



RELATIVAL DESCRIPTION OF KIDNEY MORPHOMETRIC PARAMETERS IN POLYPHARMACY OF ANTI-INFLAMMATORY PILLS

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✓ *Resume*

In connection with the rapid development of nephrology and kidney transplantation, the interest of morphologists in studying the structure of the kidney as an important organ of the urinary system is constantly increasing. At the moment, diseases of the urinary system are increasing in the world, and many researchers point out that the main reason for the increase in the number of diseases is environmental pollution, which leads to a violation of the protective functions and adaptive reserves of the human body. The kidney is a very vulnerable organ to exogenous and endogenous influences. Morphological changes in this body as a result of exposure to various substances of a physical, chemical and biological nature, as well as the effects of stress and severe pathological conditions, hypergravity and ionizing radiation have been widely studied.

Keywords: urinary system, pathogenic factors, protective functions, exogenous and endogenous influences.

СРАВНИТЕЛЬНАЯ ХАРАКТЕРИСТИКА МОРФОМЕТРИЧЕСКИХ ПОКАЗАТЕЛЕЙ ПОЧЕК ПРИ ПОЛИФАРМАЦИИ ПРОТИВОВОСПАЛИТЕЛЬНЫХ ПРЕПАРАТОВ

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✓ *Резюме*

В связи с бурным развитием нефрологии и трансплантации почки постоянно возрастает интерес морфологов к изучению строения почки как важного органа мочевыделительной системы. В настоящий момент в мире увеличивается количество заболеваний мочевыделительной системы, и многие исследователи указывают, что основной причиной роста числа заболеваний является загрязнение окружающей среды, что приводит к нарушению защитных функций и адапционных резервов мочевыделительной системы. человеческое тело. Почки очень уязвимы к экзогенным и эндогенным воздействиям. Широко изучены морфологические изменения в этом организме в результате воздействия различных веществ физической, химической и биологической природы, а также воздействия стрессов и тяжелых патологических состояний, гипергравитации и ионизирующих излучений

Ключевые слова: мочевыделительная система, патогенные факторы, защитные функции, экзогенные и эндогенные воздействия

YALLIG'LANISHGA QARSHI DORI VOSITALARINI POLIFARMATSIYA QILISHDA BUYRAKLARNING MORFOMETRIK KO'RSATKICHLARINING QIYOSIY XARAKTERISTIKASI

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Nefrologiya va buyrak transplantatsiyasining jadal rivojlanishi munosabati bilan siydik tizimining muhim organi sifatida buyrak tuzilishini o'rganishga morfologlarning qiziqishi doimiy ravishda oshib bormoqda. Hozirgi vaqtda dunyoda siydik tizimi kasalliklari soni ortib bormoqda va ko'plab tadqiqotchilar kasalliklar sonining ko'payishining asosiy sababi atrofmuhitning ifloslanishi ekanligini ta'kidlamodalar, bu esa himoya funksiyalari va adaptiv funksiyalarning buzilishiga olib keladi, bu esa o'z navbatida siydik tizimi va inson tanasi zararlanishiga olib keladi.

Buyraklar ekzogen va endogen ta'sirlarga juda zaifdir. Bu organizmdagi morfologik o'zgarishlar fizik, kimyoviy va biologik xarakterdagi turli moddalar ta'sirida, shuningdek, stress va og'ir patologik holatlar, gipergravitatsiya va ionlashtiruvchi nurlanish ta'sirida keng o'rganildi.

Kalit so'zlar: siydik tizimi, patogen omillar, himoya funksiyalari, ekzogen va endogen ta'sirlar.

