ORIGINAL ARTICLE

CONTENTS

The morphofunctional peculiarities of renal nephrons under the condition of cellular dehydratation and periods of adaptation and readaptation

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ABSTRACT

Aim: To assess, under experimental conditions of cellular dehydration of varying severity, the nature of structural changes in the nephron and the dynamics of reparative processes during the recovery period.

Materials and Methods: The study was conducted on 110 young male Wistar rats, divided into two groups. The first group (30 rats) remained intact, while the second group (80 rats) was adapted to dehydration. Adaptation was achieved through alternating a low-mineral diet with 1.5% hypertonic sodium chloride solution (for two days) and a standard vivarium diet (for one day) over 42 days. Cellular dehydration in the second group was induced by administering 1.5% hypertonic sodium chloride solution along with dried oats and crackers. The degree of dehydration was determined based on the water deficit. In the next stage of the experiment, animals were returned to a normal diet, and readaptation changes were assessed at 1, 3, 6, and 12 weeks after the cessation of the dehydrating factor. The morphological state of the kidney structures was examined using microscopic, electron-microscopic, morphometric, and statistical methods.

Results: As a result of exposure dehydrating factor, the renal parenchyma shows functional tension in the glomeruli and tubular epithelial cells due to the increased load on the kidney. Changes of podocyte pedicels affect the size of filtration slits that regulate glomerular filter permeability. The first indicators of disorders in the glomerular-tubular system are the basal membranes in the composition of capillaries and epithelium. Even in mild dehydration, as the dehydrating factor increases, the basal membrane thickens, loses its three-layer structural organization, becomes homogeneous and osmiophilic. Gradually, podocytes and endothelial cells of capillaries are damaged, undergoing dystrophy. The process of readaptation after rehydration of the previously dehydrated organism involves a complex of morphological changes following cellular dehydration, aimed at restoring lost or weakened functions of cells and tissues, their adaptive-compensatory changes, which ensure adaptation to certain conditions. Structural transformations of cells during readaptation may manifest in the enhanced stabilization of cell membranes and the resistance of tissues to intensive influences. Previous adaptation under dehydration leads to the mitigation of the dehydrating factor's impact, manifested in a lower severity of structural-metabolic disturbances and increased energy exchange.

Conclusions: The structural components of the nephron immediately respond to disturbances in the body's water-electrolyte balance by changing their structural organization. These changes are significant in severe cellular dehydration, and their restoration requires a long period of time.

KEY WORDS: nephron, dehydration, experiment, electrolytes, blood capillaries, adaptation

Wiad Lek. 2025;78(7):1207-1212. doi: 10.36740/WLek/208985 DOI

INTRODUCTION

Various environmental factors such as temperature, humidity, radiation, and atmospheric pressure affect mainly sweating and urinary water loss. Under conditions where environmental factors increasingly harm health, the problem of body dehydration and the study of adaptive-compensatory processes during dehydration are particularly relevant [1, 2]. These disorders often lead to severe functional impairments and determine the severity of the disease course [3, 4]. Mild dehydration can cause problems with blood pressure, heart rate, and body temperature. Severe dehydration can also cause weakness or confusion. In extreme cases, it can lead to kidney damage, brain damage and even death. It is not always easy to differentiate normal cellular and tissue responses to various influences that remain within physiological norms [5-7]. Dehydration caused by an imbalance between fluid intake and loss, often leading to disturbances in the balance of total body electrolytes.

There are a lot of information about the structural changes in the heart, thyroid gland, liver, and adrenal glands under dehydration conditions [5-9]. However, the reactive physiological and destructive changes occurring in the kidney during cellular dehydration remain insufficiently studied.

AIM

To assess, under experimental conditions of cellular dehydration of varying severity, the nature of structural changes in the nephron and the dynamics of reparative processes during the recovery period.

MATERIALS AND METHODS

The study was conducted on 110 young male Wistar rats, divided into two groups. The first group (30 rats) remained intact, while the second group (80 rats) was adapted to dehydration. Adaptation was achieved through alternating a low-mineral diet with 1.5% hypertonic sodium chloride solution (for two days) and a standard vivarium diet (for one day) over 42 days.

Cellular dehydration in the second group was induced by administering 1.5% hypertonic sodium chloride solution along with dried oats and crackers. The degree of dehydration was determined based on the water deficit. In the next stage of the experiment, animals were returned to a normal diet, and readaptation changes were assessed at 1, 3, 6, and 12 weeks after the cessation of the dehydrating factor.

