DYNAMICS OF ELECTROLYTE METABOLISM AND PATHOLOGICAL CHANGES IN THE MYOCARDIUM IN UREMIA (EXPERIMENTAL INVESTIGATION)

V. P. Krotov and V. M. Popov

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Renal insufficiency causes changes in the relative proportions of anions and cations in the plasma and interstitial fluid. These changes mostly affect the potassium balance. Whereas during the development of uremia a marked hyperkaliemia and a slight hyponatriemia are almost constantly observed [1, 3], conflicting data have been obtained for the concentrations of these ions in the tissues of different organs, including the heart [2, 4, 5].

The object of the present investigation was to study the relationship between the changes in the potassium and sodium concentrations in the blood plasma and the myocardium and the tissue enzyme changes in the myocardium in uremia.

EXPERIMENTAL METHOD

Experiments were conducted on 32 male rabbits weighing from 2500 to 3000 g, kept in identical conditions and on the same diet. Uremia was produced by a one-stage bilateral nephrectomy. During the experiments in the course of development of uremia the potassium and sodium concentrations in the blood plasma and myocardium were determined. To study the pathological changes in the myocardium, the rabbits were sacrificed at various times after the operation. Serial transverse histotopographic sections were cut from the fresh, unfixed hearts in a cryostat to a thickness of 10-15 μ and stained for fat with Sudan III; 8 tests also were performed for oxido-reduction enzymes. In addition to these investigations, 14 histological staining methods and histochemical reactions were carried out on sections 5-6 μ in thickness cut from the myocardium fixed in acetone and embedded in paraffin wax.

EXPERIMENTAL RESULTS

The blood potassium concentration in the animals before the operation varied from 3.5 to 4.2 meq/liter. Twenty four hours after nephrectomy the potassium level in some animals had risen to 6.0-6.2 meq/liter (mean 5.5 meq/liter). On the 2nd day of development of uremia a further increase in the potassium content in the blood plasma on the average by 1 meq/liter was observed. The continued development of uremia led to an increase in the potassium concentration to 7.1 meq/liter after 72 h and to 9.4 meq/liter after 4 days had elapsed since the operation. In this period, however, considerable deviations of the potassium level from the mean values in the blood were found in individual animals. On the 5th day after operation the range of deviation of the blood potassium concentration from the arithmetical mean value was essentially narrowed, reaching only ±0.8 meq/liter. By this time the mean plasma potassium concentration had risen to 12.1 meq/liter.

The changes in the potassium content in the myocardium in uremia were determined in a weighed sample of fresh and dried tissue. The trend of these changes in dry myocardial tissue is illustrated in Fig. 1. The mean potassium content in the myocardium of the healthy rabbits was 35.3±0.74 meq/100 g dry tissue. In the first 24 h after the operation the potassium concentration rose by only 0.7 meq/100 g, although this change is statistically significant ($P < 0.05$). In the course of development of uremia a further increase itself increasing on each successive day, so that on the 4th day it reached 40 meq/100 g dry tissue. However, from the 4th day after the operation the potassium content began to fall, and on the 5th day its value was 39.1 meq/100 g tissue.

Laboratory of General and Experimental Cardiology, Institute of Normal and Pathological Physiology, Academy of Medical Sciences of the USSR; Laboratory of Cardiovascular Pathology, Institute of Human Morphology, Academy of Medical Sciences of the USSR, Moscow (Presented by Academician V. V. Parin).
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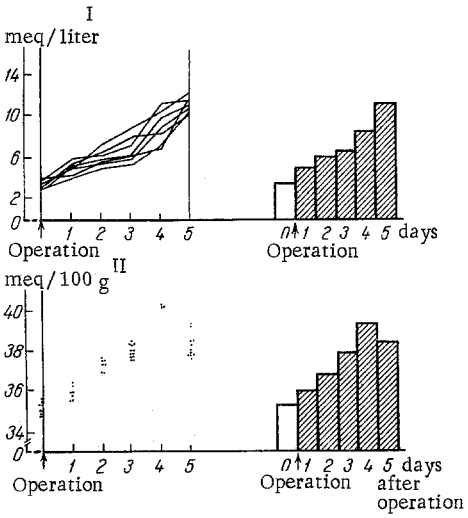

Fig. 1. Effect of nephrectomy on potassium concentration in the blood plasma (in meq/liter, I) and myocardium (in meq/100 g dry tissue, II) on the left—data for each experiment, on the right—mean data. Unshaded columns—normal.

As these results show, the hyperkaliemia was thus accompanied by an increase in the potassium concentration in the myocardium only during the first 4 days of development of uremia; later, despite the increase in the potassium concentration in the plasma, its concentration in the myocardium fell.