Relevance

There is no clear understanding of the rules of formation of the kidney structure at different ages, the structural basis of the reaction of the vascular-tissue structures of the kidney of animals when polypharmacy is used. The relevance and necessity of studying these problems is very clear, because revealing the adaptive mechanisms and morphological bases of the urinary system allows to determine very important points - morphological, as well as functional characteristics at different ages, inter-organ and interactive periods. Nonsteroidal anti-inflammatory drugs (NSAIDs) are one of the most widely used drug groups in medicine. The advantage of these drugs is their complex effect (antipyretic, anti-inflammatory and pain reliever), as well as a wide range of possible indications. The drugs used in our experiment are 5 types of anti-inflammatory drugs that are common and frequently prescribed by doctors, and they belong to the same group according to their pharmacodynamic effects. However, the data available today on the results of treatment with these drugs do not allow us to make clear conclusions about their effectiveness or ineffectiveness, as well as the development of side effects in such combinations. The side effects of these agents are naturally associated primarily with damage to the mucous membrane of the gastrointestinal tract and the urinary system. Not including polyphragmasia, that is, long-term uncontrolled intake of any drugs with anti-inflammatory, pain-relieving, hormonal effects can cause structural damage to kidney nephrons. At the same time, the information presented in the literature about the toxic effect of these drugs on the kidneys is somewhat contradictory. Thus, there are also cases where damage to the kidney nephrons caused by taking anti-inflammatory drugs leads to the development of life-threatening situations, poisoning of the body and a decrease in its adaptive response.

At the moment, active work is being done to reduce the incidence of polyphragmosis in medical practice in the healthcare sector in Uzbekistan. Decision of the President of the Republic of Uzbekistan No. PQ-4554 dated December 30, 2019 "On additional measures to deepen reforms in the pharmaceutical sector of the Republic of Uzbekistan", Decree No. 191 of the Ministry of Health of the Republic of Uzbekistan dated June 18, 2010 "Prescription of drugs and patient treatment-order "On approval of the regulation on the procedure for receiving, storing and using drugs in preventive institutions, as well as the procedure for providing drugs to the population by prescription in pharmacies" among them. Our study was devoted to determining the morphometric characteristics of the 5-month-old white rat kidney under the influence of polypharmacy of anti-inflammatory drugs (AID). During the years of independence, fundamental changes were made in the healthcare system of our country, special attention was paid to early diagnosis of diseases arising from various sources and reduction of negative consequences. In recent years, the level of medical services to the population has improved in our country. A number of large-scale measures have been implemented to prevent and treat diseases. A number of tasks aimed at adapting the medical system to the requirements of world standards, reducing diseases that develop under the influence of anthropogenic factors from natural and technical sources, "...increasing the efficiency, quality and popularity of medical care provided to the population in our country, as well as forming

a system of medical standardization, diagnosing and introducing high-tech methods of treatment, by creating effective models of patronage service and dispensation, supporting a healthy lifestyle and preventing diseases..." Decree No. 5590 [www.lex.uz] was launched. These tasks make it possible to reduce the pathological conditions that develop in the body under the influence of polypharmacy, related to the damage of the kidneys, to raise the level of modern medical services in the diagnosis, treatment and prevention of their complications to a new level, and to improve the use of modern technologies in the provision of quality medical services, and to reduce the rate of disability and death as a result of complications of diseases gives. The level of study of the problem. Currently, the issue of widespread use of anti-inflammatory drugs for the purpose of mobilizing the body's natural defenses, forming physiological and immunobiological reactions for the prevention and treatment of all types of baldness remains relevant.

It is important to study the changes in kidney morphometric indicators when using drugs in an unreasonable combination at the same time.

In the developed countries of the world, the death rate from side effects of drugs ranks 4-5 among the population deaths. Statistics show that polypharmacy of NSAIDs is common and any specialist doctor can do it.

Reactive morphofunctional changes in the kidneys observed under the influence of damaging factors in the body allow to determine the nature and intensity of the adaptive response of the kidney to this effect. Objective assessment of changes in the structural and functional state of the kidney paves the way for morphometric research methods that meet the modern requirements of evidence-based medicine. During the study of the available literature data, it was found that the data on the morphometric changes of the kidney structure under the influence of polypharmacy were not sufficiently studied.