The morphological state of the kidney structures was examined using microscopic, electron-microscopic, morphometric, and statistical methods. All animal experiments were conducted in compliance with the International Principles of the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Strasbourg, 1985).

Tissue samples were collected under ether anesthesia from pre-weighed animals of all groups. The samples were fixed in a 10% neutral formalin solution, dehydrated in alcohols of increasing concentration, and embedded in paraffin blocks. Sections 5-6 μm thick were stained with hematoxylin-eosin, examined under a light microscope, and documented.

For electron-microscopic analysis, samples were fixed in a 2.5% glutaraldehyde solution (pH 7.3-7.4) prepared in Millonig's phosphate buffer. The fixed material was transferred to a buffer solution, washed, and post-fixed in a 1% osmium tetroxide solution on Millonig's buffer. After dehydration in alcohols and acetone, the samples were embedded in a mixture of epoxy resins following standard techniques. Ultrathin sections were stained with a 1% aqueous solution of uranyl acetate, contrasted with lead citrate using Reynolds' method, and examined using an EMI-100 PM electron microscope.

Morphometric and quantitative studies were performed using a visual analysis system for histological specimens. To objectively characterize the adaptive and destructive changes in renal corpuscles and tubules, their morphometric parameters were assessed. Within the renal cortex, measurements included the areas of renal corpuscles, glomeruli, Bowman's capsule, proximal tubules, distal tubules, their cells, and nuclei, as well as the height of proximal and distal tubular epithelial cells.

Statistical analysis was conducted using Student's t-test on a personal computer. A probability of error below 5% ($p < 0.05$) was considered statistically significant.

RESULTS

As a result of periodic exposure to an unfavorable dehydrating factor, minor changes in the structural components of the nephron were observed in the kidney parenchyma of the rats. These changes manifested as an increase in the size of the renal corpuscles (the average area was 4122±1.12 μm^2), with preservation of their structural integrity. However, there was moderate vascular filling, and a reduction in the diameter of the Bowman's capsule from 786 ±2.4 μm^2 to 668±2.5 μm^2.

Electron microscopy revealed that during this period, which was considered the adaptation phase to dehydration, glomerular vessels and epithelial cells of the tubules were in a state of functional tension as a result of the increased load on the kidney. Podocytes in the inner layer of the capsule had large, massive cytotrabeculae, and the cytopodia closely adhered to the basal membrane. Prolonged adaptation led to mitochondrial hypertrophy, with a small number of crystals observed in the lumen of the matrix.

In the study of the renal corpuscles and nephron tubules via electron microscopy during mild, moderate, and severe dehydration, the changes were categorized into two groups: hypertrophic-hyperplastic and dystrophic-atrophic. In the case of severe dehydration, dystrophic changes predominated over compensatory ones.

Hypertrophic changes led to an increase in the size of the renal corpuscles: in mild dehydration, the area increased to 4242±1.34 μm^2, in moderate dehydration to 4614±1.22 μm^2, and in severe dehydration to 4943±1.23 μm^2.

The studies also found that in severe dehydration, the apical part of the epithelial cells of the nephron tubules containing microvilli was subject to destruction. There were also changes at the basal poles of the cells, where the "transverse striation" disappeared.

Morphometric studies revealed an increase in the area of the proximal tubules, a reduction in the height of the epithelial cells, and an expansion of their lumen. Partial loss of microvilli from the apical surfaces and a 25.7% reduction in cell height led to a 13.9% increase in the lumen of the tubules, while the diameter of the tubule lumens increased by 4.9% compared to the normal values. Morphometric analysis of the proximal tubules showed that the diameter of the tubules in severe dehy-

dration was 7.0% greater than normal. The height of the cells in this part of the nephron decreased to 6.58±0.23 μm, while the diameter of the tubule lumen increased to 20.81±0.63 μm, which was 29.5% larger than normal.

Rehydration of the previously dehydrated organism during the re-adaptation phase following cellular dehydration at different time intervals (1, 3, 6, and 12 weeks) showed structural changes due to rehydration.

Light optical, morphometric, and electron microscopic studies after 7 days of re-adaptation following cellular dehydration showed no significant improvement in the nephron structure.

