ISSN 1820-0254

The New ARMENIAN MEDICAL JOURNAL

Vol.11 No 2 June 2017

OFFICIAL PUBLICATION OF THE YEREVAN STATE MEDICAL UNIVERSITY

YEREVAN

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THE NEW ARMENIAN MEDICAL JOURNAL

1920 Toward the 100th anniversary of Yerevan State Medical University after Mkhitar Heratsi 2020

Volume 11, Number 2, June 2017

Our home page on Internet
www.ysmu.am

YEREVAN

The Journal is founded by
Yerevan State Medical
University after M. Heratsi.

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Scientific impact of the journal and articles is indexed by

THOMSON REUTERS SCOPUS VINITI

Copy Editors and Translators:

Tatevik R. **Movsisyan** (English)
Lilit H. **Hovhannisyan** (Russian)
Hovhanush H. **Mkrtchyan** (Armenian)

Printed in "UNIPRINT" Publishing House LLC
Director: Tigran Dilanjyan
Address: Armenia, 0002, Yerevan,
Leo St., 7 Building
Phone: (+374 10) 530914,
E-mail: uniprint@list.ru

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Professor VLADIMIR LESOVOY

Rector of Kharkiv National Medical University
Corresponding Member of the National Academy of Medical Sciences of Ukraine
Laureate of the State Prize of Ukraine in Science and Technology
Honoured Doctor of Ukraine

Dear readers of "The New Armenian Medical Journal"!

I am very pleased to present the publications of the staff of Kharkiv National Medical University in such an authoritative medical edition as "The New Armenian Medical Journal".

Kharkiv National Medical University is one of the oldest higher medical schools in Ukraine, which is now preparing to celebrate its 215th anniversary. Our University traces its history from the medical faculty of the Imperial Kharkiv University, founded in 1804.

Kharkiv National Medical University has served the development of medical science and practice, striving for the best quality of education and research.

In the list of the names that created the history of our University, there are the names of professors I.I. Mechnikov, V.F. Groube, L.L. Girshman, A.G. Podrez, I.P. Lazarevitch, V.Ya. Danylevsky, N.S. Bokarius, M.P. Trinkler, V.P. Vorobyov, A.M. Gasparyan, L.A. Oganesyan, L.T. Malaya, V.I. Grischenko, A.A. Shalimov and many others, who made a significant contribution to world medicine and brought well-deserved fame to Kharkiv. These professors of the Faculty of Medicine of Kharkiv University were the first who performed such surgeries as ovariotomy, definitive resection of stomach, open heart surgery, and made significant scientific discoveries in the Russian Empire.

Today, Kharkiv National Medical University is a modern multi-discipline educational institution with a strong scientific, material and technical base. Our University has six educational research and production associations, seven educational, scientific and scientific-practical centres: Training and Research Medical Complex "The University Clinic", Research Institute of Occupational Hygiene and Occupational Diseases, Medical Training and Research Division "The Dental Centre", Medical College, Scientific and Practical Centre for Preclinical and Clinical Trials, Centre for Gender Education and Centre for Medical Regional Studies, etc.

The University has 70 departments. The University staff counts 933 academic and research professionals, including 116 professors, 72 associate professors, 129 doctors of medical science and 543 candidates of sciences (PhDs). Among them there is one academician of the NAMS of Ukraine, five corresponding members of the Ukrainian National Academy of Sciences, 15 Honoured Workers of Science and Technology of Ukraine, 15 Honoured Doctors of Ukraine, Honoured Worker of Pharmacy of Ukraine, three Honoured Workers of Education of Ukraine, nine laureates of the State Prize of Ukraine in Science and Technology, 19 academicians of state and public academies of Ukraine.

Over the period of KhNMU's existence, more than 62.000 doctors have been trained in its walls.

Currently, more than 7.000 students are studying at the University, including more than 3.000 foreign citizens from 82 countries. KhNMU was one of the first in Ukraine (1951) to start training medical personnel for different countries of the world. Over this period, the University has trained more than 3.600 professionals for 86 countries in Western Europe, Asia, Africa, Latin America, the Middle East, including three doctors of sciences and 70 candidates of medical science, more than 250 clinical residents.