The purpose of the study. Study of changes in morphometric parameters of kidneys in conditions of polypharmacy of anti-inflammatory drugs.

Research tasks:

1. To study changes in the morphological parameters of five-month-old white rat kidneys in the norm, as well as when using anti-inflammatory drugs separately.

2. To determine the morphological parameters of the kidneys of five-month-old white rats and the changes in the morphometric parameters of the kidney structural structures when using two, three, four and five types of anti-inflammatory drugs at the same time.

3. To study the morphometric parameters of kidney nephrons of five-month-old white rats in the norm, as well as the morphometric changes caused by the simultaneous use of two, three, four and five types of anti-inflammatory drugs.

Material and method

Research object. The study was conducted on 250 5-month-old inbred white rats. They were kept in normal vivarium conditions. According to the study, all experimental animals were divided into 5 comparable groups. 5 types of anti-inflammatory drugs were used in polypharmacy in different combinations.

Histological material obtained from different parts of the kidneys of experimental white rats served as the subject of the study.

Research methods. Experimental, histological, morphological, morphometric, and statistical methods were used to conduct the research and achieve the goal.

Result and discussion

Practical significance of research. The results of the study of macro- and microscopic changes in kidney formations against the background of polypharmacy help to choose the right number of drugs and to determine the interaction of drugs with similar pharmacodynamics. The study of the morphological structural changes of the kidney under the influence of two or more NSAIDs allows to create the most important combinations of these drugs. The obtained information serves to develop scientific bases for improving the condition of patients suffering from pain syndrome,

musculoskeletal system problems, and inflammatory diseases. The results of the research were introduced into the educational process of the departments of pharmacology and clinical pharmacology, pathological anatomy, and pathological physiology of the Samarkand State Medical Institute, as well as the work of doctors of polyclinics of the city of Samarkand. The reliability of the research results was determined by modern, complementary experimental, morphometric, laboratory and statistical methods used in the research. The obtained results make it possible to determine the most characteristic patterns of changes in the morphological and functional parameters of nephron structures, and also help to determine the formation and development of pathological changes in the kidneys of white rats. The work was carried out in the research laboratory of the Bukhara State Medical Institute (BSMI) during 2021-2022.

The experiment was conducted in vivarium conditions on 250 white rats. White rats aged up to 5 months were involved in it. At the beginning of the experiment, all sexually mature rats were quarantined for a week, and after exclusion of somatic or infectious diseases, they were transferred to the usual vivarium regimen with 3 meals a day. The following anti-inflammatory drugs were used to study the effects of polypharmacy in experimental groups of animals: Aspirin (SAQD - salicylic acid derivatives), Paracetamol (SAQD - anilide derivatives), Ibuprofen (SAQD - propionic acid derivatives), Dexamethasone (synthetic hydrocorticosteroid), Hydroxychloroquine sulfate (anti-inflammatory effective antimalarial). Experimental animals were divided into 5 groups (n = 250): I - control group (n = 50); II - group - rats that received 2 types of anti-inflammatory drugs, paracetamol 15 mg / kg, aspirin 5 mg / kg (n = 50); III - group - rats that received 3 types of anti-inflammatory drugs, paracetamol 15 mg / kg, aspirin 5 mg / kg, ibuprofen 6 mg / kg (n = 50); Group IV - white rats 4 types of anti-inflammatory drugs, paracetamol 15 mg/kg, aspirin 5 mg/kg, ibuprofen 6 mg/kg, dexamethasone 0.1 mg/kg. (n = 50); Group V - white rats receiving 5 types of anti-inflammatory drugs, paracetamol 15 mg/kg, aspirin 5 mg/kg, ibuprofen 6 mg/kg, dexamethasone 0.1 mg/kg, hydroxychloroquine sulfate 6.5 mg/kg (n = 50). Doses of this drug were calculated empirically and administered as an intragastric solution every day for 10 days.

