

MEDICINE

COMPARATIVE CHARACTERISTICS OF THE MORPHOLOGICAL CHANGES OF NEPHRON TUBULES AT THE EARLY AND LATE STAGES OF THE CHRONIC OPIOID EFFECT

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ABSTRACT

The aim of the study is the examination of the nephron tubules morphological changes at the early and late stages of the experimental chronic opioid effect. Varying degrees of the morphological changes of proximal convoluted tubules, loops of Henle and distal convoluted tubules under chronic nalbuphine effect in the dynamics have been detected. The materials of the study – kidneys of 56 sexually mature male-rats. The experimental animals received daily intramuscular nalbuphine injections for 98 days. From the first to the fourteenth day of the experiment the dose of nalbuphine was 0,212 mg/kg. Every next two weeks nalbuphine injections were done in increasing doses. For histological investigation was used commonly agreed method. The colouring was performed using hematoxylin and eosin as well as azan by Heidenhain's method. Varying degrees of morphological changes of proximal convoluted tubules, loops of Henle and distal convoluted tubules under continuous nalbuphine injection in the dynamics have been detected. The most vivid alternative changes can be observed in proximal convoluted tubules both: at the early and late stages of the experiment. At the early stages as of the 14th day of the experiment signs of granular dystrophy appear, as of the 28th day – necrotic changes, progressing further at the late stages of the experiment. The loops of Henle undergo sporadic destructive changes at the early stages and at the beginning of the late stage of the experiment. Distal convoluted tubules have been necrotic altered only at the late stages of the experiment.

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Introduction.

The given article is a part of scientific research work «Structural organization, angioarchitectonics and anthropometric peculiarities of the body organs at prenatal and postnatal stages of development under the influence of exopathogenic and endopathogenic factors» (state registration number 0115U000041) by the normal anatomy department of Danylo Halytsky Lviv National Medical University.

Taking the doubtless relevance of drug addiction problems in modern society into consideration, the experimental studies of opioid effect on body organs and systems are widely spread among

morphological studies nowadays [6,9]. Modern literature highlights the problems of opioid effect on the structure and angioarchitectonics of different body organs through the experiment [1,4,8,10,11].

The aim of the study is the examination and comparison of the nephron tubule morphological changes at the early and late stages of the experimental opioid consumption. The results of the comparative characteristics of the pathomorphological changes of the parts of convoluted tubules at the early and late stages of the experimental continuous nalbuphine effect may be used for the diagnostics of nephropathy caused by continuous opioid consumption as well as for predicting the progress of the changes. The data obtained may also be used for the comparison of nephron structures morphological changes with prolonged exposure to nalbuphine and the medication withdrawal at different stages.

Using bio- and autopsy materials, changes of some parenchymal organs of individuals consuming narcotic drugs for a long period of time have been examined [7,15]. A great number of modern research papers concern studying the changes in drug addicts' kidneys [2]. In particular according to the studies, it has been estimated that at the early stage of the disease (drug adaptation) patients with opioid addiction suffer from tubulopathy with interstitial lesions of an organ by type of chronic pyelonephritis and (or) interstitial nephritis. With further drug addiction development (more than 3 years) such patients also suffer from glomerulopathy as cell proliferation of renal glomeruli. Active nephrosclerosis with the obliteration of renal glomeruli parts develops at the late stages [3]. The experimental studies of body organs and system have a number of advantages for the estimation of pathomorphological changes dynamics under the influence of damaging factors on the human body. The changes of nephron units under the experimental nalbuphine injection have been examined [13,14]. The comparison of the detected nephron structure changes at the early and late stages of the experimental opioid injection remains relevant.

Materials and methods.

The materials of the study were kidneys of 56 sexually mature male-rats. The animals were kept in a vivarium and the research was done according to «The rules of conducting testing using experimental animals» that correspond to the Declaration of Helsinki. The experiments on the animals were conducted according to the provisions of the European Community Directive as of 24th November 1986. The conducted research studies comply with the ethical standards according to the order of the Ministry of Health of Ukraine № 231 as of 01. 11. 2000 (protocol №2 as of February 20, 2012), established by the bioethics commission of Danylo Halytsky Lviv National Medical University.

