

ABSTRACT

of the dissertation for the degree of Doctor of Philosophy (PhD) in 6D060700
Biology

RAKHMETOVA ASSEL MURZAGELDINOVNA

STRUCTURAL ORGANIZATION OF THE KIDNEY IN CONDITIONS OF PERIPHERAL TUMOR GROWTH AND CORRECTION WITH LITHIUM CARBONATE

The relevance of the topic. The relevance of the study is determined by the steady growth of malignant diseases all over the world and in Kazakhstan, including, which is associated, in particular, with environmental degradation. Environmental pollution represents a wide range of carcinogenic and mutagenic substances that can play a role in chronic systemic inflammation, oxidative stress, DNA damage and cancer development. The problem of tumor growth has recently attracted increasing attention from researchers.

It is generally accepted that a healthy body has a self-regulating system of homeostasis. The main mechanisms of regulation of this system upon ingestion of xenobiotics are the processes of absorption, utilization and excretion. The kidneys play an important role in these processes, which are not only one of the main detoxification organs, but also take part in all metabolic processes.

Also, the human kidney contains about a million nephrons, each of which is able to independently perform its main function: to regulate the chemical and ionic composition of blood plasma by filtering it.

Impaired renal function adversely affects the functional activity of all organs and systems. Kidney function is extremely important in malignant growth, characterized by the development of endogenous intoxication. The syndrome of endogenous intoxication can be aggravated by the use of antitumor drugs that promote the breakdown of tumor tissue and the increase of toxic metabolites in the blood.

It is known that hepatocarcinoma is one of the aggressive human tumors and, despite successes in early diagnosis and treatment, gives a high percentage of mortality among patients due to metastasis.

The problem of induction of tumor cell death is currently one of the most relevant areas in modern biomedical research. The complexity of solving this problem is determined by the heterogeneity of the tumor cell population, the presence of cancer stem cells and cells at different stages of the cell cycle, as well as the existence of various signaling pathways and many signaling molecules involved in the regulation of cell death – apoptosis, autophagic death and necrosis.

Recently, lithium salts have been considered as antitumor agents capable of blocking tumor growth.

It has been shown that lithium carbonate can cause the development of apoptosis and autophagic death of hepatocarcinoma cells. There are studies indicating the antitumor effect of lithium salts in other forms of cancer.

However, the use of lithium preparations may be limited by its toxic effect on the body. Therefore, it is relevant to develop methods and doses of lithium administration.

In connection with the above, it seems relevant to study the structural organization of the kidney in conditions of peripheral tumor growth and the use of lithium to block tumor growth.

The object of the study is the kidneys of mice of the NEA line

The research methods are transmission electron microscopy, immunohistochemical analysis, morphometry and statistical analysis.

The purpose of the study: To identify structural changes in the kidneys under conditions of long-term tumor growth and the use of lithium carbonate

Research objectives:

1 Using light microscopy to investigate structural changes in the kidney in the dynamics of peripheral tumor growth.

2 Using electron microscopy to identify ultrastructural changes in the components of the renal nephron in the dynamics of tumor growth.

3 Using immunohistochemical analysis to determine the contribution of autophagy in maintaining the homeostasis of kidney cells in conditions of peripheral tumor growth.

4 To investigate the effect of lithium carbonate on the kidney structure of intact animals

5 To identify structural changes in the components of the renal nephron at various stages of lithium carbonate administration in the conditions of modeling tumor growth

Scientific novelty

For the first time, new data on structural rearrangements developing in the kidney during modeling of distant tumor growth – hepatocarcinoma-29 in the thigh muscle tissue of experimental animals are presented. It was found that in conditions of distant tumor growth, in the structure of the kidney, there is a decrease in the volume density of the lumen of the capsule and glomerular capillaries of the renal corpuscle, an increase in the volume density of the extracellular matrix, a decrease in the thickness of the basement membranes of glomerular capillaries and distal tubules, a decrease in the number of fenestra in the endothelium of glomerular capillaries, an increase in the size of cytopodia.

For the first time, the use of lithium carbonate as an antitumor agent leads to an aggravation of structural changes in the kidney, which is apparently due to an increase in the toxic load on the organ due to an increase in the decay products and death of tumor cells under the influence of lithium. The use of lithium carbonate on the periphery of tumor growth has a corrective effect on the structure of the kidneys and the ultrastructure of the renal corpuscle.

It was found that in the conditions of modeling hepatocarcinoma-29 in the thigh muscle tissue of experimental animals, ultrastructural changes were observed

in the epithelial cells of the proximal nephron, indicating a violation of organ function. There is a swelling of the cytoplasm of cells, a decrease in the numerical density of mitochondria and the development of autophagy - an increase in autolysosomes and lysosomes.