The University is proud that its alumni were and continue to be the elite of their countries. Among the students of Kharkiv Higher Medical School: 34 academicians and corresponding members of various academies of sciences, six Heroes of Labour, Heroes of Socialist Labour and Heroes of Ukraine, 34 laureates of State Prizes, 23 ministers and heads of government authorities, 67 directors of research institutes and centres, 31 rectors of higher education institutions, 17 deputies of the Supreme Council of Ukraine, and six honorary citizens of Ukrainian cities.

Throughout the history of the University, international educational and scientific cooperation were one of the priorities of its activity. It included cooperation with educational and scientific institutions, with international organizations, publishing houses and scientific journals. We are very pleased that the authoritative edition of the Yerevan State Medical University after Mkhitar Heratsi "The New Armenian Medical Journal" has become our good partner and friend. I would like to congratulate the founders and editorial staff of the journal, represented by the Rector of the Yerevan Medical University after Mkhitar Heratsi, Professor Armen Muradyan and the Editor-in-Chief Professor Arto Zilfyan, with the 10th anniversary of "The New Armenian Medical Journal". I want to wish respected colleagues new interesting publications, a large number of interested readers, further leadership positions among international medical editions, peace and prosperity!

Professor VALERIY MYASOYEDOV

Vice-Rector for Research of Kharkiv National Medical University
Honoured Worker of Science and Technology of Ukraine

Dear readers of "The New Armenian Medical Journal"!

I am glad that the current issue of the journal includes the articles by the leading scientists of Kharkiv National Medical University. They demonstrate the mainstream of scientific research carried out at our University. These articles are devoted to topical issues of therapy, pediatrics, urology, nephrology, dentistry, pathological anatomy and public health, those branches of medical science and practice which today, as always, determine the trend in the development of medicine.

Research work is an important aspect of Kharkiv National Medical University's activities, which in integration with educational activities is aimed at training highly qualified personnel and solving urgent problems of medical science and the healthcare system.

Today, among the priority areas of scientific research at the University are the prevention, diagnosis and treatment of cardiovascular diseases; minimally invasive interventions in acute and chronic pathology; prevention, diagnosis and treatment of viral, bacterial infections based on the study of their pathogenetic mechanisms, etc.

At the University, 15 scientific and pedagogical schools have been formed, and they are successfully developing now. These are anatomical, pathoanatomical, histological, physiological, biochemical, pathophysiological, surgical, hygienic, pediatric, therapeutic, microbiological, urological, obstetric-gynecological, neurological, psychiatric and pharmacological schools.

At present, the University carries out 60 scientific research works. Annually, the University's staff receives about 80 patents, including more than 20 ones for inventions. About 800 reports are presented at scientific forums in Ukraine, about 150 - in the CIS countries, about 200 - in the countries of the far abroad. Printed scientific materials are about 40 monographs annually and about 2.000 publications in scientific editions.

Kharkiv National Medical University ranks 26th among all universities and 5th among higher medical education institutions in Ukraine in terms of Scopus scientometric database. Annually, about 50 scientific forums, including international ones, are held at the University and with its participation. The University provides doctoral training, postgraduate training and clinical residency in more than 40 specialties, 48 doctoral and 235 PhD dissertations are being carried out.

There are five specialized scientific councils for the defense of doctoral theses and dissertations for the degree of PhD in 16 specialties at the University. The University scientists actively cooperate with many foreign and international research institutions and organizations, in particular with the Federation of European Physiological Societies, the European Association of Urology, the European Society of Human Reproduction and Embryology, the European Society of Uroradiology, the International Brain Research Organization, the WHO Regional Office for Europe, the American Medical Research Foundation and others.

Today, the key to success in any field of human activity, science in particular, is effective communication. Scientific journals are the cornerstone of such communication. I am very pleased to congratulate honorable colleagues from Yerevan State Medical University after Mkhitar Heratsi, the editorial staff and its Editor-in-Chief Arto V. Zilfyan on the 10th anniversary of "The New Armenian Medical Journal", a beautiful star on the scientific horizon. I want to thank my dear colleagues for their friendship, mutual understanding, high publishing competence and I would like to wish you a lot of anniversaries ahead, new embodied ideas, peace and good!