The experimental animals received daily intramuscular nalbuphine injections for 98 days. From the first to the fourteenth day of the experiment the dose of nalbuphine was 0,212 mg/kg (1st experimental group). Every next two weeks nalbuphine injections were done in increasing doses, thus creating a model of a chronic opioid effect [12]. As of the fourteenth day the nalbuphine dose received by the animals was 0,225 mg/kg (2nd experimental group), as of the twenty-eighth day – 0,252 mg/kg (3rd experimental group), as of the forty-second day – 0,260 mg/kg (4th experimental group), as of the fifty-sixth day – 0,283 mg/kg (5th experimental group), as of the seventieth day – 0,3 mg/kg (6th experimental group), as of the eighty-fourth day – 0,45 mg/kg (7th experimental group). The control group received intramuscular saline injections for 98 days. Before sampling the material of the research the animals were put to a sleep by thiopental intraperitoneal injection (in proportion of 25 mg/kg). Histological preparation was done as per the commonly agreed method [5]. The colouring was performed using hematoxylin and eosin as well as azan by Heidenhain's method.

Results.

At the early stages of a chronic opioid effect (during 42 days of the experiment) alterative and destructive changes of the proximal convoluted tubules of kidney and the loops of Henle have been observed. Distal convoluted tubules have remained without any pathological changes at the early stages of a chronic opioid effect. The most visible morphological changes have been observed in proximal convoluted tubules. After fourteen days of the experiment the majority of proximal convoluted tubules have kept their normal structure, a small part of epitheliocytes have been swollen and lost their brush borders. Sometimes pyknotic nuclei, eosinophilic cylinders and desquamated epitheliocytes can be observed in the lumen of the tubules. After 28 days the majority of epitheliocytes of proximal convoluted tubules have been swollen and obtained eosinophilic granularity. Some epitheliocytes have lost their brush borders. Sporadic tubules with necrotic changes have appeared. Eosinophilic cylinders and desquamated epitheliocytes can be observed. After 42 days of the experiment some of the proximal convoluted tubules have already shown visible necrotic changes (Fig.1).

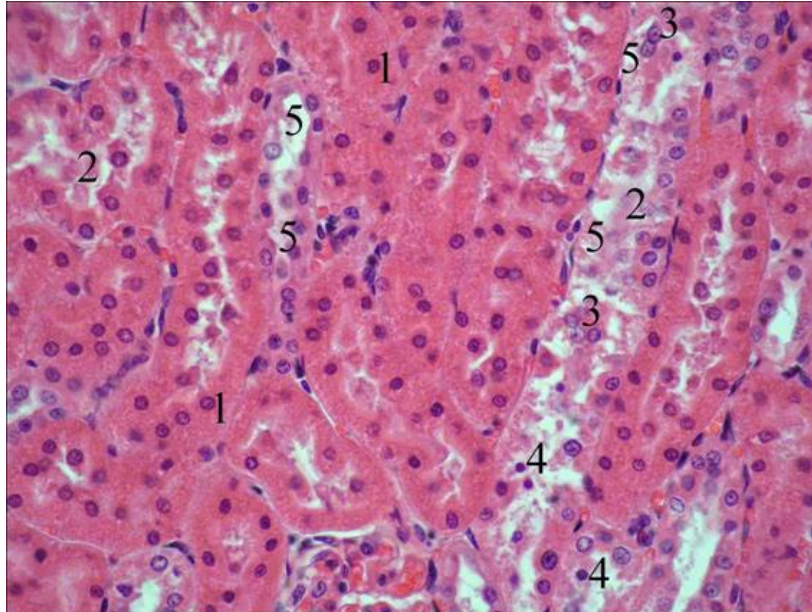


Fig.1. Micromorphological image of proximal convoluted tubules after 42 days of the experiment. The colouring has been performed using hematoxylin and eosin. Photomicrograph: x480. 1 – swollen epitheliocytes of proximal convoluted tubules; 2 – eosinophilic cylinders in the lumen of the tubules; 3 – desquamated epitheliocytes; 4 – desquamated epitheliocytes with pyknotic nuclei; 5 – necrotized tubules.