At three weeks of re-adaptation after mild dehydration, a gradual normalization of the renal corpuscle structure was observed. They became round-oval in shape, with well-organized glomerular vessels, endotheliocytes, basal membranes, and podocytes. Morphometric analysis revealed a reduction in the area of the renal corpuscles to normal values, but the glomerular vessels remained reduced, and the lumens of the capsules were still moderately dilated compared to the norm, significantly differing from the intact animals.

At this point in the re-adaptation process after moderate dehydration, submicroscopically, hypertrophic changes in the mitochondria were observed in both proximal and distal convoluted tubules. The epithelial cells of the proximal nephron had well-defined microvilli on their apical poles. Morphometric indicators corresponded with the findings of electron and light microscopy.

The period of 6-12 weeks of the animals being on a normal diet showed a good gradual progress in recovery processes. Microscopic studies at weeks 6-12 of rehydration showed that regeneration processes were uneven. Regenerative processes significantly improved the structural state of the kidneys, but there were still residual effects of the damaging factor in the cortical substance. Under light microscopy, different morphofunctional states of structural components of both the renal corpuscles and tubules were observed. In some areas of the kidney cortex, polymorphism of the renal corpuscles was seen, with atrophied ones being less frequently visualized, but many hypertrophied ones were present. Small renal corpuscles with dilated capsule lumens were noted, while a few corpuscles were smaller and isolated, with tight glomerular structures and a significant increase in the size of the Bowman's capsule lumen.

Morphometric measurements of the structural components of the nephron's renal corpuscles during different periods of re-adaptation after moderate dehydration gradually approached the values of intact animals starting from the third week of re-adaptation.

The apical poles of the epithelial cells of the proximal tubules were well-contoured, with the "transverse striation" of the basal poles of the cells improving, and mitochondria were arranged in an ordered fashion between the plasma membrane folds.

Morphometric studies during this period of re-adaptation showed that the area of hypertrophied and atrophied renal corpuscles approached the values of intact animals, being 4277±1.33 μm^2 and 3956±7.6 μm^2 in severe dehydration, respectively. The areas of the glomerular vessels in the hypertrophied Malpighian corpuscles remained enlarged at 3386±6.3 μm^2 compared to normal values.

The height, width, and area of the epithelial cells forming the walls of the distal tubules did not significantly differ from the values at 6 or 12 weeks of re-adaptation following moderate dehydration, being 7.81±0.32 μm, 9.68±0.37 μm, 68.9±2.3 μm^2 at 6 weeks, and 7.20±0.44 μm, 9.71±0.36 μm, 74.72±1.9 μm^2 at 12 weeks. Similar positive changes were observed in the dynamics of the diameter and area of the nephron tubules.

Submicroscopic studies of the kidney cortex after 12 weeks of re-adaptation showed that despite the long experimental period, some pathological changes remained in the structure of certain nephrons. Specifically, in 27% of glomeruli, large nuclei were observed in the endothelial cells, with high levels of ribosomal granules and uneven thickening of the perinuclear space. In the perinuclear zone of the cytoplasm, hypertrophied mitochondria, many ribosomes, and large vacuole-like structures were visualized. However, the basal membrane maintained a clear structural organization, was tripartite, and showed clear fenestration of the peripheral endothelial areas. In some areas, small cytopodia were visualized, tightly adhering to the basal membrane and closely arranged, contacting each other.

Prolonged rehydration also had a positive effect on the submicroscopic structure of the tubules. On the apical surface of the epithelial cells of the proximal tubules, a well-organized microvillus system was visualized, and at the basal pole, the "basal striation" was clearly expressed, indicating active functioning of the reabsorption barrier components.

In most of the epithelial cells in the proximal tubule wall, well-structured organelles were visualized in the light cytoplasm. These mainly included mitochondria of various sizes and shapes with moderately osmiophilic matrices, individual granular endoplasmic reticulum tubules, cisterns, and vacuoles of the Golgi complex, small lysosomes, and vesicles. Large nuclei with predominant euchromatin in the karyoplasm and clear nucleoli were observed. The nuclear membrane was uniform, and the perinuclear spaces were small and well-contoured.

DISCUSSION

Dehydration is a condition, which is caused by imbalance between fluid intake and loss, very often leading to disturbances in the balance of total number of body electrolytes. Intensive training, exhausting work, and infectious diseases are often accompanied by dehydration of the body, which can be caused by both restricted water intake and excessive water loss [4, 10, 11]. Dehydration, especially severe dehydration, can lead to the development of a serious complication such as hypovolemic shock. Dehydration affects individuals of all ages, but older persons are disproportionately impacted due to physiological changes in the organism, reduced thirst sensation, the higher prevalence of the comorbid conditions.