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THE FEATURES OF SMOOTH MUSCLE ACTIN EXPRESSION IN THE KIDNEYS, URETERS AND BLADDER OF THE NEWBORNS EXPOSED TO CHRONIC INTRAUTERINE, ACUTE POSTNATAL AND MIXED HYPOXIA

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Received 5/04/2016;accepted for printing 18/06/2017

Abstract

The study aimed to determine the characteristics of smooth muscle actin expression in the kidneys, ureters and bladder of the newborns exposed to experimental chronic intrauterine, acute postnatal and mixed hypoxia.

In this study an experiment was carried out on WAG rats on modeling chronic intrauterine, acute postnatal and mixed hypoxia. The material of the study was the tissue of the kidney of newborn rats. Immunohistochemical study was performed by the standard method using monoclonal antibodies against smooth muscle actin. Morphometrical investigation was conducted while studying the slides.

In newborns, chronic intrauterine and mixed hypoxia result in significant reduction of mean value of the muscular fiber thickness in the muscular layer of the ureter and bladder, as well as in non-uniform expression of smooth muscle actin by the muscular layer cells of these organs. Acute postnatal hypoxia does not produce a damaging effect on the qualitative and quantitative characteristics of the muscular layer of the ureter and bladder of the newborns. In infants, acute postnatal hypoxia does not affect the mean value of the muscular fiber thickness in the arterioles and venules of the kidneys, ureters and bladder, while chronic intrauterine and mixed hypoxia result in a significant reduction of these indicators. Chronic intrauterine hypoxia and mixed hypoxia amplify severity of expression of smooth muscle actin by myofibroblasts in the kidneys, ureters and bladder, as well as by mesangiocytes, glomerular epithelial cells, and epithelial cells of renal tubules, which can lead to the further development of sclerotic changes in these organs in children at different stages of ontogenesis.

The analysis of the features of smooth muscle actin expression in the urinary system organs of newborns found that chronic intrauterine and mixed hypoxia have a damaging effect on the urinary system organs of newborns while acute postnatal hypoxia has no damaging effect.

Keywords: *kidney, ureter, bladder, newborn, hypoxia, smooth muscle actin, experiment.*

Introduction

At present, pathology of the urinary system in children not only loses its relevance, but also remains a serious and significant problem in medicine. Epidemiological studies in Ukraine and in the countries around the world testify to the widespread disease of the urinary system among children [*Makovetskaia G, Kozlova T, 2000; Harambat J et al., 2012; Kolibaeva T et al., 2013*]. Nowadays, the researchers note an atypical clinical picture of the urinary system diseases in children, prevalence of both chronic, latent forms and manifest, aggressive, severe forms of the disease that are resistant to conventional therapies, combination of different pathologies of this system in one patient against a background of anomalies, dismetabolic disorders and microbial-inflammatory pro-

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cesses [*Chugunova O, Panova L, 2010; Kolibaeva T et al., 2013*]. Pathology of the urinary system in children dramatically reduces their quality of life, in some cases leads to development of chronic renal failure, requiring the use of expensive methods of replacement therapy [*Chugunova O, Panova L, 2010; Erman M, Pervunina T, 2012*].

Currently, the concept of a close relationship between the development of the urinary system pathology in children and the effect of different unfavorable factors in the antenatal, intranatal or postnatal periods of the organism development is intensively developing [*Erman M, Pervunina T, 2012; Koleganova N et al., 2012; Gafarova F, 2015*]. The most frequent cause of problems in an embryo, fetus and newborn is oxygen deprivation or hypoxia [*Shevchenko L et al., 2011*], which can be acute, chronic, or mixed. Acute hypoxia occurs at premature detachment of the placenta, development of multiple infarctions in it, loss of the umbilical cord, umbilical cord knots or its loops around the neck or limbs of the fetus, leading to acute disorders of uteroplacental or fetoplacental circulation. Chronic fetal hypoxia is a manifestation of chronic placental insufficiency, which develops due to the presence of various maternal genital or extragenital pathologies [*Gilany K, Vafakhah M, 2010*].