Moderate morphological changes have been observed in the loops of Henle. After 14 days of the experiment swollen cytoplasm has been detected in some cells, after 28 and 42 days – destructive changes.

At the late stages of a chronic opioid effect (from the 56th to 98th day of the experiment) visible alterative and destructive changes of the proximal convoluted tubules have been observed. As for the loop of Henle, after 56 days of the experiment destructive changes have been observed in sporadic cases, however as of the 70th day and till the end of the experiment these changes have not been detected any more. During the given stage, it has been noticed that some cells of the loop of Henle contain enlightened and sealed cytoplasm which may testify to regenerative processes. As of the 56th day of the experiment necrotic changes first occur in distal convoluted tubules and last till the end of the experiment (Fig.2).

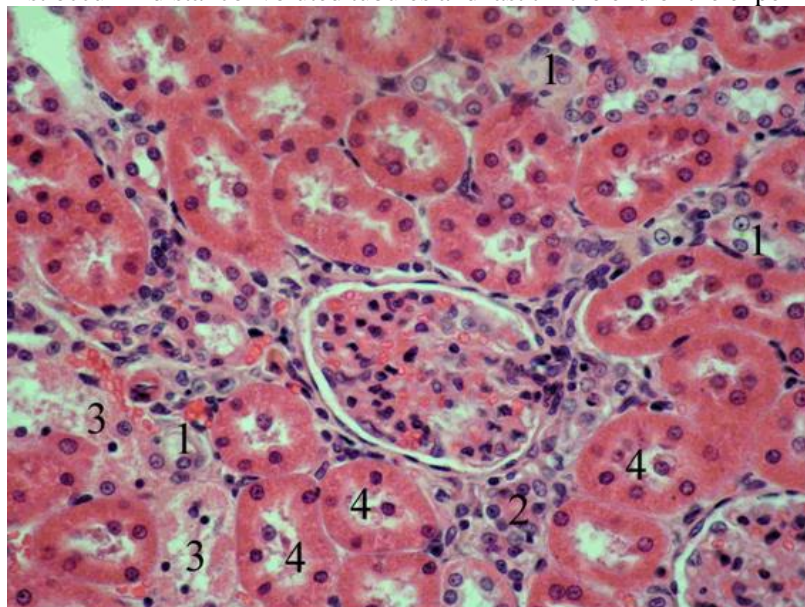


Fig.2. Micromorphological image of the cortical substance of the kidney after 70 days of the experiment. The colouring has been performed using hematoxylin and eosin. Photomicrograph: x480. 1 – desquamated epitheliocytes with pyknotic nuclei in the lumen of the distal convoluted tubule; 2 – eosinophilic masses in the lumen of the distal convoluted tubule; 3 – necrotized proximal convoluted tubules; 4 – desquamated epitheliocytes in the lumen of the proximal convoluted tubule.

Conclusions.

1. Varying degrees of morphological changes of proximal convoluted tubules, loops of Henle and distal convoluted tubules under continuous nalbuphine effect in the dynamics have been detected.
2. The most vivid alterative changes can be observed in proximal convoluted tubules both: at the early and late stages of the experiment. At the early stages as of the 14th day of the experiment signs of granular dystrophy appear, as of the 28th day – necrotic changes, progressing further at the late stages of the experiment.
3. The loops of Henle undergo sporadic destructive changes at the early stages and at the beginning of the late stage of the experiment.
4. Distal convoluted tubules have been necrotic altered only at the late stages of the experiment.

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