Provisions to be defended:

1. In conditions of distant tumor growth, structural changes develop in the kidney, indicating a violation of the filtration barrier of the organ. There is a decrease in the volume density of the lumen of the capsule and glomerular capillaries of the renal corpuscle, an increase in the volume density of the extracellular matrix, a decrease in the thickness of the basement membranes of glomerular capillaries and distal tubules, proximal tubules unchanged, as in the control group of animals, a decrease in the number of fenestras in the endothelium of glomerular capillaries, an increase in the size of cytopodia.

2. In the conditions of modeling long-term tumor growth, morphological changes develop in the kidneys during the development of hepatocarcinoma in the thigh muscle tissue of experimental animals. There is an increase in the size of the lumen of the capsule and interstitial spaces of the renal corpuscle and a decrease in the volumetric density of the capillary glomeruli. When lithium carbonate is administered per os, the size of the lumen of the renal corpuscle capsule decreases, the volume density of the capillary glomeruli and the size of the interstitial spaces of the renal corpuscle increase. When lithium carbonate per os was administered to intact animals in the kidney structure, an increase in the size of the lumen of the renal corpuscle capsule and a decrease in the volume density of capillary glomeruli and the size of the interstitial spaces of the renal corpuscle were noted. The use of lithium carbonate on the periphery of tumor growth has a corrective effect on the structure of the kidneys and the ultrastructure of the renal corpuscle.

3. When modeling hepatocarcinoma-29 in the thigh muscle tissue of experimental animals, ultrastructural changes are observed in the kidney, indicating a violation of organ function. There is a decrease in mitochondria, an increase in primary and secondary lysosomes, and swelling of epithelial cells of the proximal nephron.

Theoretical and practical significance.

The results of the study contribute to fundamental lymphology and cell biology and morphology and may have applied significance. It was found that in conditions of distant tumor growth, structural changes develop in the kidneys: a decrease in the volume density of the lumen of the capsule and glomerular capillaries of the renal corpuscle, an increase in the volume density of the extracellular matrix, a decrease in the thickness of the basement membranes of glomerular capillaries and distal tubules, proximal tubules unchanged, as in the control group of animals, a decrease in the number of fenestrae in the endothelium of glomerular capillaries, an increase in the size of cytopodia.

The results obtained have found practical application in the laboratory of physiology of the Scientific Research Institute Of Clinical And Experimental Lymphology design system, a branch of the Institute of Cytology and Histology

SB RAS in Novosibirsk, research works of the Scientific Research Institute of Human and Animal Physiology of the NC MES RK (Almaty, Kazakhstan).

The main provisions of the dissertation are included in the course of lectures on the discipline "Cell Biology" for students of the specialty "5B060700-Biology" at S. Toraighyrov PSU in Pavlodar (the acts of implementation are attached)

Approbation and implementation of research results: 16 scientific papers on the topic of the dissertation have been published. International scientific and practical conference "IX toraighyrov readings". Pavlodar, Kazakhstan, 2017; international conference on lymphology. Bishkek, Kyrgyzstan, 2018; XIII International Scientific and Practical Conference "Lymphology: Medical technologies from basic research". Novosibirsk, Russia, 2018; Biotechnology and Biotechnological experiments, special issue: European Biotechnology Congress, Poland, 2020.; IEEE International Multi-Conference on Engineering, Computer and Information Sciences 2022 (SIBIRCON), Novosibirsk, Russia, 2022; scientific article published in the foreign journal "The influence of lithium carbonate salts on the structural organization", registered in the information base of the International Journal with a non-zero impact factor (WoS and Scopus database of cells and vessels in the development of experimental hepatocarcinoma", European Biotechnology Congress Nanotechnology, the Netherlands, 2018; «Accumulation and neuroprotective effects of lithium on hepatocellular carcinoma mice model», Behavioural Brain Research. Volume 456, 5 January 2024; "Ultrastructure of the kidney proximal tubular epithelium during peroral administration of lithium carbonate in tumor growth", Clinical and Experimental morphology. 2023 in journals recommended by the Committee for Control in the field of education and Science of the Ministry of Education and Science of the Republic of Kazakhstan: "Structural organization of labor in conditions of excluded tumor growth", "Bulletin of L. N. Gumilev YSU", series "Biological Sciences", 2019; "The effect of lithium carbonate on the structure of mail in conditions of peripheral tumor growth", "Astana Medical Journal", medical journal Astana, Kazakhstan, Astana, 2020; "Effect of lithium carbonate op sydney structures sondiones of dystant tumour growth", "Bulletin of Karsu" Series "Series"biological sciences", Kazakhstan, Karaganda, 2020

The relationship of the presented work with other research papers and various state and international programs

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The scope and structure of the work: the dissertation work includes the main 102 pages, normative references, definitions, designations and abbreviations, introduction, three sections, conclusion, references – 264, table – 15, figures – 20, graphics – 3 and appendices.