According to different authors, under the influence of hypoxia on the organism of the infant, the signs of the urinary system involvement in the pathological process are diagnosed in 80% of cases [*Pogodaeva T, Luchaninova V, 2012; Dorey E et al., 2014*]. As a result of hypoxia the child can develop respiratory distress syndrome, central nervous and cardiovascular systems, disorders, which further increase the chances of the damage to the urinary tract organs in these children [*Galyant O et al., 2013*]. The reason is simple: the kidneys are integrating bodies; therefore, whatever disease develops in a child, the organs of urine production and excretion suffer in varying degrees [*Pogodaeva T, Luchaninova V, 2012; Alaro D et al., 2014*].

It should be noted that the literature data on the effect of hypoxia on the urinary system organs in fetuses and newborns are unstructured, in the majority of cases they have clinical orientation and are not morphologically confirmed [*Gupta B et al., 2005; Makovetskaia G, Kozlova T, 2000; Shunkina G, 2010; Erman M, Pervunina T, 2012; Koleganova N et al., 2012*]. In addition, the data on the effect of acute postnatal and mixed hypoxia on the structural and functional features of the urinary system in newborns are absent. All this testifies to the urgency and necessity of present research.

The study aimed to determine the characteristics of smooth muscle actin expression in the kidneys, ureters and bladder of the newborns exposed to experimental chronic intrauterine, acute postnatal and mixed hypoxia.

Material and methods

This study involved an experiment simulation of high-altitude hypoxia in Wistar Albino Glaxo rats at the experimental biological hospital of Kharkiv National Medical University. The study was approved by the Commission on Ethics and Bioethics of Kharkiv National Medical University and conforms to the principles of the Guide for the Care and Use of Laboratory Animals published by US NIH (No 85-23, revised in 1985) [*International Ethical Guidelines for Biomedical Research Involving Human Subjects, 1993*].

High-altitude hypoxia was simulated using a sealed pressure chamber, from which the air was pumped out creating the conditions of sharp reduction in the atmospheric pressure. The rats were placed daily for 20 minutes at the same time in the conditions corresponding to the altitude of 7500 *m* with the respective pressure of 287 *mm Hg*.

The animals were divided into four groups: I (control) – pregnant female rats (n=3) were not subjected to high-altitude hypoxia and the resulting offspring from them (n=11) in the first day after birth were taken out of the experiment, II (simulation of chronic intrauterine hypoxia) – pregnant female rats (n=4) were exposed to high altitude hypoxia and the resulting offspring from them (n=10) in the first day of life were taken from the experiment, III (modeling of acute postnatal hypoxia) – pregnant female rats (n=2) were not subjected to high-altitude hypoxia, however, the resulting offspring from them (n=8) in the first day of life were exposed to single high-altitude hypoxia and then taken out of the experiment, IV (modeling mixed hypoxia) – pregnant female rats (n=3) during pregnancy were exposed to high-altitude hypoxia, and then their offspring (n=8) in the

first day of life were exposed to single high-altitude hypoxia and taken out of the experiment.

The materials of the study were the kidneys of the newborns. Immunohistochemical investigation was performed by standard methods using monoclonal antibodies against smooth muscle actin (DAKO, Denmark). These slides were examined under "Olympus BX-41" microscope (Japan) with processing using "Olympus DP-soft version 3.1" software (Japan), which determined the thickness of the muscular fibers, the cells of which expressed smooth muscle actin in the muscular layer of the ureter and bladder, as well as arterioles and venules of the kidneys, ureter, and bladder of the rats. In other cases, to assess the grade of immunohistochemical reaction, a semiquantitative scale, i.e. "+" – poor, "++" – fair, "+++" – pronounced reaction, was used.

Non-parametric U-Mann-Whitney criterion was used for statistical evaluation of the values obtained in the groups. Significance of differences between the values was taken at significance level of $p < 0.05$. Statistical calculations were performed using Statistic Soft 6.0 and Microsoft Excel 2007 software.