One of the physiological laws is the law of constancy of the internal environment of the body, or the law of homeostasis preservation [1, 12]. The concept of the constancy of the "internal environment" includes not only the quantity but also the quality, which provides cells with nutrients, building materials, and supports their physicochemical constants of temperature, osmotic pressure, pH, concentration of organic and inorganic substances and their compounds.

Among the internal organs that maintain homeostasis and ensure its stability, the kidneys play the most significant role, as their primary functions include regulating water balance, acid-base balance, blood ion composition, blood pressure, excreting nitrogenous waste products from protein metabolism, as well as performing endocrine and other important functions [2, 4, 10].

As a result of periodic exposure to the adverse dehydrating factor, the renal parenchyma of rats shows functional tension in the glomeruli and tubular epithelial cells due to the increased load on the kidney. Changes in the configuration and size of podocyte pedicels affect the size of filtration slits that regulate glomerular filter permeability [10, 11]. Consequently, an increase in permeability is accompanied by a restructuring of the ultrastructure of proximal nephron cells.

The first indicators of disorders in the glomerular-tubular system are the basal membranes in the composition of capillaries and epithelium, as evidenced by other researchers [11, 13].

Under dehydration, morphological signs of disturbances in glomerular filtration appear, as indicated by changes in the structural components of the glomerular filter. Even in mild dehydration, as the dehydrating factor increases, the basal membrane thickens, loses its three-layer structural organization, becomes homogeneous and osmiophilic. Gradually, podocytes and endothelial cells of hemocapillaries are damaged, undergoing dystrophy.

Atrophic-dystrophic changes in the renal corpuscles, which occur in severe dehydration, manifest not only in the shrinkage of the glomeruli but also in the atrophy of the renal corpuscles, negatively affecting the trophism of proximal and distal tubules, causing disturbances in their structural organization and urinary function [5, 14].

In the case of cellular dehydration, the structure of the entire nephron is damaged, although changes in the tubular part are usually more pronounced than in the glomerular part. This depends on the morphological-functional features of the nephron segments, the nature of their metabolism, their sensitivity to the altered conditions, and the sequence of reserve nephrons involved in compensatory-adaptive responses.

The process of readaptation after rehydration of the previously dehydrated organism involves a complex of morphological changes following cellular dehydration, aimed at restoring lost or weakened functions of cells and tissues, their adaptive-compensatory changes, which ensure adaptation to certain conditions.

Structural transformations of cells during readaptation may manifest in the enhanced stabilization of cell membranes and the resistance of tissues to intensive influences. Mitochondrial membranes are the first to undergo changes, followed by the granular endoplasmic reticulum, leading to the disintegration of protein synthesis and disorders in the intracellular transport system. These changes are aimed at restoring homeostasis and are observed when the body is affected by chemical, physical, and biological factors, as well as during physiological regeneration and pathology. Thus, there are patterns of structural changes that determine the direction, depth, and reversal of compensatory-adaptive reactions [2, 10, 15].

Previous adaptation under dehydration leads to the mitigation of the dehydrating factor's impact, manifested in a lower severity of structural-metabolic disturbances and increased energy exchange.

Positive changes in the structural organization of the renal cortex, which occur as early as the 3rd week of readaptation after cellular dehydration, and the tubules of the nephron at the 6th week, indicate that the readaptation processes in animals adapted to cellular dehydration occur more actively and quickly in all structural components of the nephron, promoting the relative normalization of their structure and urinary function.

CONCLUSIONS

The structural components of the nephron immediately respond to disturbances in the body's water-electrolyte balance by changing their structural organization. These changes are significant in severe cellular dehydration, and their restoration requires a long period of time.

However, the influence of the adverse factor triggered the activation of compensatory-adaptive reactions, and the process of readaptation occurs more rapidly in an organism that is adapted to dehydration.

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The work is carried out within the framework of the initiative research work of the I. Horbachevsky Ternopil National Medical University (Ternopil, Ukraine) "0116 U003390 Systemic and organ disorders due to the action of extraordinary factors on the body, the mechanisms of their development and pathogenetic correction".

CONFLICT OF INTEREST

The Authors declare no conflict of interest

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RECEIVED: 10.01.2025
ACCEPTED: 27.06.2025