Diametrically opposite changes were found in the sodium concentration in the blood plasma and myocardium (Fig. 2). The plasma sodium concentration of the healthy rabbits in these experiments was 137.4±1.55 meq/liter. A significant decrease in the plasma sodium level was not observed until 2 days after the operation. With the development of uremia the sodium concentration fell progressively. The fall in the plasma sodium concentration was greatest on the 5th day, when its value was 123 meq/liter.

The sodium concentration in the myocardium fell only during the first 4 days of development of uremia. On the 5th day a statistically significant increase (compared with the 4th day) in the sodium concentration in a weighed sample of dried myocardium was observed.

Consequently, hyponatriemia developed parallel to the decrease in the sodium content in the myocardium only during the first 4 days of development of uremia. On the 5th day a significant decrease in the plasma sodium concentration was accompanied by a slight increase in its concentration in the heart muscle.

Morphological investigations of the hearts of these rabbits showed that the first changes in the myocardium became apparent 12 h after bilateral nephrectomy. They took the form of an increase in the permeability of the blood vessel walls with edema, an increase in the content of acid mucopolysaccharides in the adventitia, a marked and diffuse edema of the myocardial stroma, and small areas of diapedesis of erythrocytes to produce small hemorrhages. Twenty-four hours after the operation an increase in the edema of the myocardial stroma and in permeation of the walls of the small blood vessels with plasma proteins were observed. The content of acid mucopolysaccharides was increased near the vessels. Two days after nephrectomy a progressive edema was seen around the vessels and between the muscle fibers of the papillary muscles of both ventricles. Some muscle fibers in these parts of the heart appeared slightly swollen, with signs of vacuolation of the cytoplasm near the nuclei. Other muscle fibers were reduced in thickness, with pycnomorphic nuclei. No glycogen was present in these muscle fibers in some places, while in other places its content was greatly reduced. With the development of uremia (72 h after operation) progressive degeneration of individual muscle fibers was observed. Besides the loss of glyoogen, in some fibers of the heart no enzyme activity was present: this was especially true of succinate, α-glycerophosphate, and lactate dehydrogenases, and NAD-diaphorase. Fuchsinophilia, picrinophilia, and pyroninophilia of these muscle fibers were noted. In later periods after bilateral nephrectomy (96 h), besides the changes listed above, single muscle fibers were seen with tiny lipid droplets in their cytoplasm. These fibers appeared swollen, with a homogeneous myoplasm and an ill-defined cross striation. An increase in lactate dehydrogenase activity was clearly exhibited in the unchanged muscle fibers, indicating an increase in anaerobic oxidation of substances in the myocardium. On the 5th day after the operation small areas were found in the myocardium (mainly in the papillary muscles and beneath the endocardium) where the myofibrils had undergone lysis and the nuclei were slightly swollen. The sarcolemma of these muscle fibers was intact. As a result of this, these fibers of the myocardium appeared honeycombed in transverse section. No leukocytic reaction was present around the lysed muscle fibers.

From the results of this investigation the morphological changes in the heart can be compared with the disturbances of the potassium and sodium balance. The disturbance of the sodium and potassium concentration in the myocardium took place parallel to the changes in the structural proteins of the myocardium and in the activity of the enzymes catalyzing the principal reactions of energy metabolism. On the 5th day after nephrectomy, when a marked loss of potassium in the muscle fibers of the myocardium was accompanied by an increase in the sodium concentration, hyperhydration and lysis of the myofibrils with uncovering of the stroma of the heart were found.

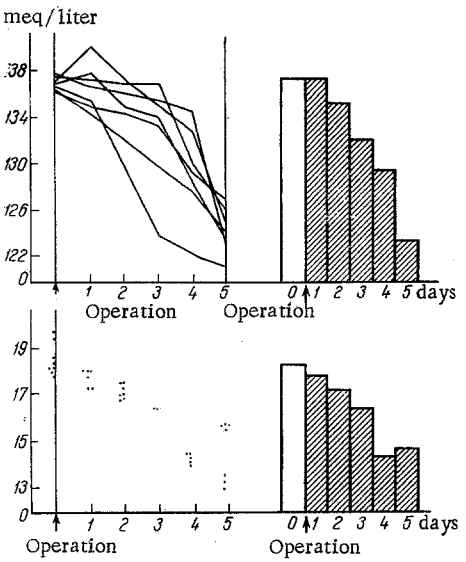

Fig. 2. Effect of nephrectomy on sodium concentration in blood plasma (in meq/liter, above) and myocardium (in meq/100 g dry tissue, below). Legend as in Fig. 1.

The changes in the subendocardial portions of the myocardium and in the papillary muscles of both ventricles may be attributed to the increased functional load placed on these parts of the heart in the conditions of severe toxemia (gross disturbances of the water and electrolyte metabolism).

It may be postulated on the basis of these results that the necrobiotic changes in individual myocardial fibers during uremia are connected with disturbances of the electrolyte balance of the heart tissues and of their metabolism.

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