RESULTS AND DISCUSSION

All four groups demonstrated smooth muscle actin expression on immunohistochemical investigation in the form of a clear brown cytoplasmic staining of the smooth muscle cells that formed muscular fibers of the muscular layer of the bladder and ureter (Fig. 1). The analysis of muscle fiber thickness in the ureter and bladder (Table 1)

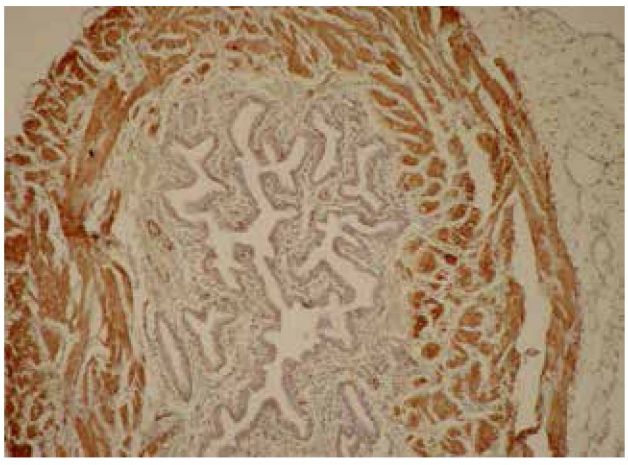

Figure 1. *Expression of smooth muscle actin in the ureter of the newborn exposed to chronic intrauterine hypoxia. Peroxidase reaction with monoclonal antibodies to smooth muscle actin, ×100*

TABLE 1

Mean value of the muscular fiber thickness in the muscular layer of the ureter and bladder in newborn rats of four groups ($\times 10^{-6} m$)

Groups	Location	
	Ureter	Bladder
I	8.09±0.547	12.55±0.562
II	5.20±0.327 $p_1<0.05$	8.50±0.543 $p_1<0.05$
III	8.38±0.497 $p_1>0.05$ $p_2<0.05$	11.95±0.563 $p_1>0.05$ $p_2<0.05$
IV	4.75±0.250 $p_1<0.05$ $p_2>0.05$ $p_3<0.05$	8.13±0.295 $p_1<0.05$ $p_2>0.05$ $p_3<0.05$

Notes: *p_1 – significance of differences compared to I group; p_2 – significance of difference compared to II group; p_3 – significance of difference compared to III group.*

revealed a significant decrease in this indicator in II and IV groups compared with I group, which suggests of the damaging effect of chronic intrauterine and mixed hypoxia on quantitative parameters of the muscular membrane of the ureter and bladder in the newborns that can manifest by certain functional disorders in these organs. While comparing to I group, in III group significant differences were absent in terms of the mean value of the thickness of the muscular fibers in the muscular layer of both ureter and bladder, which suggests that acute postnatal hypoxia does not have a damaging effect on the quantitative indicators of the muscular membrane of the ureter and bladder in newborns. In II and IV groups, no significant differences were observed in terms of mean thickness of the muscular fiber in the muscular layer of the ureter and bladder.

In II and IV groups, the muscular fibers of the muscular layer of the ureter and bladder demonstrated heterogeneity in expression of smooth muscle actin. Thus, some muscular fibers expressed smooth muscle actin well, while the others expressed it slightly or moderately. Uneven expression by the muscular fibers of smooth muscle actin is possible due to the fact that some of the fibers develop dystrophic and atrophic changes induced by chronic intrauterine or mixed hypoxia, while the others develop hypertrophy of the muscular fi-

bers, which is a unique compensatory-adaptive response necessary to compensate for the quantitative deficiency of smooth muscle cells resulting from their destruction and elimination under the action of the above damaging factor.

It is known that smooth muscle tissue is an obligatory structural and functional component of the wall of the bladder and ureters; it plays an important role in their normal function. Smooth muscle cells are traditionally classified into two main types – visceral and vascular. Visceral smooth muscle cells are referred to the so-called "phase" smooth muscle cells, which are electromechanically paired and function as a single syncytium. The action potential in this syncytium is transferred from one smooth muscle cell to another through gap junctions. An important feature of these cells is the ability of a small number of cells spontaneously to generate action potential, i.e. to be pacemakers. The vascular smooth muscle cells are "tonic" and function as individual units [*Lushnikova E et al., 2012*].

