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MORPHOLOGICAL CHANGES OF STRUCTURES OF TUBULAR AND VASCULAR KIDNEY SYSTEMS ON PROTEIN LOAD

Abstract

Objective. Protein is an important component in the process of functioning of the body. But for those who have kidney disease, excessive consumption of protein leads to the opposite effect. Since the glomeruli cannot completely filter blood, toxic substances accumulate in the body. This leads to the disease of other organs. Therefore, the topic is important for research. The main objective of the is to study the morphological changes in the structures of the tubular and vascular systems of the kidneys on protein load. Regulation of protein homeostasis is provided by structural and functional systems and may be accompanied by proteinuria.

Materials and methods. Therefore, in order to study the structural bases of integration of functional kidney systems in the regulation of protein homeostasis, the author created a model of protein homeostasis disruption in rats. For the experiments, adult white outbred rats weighing 140–160 g were used, which were divided into three groups.

Results. On the first day after the experiment, dilation of the afferent and constriction of the efferent arterioles, and an increase in the percentage of glomeruli were seen. The structure of the proximal tubule cells did not change. On the third day, the degree of opening of the blood capillaries, surface and juxtamedullary nephrons exceeds the parameters of the control animals. As a result of the morphological study of the kidney, it was established that under different physiological conditions there are regular changes in the cells of JGA and capillaries of the glomeruli of superficial and juxtamedullary nephrons, which are aimed at increasing the functional reserve of the kidneys in regulating protein homeostasis.

Conclusion. It was established that a single protein load is accompanied by activation of the juxtaglomerular complex, and by changes of nephrons functioning.

Key words: *protein load, kidneys, glomerular filtration rate, arterioles, juxtamedullary nephrons*

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SG – secretory granules, COR – capillary opening rate, JGA – juxtaglomerular apparatus

Introduction

The life of an organism is a broad spectrum of genetically programmed constant reorganizations in response to different environmental and internal factors and changes in homeostasis arising from fluctuations of continuous metabolic processes. Adaptive reactions that have developed over the course of evolution are realized in ontogeny as genetically programmed reactions.

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They are highly diverse but can be divided into those realized relatively quickly (fractions of a second, seconds) and slowly (days, months, years) [1, p. 54].

The kidneys play role in homeostasis and, thus, are very sensitive to any changes in the diet. The kidneys perform not only excretory function but also a number of other most important functions, including ones related to metabolism and homeostasis. Despite their sensitivity to the slightest changes in the ratio of ingredients in the diet, the duration of the complete renal response to a change in any individual ingredient can vary. To decode mechanisms of renal homeostatic functions and integration of functional systems ensuring the performance of kidneys, a protein load model has been proposed for different age groups. However, the structural mechanism governing interactions between different functional systems of the kidneys in different physiological states remains understudied [2, p. 14].

The **objective** of this study was to define structural bases of integration of certain renal functional systems in the regulation of protein homeostasis.

Materials and Methods

The experiments were performed in adult white outbred rats with body weights of between 140 and 160 g. The first group (n = 15) received a protein load on their kidneys via single and multiple parenteral doses of albumin. The second group (n = 15) was subjected to protein deprivation, with ad libitum access to water. The third group (n = 15) was a control group.

In all experiments, the right kidney was dissected through the middle line from the convex surface to the portal area. A 1.5 mm slice was taken parallel to the dissection plane, and the cortex and medulla were separated. Then the cortex was cut into three equal parts: internal, intermediate, and superficial. Renal tissue corresponding to superficial and juxtamedullary nephrons was fixed in a 2.5% buffered glutaraldehyde solution. Sections of the tissue were prepared in an ultramicrotome according to the general technique used in electronic microscopy. The sections were mounted on slides, dried at room temperature and stained with methylene blue and basic fuchsin. Microscopic images were made using a light microscope equipped with a digital camera.

Renal tissue obtained on days 1, 3, and 7 was studied using morphometry and electron microscopy.

Results and Discussion

Results showed dilation of the afferent and constriction of the efferent arterioles, increase in the proportion of glomeruli with higher capillary opening rate (COR) and activation of cells in the juxtaglomerular apparatus (JGA) on the first day of protein load [3, pp. 79–80].

The cell structure of proximal tubules was unchanged. The cells are characterized by light and homogeneous cytoplasm with nuclei in the basal area. Mesangial matrix is scarce, with single mesangial cells (Fig. 1).

Three days later, when the JGA structure had normalized, COR of both superficial and juxtamedullary nephrons exceeded that observed indicators in the control animals.

Cells in the macula densa were cleared, and the length of basal and lateral parts of their membrane was increased. Juxtavascular cells were hypertrophic and contained secretory granules.

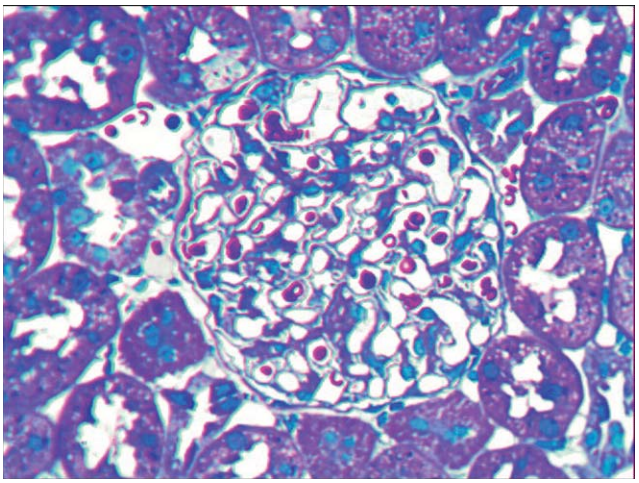

Figure 1. *Coloring: methylene blue. Inc. 40×10*

Mesangial cells grow in size and become irregular in shape under protein load (Fig. 2).