From 141 days to 150 days, 0.5 ml of distilled water was administered through the gastrointestinal tract to non-white rats in the control group. It was conducted in compliance with the rules of humane treatment of animals, regulated by the "Rules for conducting work using experimental animals" approved by the ethics committee of the Bukhara State Medical Institute named after Abu Ali Ibn Sina.

A total of 250 rats were involved in the experiments, of which only 1 died during the experiment (table 1).

Distribution of animals into groups depending on the content of the experiment.

It was observed that there was no deviation in the general condition and behavior of the animals. After that, the experimental animals were weighed at the appropriate time in the morning, slaughtered by beheading under ether anesthesia on an empty stomach, and subjected to the experiment. Animal sacrifice was performed in accordance with international recommendations for medical-biological research using laboratory animals.

Research methods included organometric, histological, histomorphometric, microscopic and statistical methods.

Using organometric, histological, histomorphometric and microscopic methods, kidney morphogenesis in white rats was studied at various levels (organ, tissue and cell level). Statistical (methodological) information was used to process the research results. After extraction, the kidneys were cleaned, their weight was measured on a VLR-200 laboratory balance (2019y) to an accuracy of 0.25 mg, and the length, width, and thickness of the organ were measured to an accuracy of 0.05 mm using a caliper. Information about the obtained results was recorded in the records of material selection.

Absolute and relative kidney mass and kidney volume were calculated using the standard empirical coefficient formula that replaces the sonographic study.

After organometry, the kidneys were preserved in a 10% solution of neutral formalin. After fixation, the preparations were washed in running water for one hour. The material was embedded in paraffin blocks according to a standard technique that included dehydration with a high-concentration alcohol solution. Next, paraffin sections with a thickness of 4-6 μm were prepared

using an MC-2 microtome, stained with hematoxylin-eosin and Van Gison methods. Sections were examined morphometrically using an ocular micrometer DN-107T / Model NLSD-307B (Nobel, China), at the level of the renal medulla, the renal corpora, vascular glomeruli, and glomerular capsule cavity were measured, as well as the diameter and lumen diameter of their proximal and distal convoluted tubules. was measured. In order to directly determine the mathematical processing of the morphological data obtained during the research, using the capabilities of the "STTGRAPH 5.1" program, the Microsoft Office software package "Excel 7.0" was implemented on a Pentium-IV personal computer. Standard deviation and representative errors were determined.

Table 1

The essence of the experiment

Group	The essence of the experiment	5-month-old white rats in the experiment	Total number of animals
I	Control group	50	50
II	Rats treated with 2 types of anti-inflammatory drugs, paracetamol 15 mg/kg, aspirin 5 mg/kg (n=50)	50	50
III	Rats receiving 3 types of anti-inflammatory drugs, paracetamol 15 mg/kg, aspirin 5 mg/kg, ibuprofen 6 mg/kg (n=50)	50	50
IV	Group IV - rats 4 types of anti-inflammatory drugs, paracetamol 15 mg/kg, aspirin 5 mg/kg, ibuprofen 6 mg/kg, dexamethasone 0.1 mg/kg. (n = 50)	50	50
V	Group V - rats receiving 5 types of anti-inflammatory drugs, paracetamol 15 mg/kg, aspirin 5 mg/kg, ibuprofen 6 mg/kg, dexamethasone 0.1 mg/kg, hydroxychloroquine sulfate 6.5 mg/kg (n = 50)	50 (1)	49 (1)
Total		250 (1)	249 (1)

