramedullary local blood flows was observed (Fig. 2) and was explained by the primary vasodilator and hypotensive effect of guanethidine against the background of postnephrectomy hyperperfusion of the remaining kidney. Later and until the end of the experiment, the cortical local blood flow progressively declined in the experimental kidneys and the medullary local blood flow increased, also evidence of redistribution of the blood flow into the juxtamedullary and medullary zones as a result of extraglomerular shunting of blood. A shift of this nature may be due to activation of the renin-

angiotensin mechanism during chronic overloading of the organ and systemic blocking of the peripheral sympathetic neurotransmitter system, and may be aimed at maintaining homeostasis of sodium by the remaining kidney during its adaptation to chronic hypotension and to the tissue mediator deficiency.

Chronic pharmacological blockade of neurotransmitter influences can thus have a significant influence on the intrarenal hemodynamic shifts in CHK. It is logical to sugggest that reduction of cortical perfusion and redistribution of the blood flow in the medullary zone at different stages of the experiment are stereotyped mechanisms of adaptation in response to the blocking of mediator influences of the autonomic nerves on the residual kidney, which are probably based on tubulomedullary feedback, resulting from neurogenic injury to the tubular transport systems and the switching of the single kidney, under these conditions, to a phylogenetically older humoral-glomerular type of regulation of its many diverse functions.

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HYPERBARIC OXYGENATION IN THE TREATMENT OF EXPERIMENTAL HYPOTHYROIDISM

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Rehabilitation of patients after resection of the thyroid gland remains an urgent problem. One of the factors aggravating the state of such patients is the development of postoperative hypothyroidism. Besides specific correction of the pathological syndromes arising under these circumstances, nonspecific treatment of hypothyroidism also is possible. Our clinical observations have shown that hyperbaric oxygenation (HBO) is very effective in such patients [2]. However, the nature of the therapeutic effect of HBO on manifestations of hypothyroidism has not been explained.

The aim of this investigation was to study the effect of HBO on the functional state of the heart, on the microcirculation in skeletal muscle and the thyroid gland, and on some parameters of lipid peroxidation (LPO) in the myocardium of hypothyroid rabbits.

EXPERIMENTAL METHOD

Experiments were carried out on male chinchilla rabbits weighing 2.5-3 kg. A model of hypothyroidism was created by giving a single intravenous injection of ^{131}I in the composition

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