After three days of protein deprivation, COR is increased; however, no JGA activation is observed [4, p. 147].

7 days later, COR remains high in juxtamedullary nephrons only [5, p. 53].

Light microscopy results showed natural morphologic changes in different parts of the nephron. The size of glomeruli was increased, the urinary space of the Bowman's capsule was dilated, the mesangial matrix expanded and the number of mesangial cells increased, and capillary loops formed adhesions to capsule's walls and were compressed. In addition, focal sclerosis of the capsule and sclerosis of capillary loops were observed in single glomeruli. Significant changes were registered in proximal tubules. They included an increased number of secretory granules in cell cytoplasm, extrusion of the apical membrane of tubule cells into the tubular lumen, as well as nuclei in the apical or intermediate areas in significant number of cells (Fig. 3).

Therefore, different physiological states induce characteristic changes in JGA cells, glomeruli capillaries, and tubules of superficial and juxtamedullary nephrons. These changes aim to increase the functional reserve of the kidneys [6, pp. 54–55].

In control animals, juxtaglomerular cells of the afferent arteriole are the main renin-producing component of the juxtaglomerular apparatus [7, p. 84; 8, p. 102; 9, pp. 91–92]. They are polygonal in shape and contain numerous organelles: rough endoplasmic reticulum evenly distributed throughout cytoplasm and closely interacting with round-shaped moderate-size mitochondria; the Golgi apparatus is located close to the nucleus. Secretory granules (SG) are moderate in quantity, round-shaped, with high electron density, and are evenly distributed throughout cytoplasm. These data indicate their moderate functional activity [10, pp. 8–12; 11, pp. 8–82–85].

Juxtamedullary cells in the wall of the efferent arteriole are smaller and contain fewer SGs than those in the wall of the afferent arteriole. Cells in the macula densa are cylindrical, basal folds are single, low, do not contact with mitochondria, and are diffusely distributed in cytoplasm. The basement membrane is thin and non-continuous in the areas of cell membrane contact [12, p. 49].

Juxtavascular cells located between the afferent and efferent arterioles are irregular and elongated, have few organelles, numerous ribosomes and polyribosomes. Mesangial cells are located between capillaries in the glomerulus and are almost identical in structure to juxtavascular cells [13, p. 23].

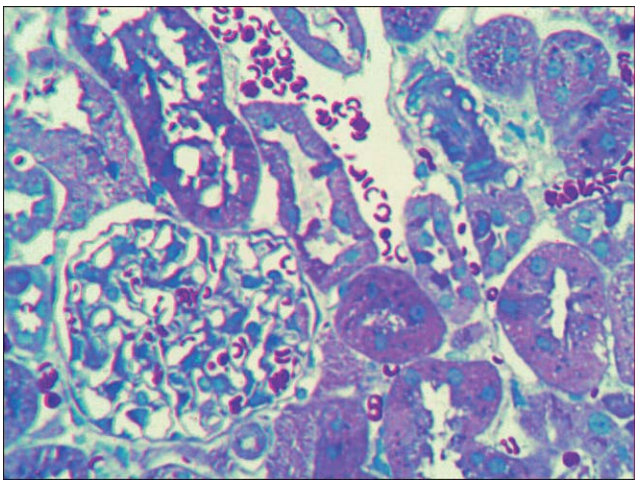

Figure 2. *Coloring: methylene blue. Inc. 40×10*

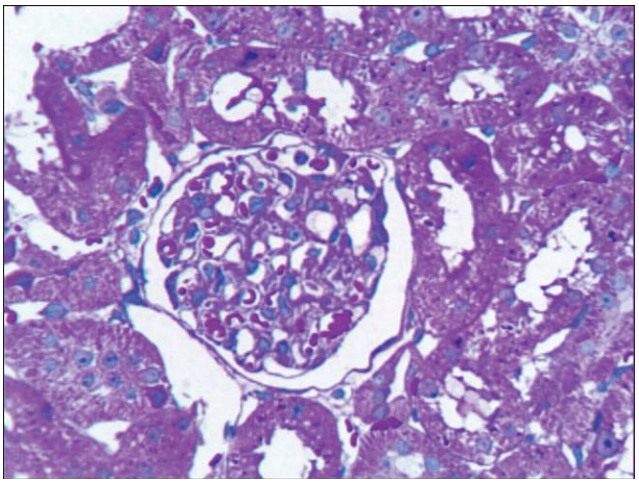

Figure 3. *Coloring: methylene blue. Inc. 40×10*

Conclusion

The obtained data indicate that single protein load is accompanied by activation of the juxtaglomerular complex and changes in nephron performance.

Morphological data characterize relatively early stages of experimentally-induced chronic renal dysfunction, since only the first signs of nephrosclerosis development were found together with clear morphological signs of changes in the glomerular hemodynamics and dystrophic changes in tubules.

The obtained data reveal new opportunities to study the role of the kidneys in protein metabolism in the event of the development of kidney failure, including tubular reabsorption of not only endogenous but also exogenous proteins. The data also point out the need to study the most important non-excretory renal functions and their effects in the analysis of nephropathies progression.

Conflict of Interests

The authors declare no conflict of interests.

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