Variance series of numerical data were plotted, arithmetic mean deviation was calculated, and mean error, coefficient of variation, and percent deviation of measurements from control were calculated. The statistical significance of deviations from the corresponding control of the obtained results was evaluated using the parametric method - Student's criterion (in the case of normal distribution) for comparing two independent samples. When bifurcation was observed in the obtained data, the Mann-Whitney test was used to compare two independent samples. The difference was considered significant with a probability of error of 5% ($r < 0.05$). Microscopic examinations showed that the main component of the nephron is the renal corpuscle, which is surrounded by a two-layered capsule consisting of an outer and an inner layer. The outer layer of the capsule is covered with a single layer of flat epithelial cells. Morphologically, the balls have thin connective tissue, the number of capillaries is evenly distributed. At the level of the capsule cavity of the ball. Signs of this appearance were mainly evident in the proximal convoluted tubules. In addition, research microscopy, in addition to the views described above, is explained by a significant number of widths in the space of the nephron tubules (figure 1).

Figure 1. Cortical material of the kidneys of 5-month-old control rats.



Thus, as a result of macroscopic, histological, and morphometric studies, the structure of kidney nephron components of 5-month-old rats in the control group was determined, which corresponds to the laws described in the literature.

According to our data, the experimental dynamics in the group receiving two types of anti-inflammatory drugs gave the following information on the results of modeling in 5-month-old rats:

The body weight of 5-month-old rats in group 2 ranged from 228.23 g to 273.34 g, with an average of 235.72 ± 1.37 g. There were no deviations in the body weight of rats compared to group 1 of the experiment. No differences were found in the kidneys of 5-month-old rats compared to group 1 of the experiment (fig. 2.). The organometric parameters of the kidneys of the experimental animals did not differ from the values of the control group in all periods, mainly during the observation period.



Figure 2. Cross-section of kidney of 5-month-old rats of group 2. Magnified 2.5 times

Experimental animals Group 2 5-month-old rats, the absolute weight of the kidneys is from 1505.11 mg to 1791.08 mg, the average is 1674.11 ± 6.21 mg, the length of the right kidney is from 16.12 mm to 17.09 mm, the average is 16.52 ± 0.31 mm, the width From 8.37 mm to 9.43 mm, the average is 8.91 ± 1.03 mm, and the thickness is from 7.08 mm to 8.33 mm, the average is 7.67 ± 0.5 mm. These indicators indicate that there were no deviations compared to the 1st group of the experiment.

At the same time, during the observation period, the volume of the right kidney ranged from 1339.92 mm³ to 1897.6 mm³, the average was 1553.47 ± 8.12 mm³, which shows no change compared to the 1st group of the experiment.

When the kidneys of rats in the group that received two types of anti-inflammatory drugs were examined microscopically, a number of specific features were revealed in the structure of nephrons.

In this case, the renal corpuscles of the nephrons retain their structure, but destroyed renal corpuscles are often detected between the preserved tubules. In some kidney bodies, destroyed vascular balls were found, which indicates the presence of erythrocytes in the capsule cavity. The cortical nephrons in the kidneys of 5-month-old irradiated rats of the experimental group appeared to be smaller due to the narrowing of the capsule space, while most of the renal corpora were compared to the control group of experimental animals.

Conclusion

Polypharmacy of anti-inflammatory drugs had a negative effect on parameters of kidney structures. It was found that the area of the renal corpuscle (up to 6.23%), the area of the renal capsule cavity (up to 12.36%), and the area of the renal corpuscle (up to 7.04%) decreased. Under the influence of polypharmacy, the renal nephron proximal convoluted tubules (up to 8.27%) and distal convoluted tubules (up to 8.77%), as well as the diameter of their cavities (up to 16.97% and 8.77%) decreased indicators were observed.

In polypharmacy rats, the initial parameters describing the structural and functional state of nephrons underwent negative changes, and it was found that the diameter of the proximal and distal convoluted tubules and their spaces was smaller than the kidney elements of the control group of the experiment.

Compared with the experimental groups under the influence of YaQDV polypharmacy, it was observed that the area of renal corpuscles, the area of the capsule space of the kidney ball, the diameter of proximal and distal convoluted tubules and their spaces decreased in different sizes. These changes in the parameters of the kidneys of experimental animals depended on the number of drugs that the rats received.

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