Expression of smooth muscle actin by the smooth muscle cells that form muscular fibers of the tunica of the arterioles and kidney venules of the kidneys, ureters and bladder was identified. In the urinary organs in all groups, the muscle fibers were significantly thicker in the wall of the arterioles compared to the venules, which is a variant of the norm and is due to their functional characteristics (Table 2). The analysis also revealed a significant decline in the mean muscular fiber thickness

Table 2

Mean value of the muscular fiber thickness in the arterioles and venules of the kidney, ureter and bladder in newborn rats of four groups ($\times 10^{-6} m$)

Location	Vessel type	Groups			
		I	II	III	IV
Ureter	Arteriole	2.19±0.229	1.51±0.270 $p_1<0.05$	2.15±0.073 $p_1>0.05$ $p_2<0.05$	1.49±0.050 $p_1<0.05$ $p_2>0.05$ $p_3<0.05$
	Venule	1.38±0.189 $p_4<0.05$	0.88±0.107 $p_1<0.05$ $p_4<0.05$	1.35±0.056 $p_1>0.05$ $p_2<0.05$ $p_4<0.05$	0.83±0.117 $p_1<0.05$ $p_2>0.05$ $p_3<0.05$ $p_4<0.05$
Bladder	Arteriole	2.92±0.207	2.20±0.198 $p_1<0.05$	2.94±0.080 $p_1>0.05$ $p_2<0.05$	2.24±0.081 $p_1<0.05$ $p_2>0.05$ $p_3<0.05$
	Venule	2.11±0.160 $p_4<0.05$	1.49±0.239 $p_1<0.05$ $p_4<0.05$	2.16±0.082 $p_1>0.05$ $p_2<0.05$ $p_4<0.05$	1.52±0.059 $p_1<0.05$ $p_2>0.05$ $p_4<0.05$
Kidney	Arteriole	1.79±0.048	1.19±0.059 $p_1<0.05$	1.70±0.046 $p_1>0.05$ $p_2<0.05$	1.10±0.073 $p_1<0.05$ $p_2>0.05$ $p_3<0.05$
	Venule	1.28±0.086 $p_4<0.05$	0.73±0.030 $p_1<0.05$ $p_4<0.05$	1.20±0.057 $p_1>0.05$ $p_2<0.05$ $p_4<0.05$	0.70±0.060 $p_1<0.05$ $p_2>0.05$ $p_3<0.05$ $p_4<0.05$

Notes: *p_1 – significance of differences compared to I group; p_2 – significance of difference compared to II group; p_3 – significance of difference compared to III group; p_4 – significance of difference compared to the arteriole in this group.*

in the arterioles and venules of the kidney, ureter and bladder in the newborns from II and IV groups, compared to I group, which indicates the damaging effect of chronic intrauterine and mixed hypoxia on the muscular component of the vascular walls of microcirculatory basin that can disrupt tissue nourishment in these organs and further result in sclerotic changes in them. Acute postnatal hypoxia does not produce a damaging effect on quantitative indicators of muscular fibers of the arterioles and venules of the urinary system in newborns. In the newborns from II and IV groups, no significant differences were observed in terms of the mean value of thickness of the muscular fibers of arterioles and venules.

The kidneys, ureters and bladder of the newborns from I group demonstrated moderate expression of smooth muscle actin by myofibroblasts, which were defined in the stroma of these organs (Fig. 2, 3). Myofibroblasts were identified in the process of development and maturation of the urinary system of humans and laboratory animals by many researchers [*Carey A et al., 1992; Naruse K et al., 2000*].

It is known that myofibroblasts are main profibrogenic cells characterized by unique functional capabilities. Thus, myofibroblasts are able to produce a number of key components of the extracellular matrix, including I, III, V, VII type collagens. Possibility of production of the basal membrane components, i.e. type IV collagen and laminin by myofibroblasts have been proven. In addition, this cell line produces a wide range of sulfated proteoglycans of the matrix and basement membrane (in particular, decorin, nidogen and perlecan) influencing the migratory and proliferative anility of the connective tissue cells and epithelium. Important products of myofibroblast secretion are fibronectin and tenascin-C. In addition to the components of the extracellular matrix, myofibroblasts produce a great variety of metalloproteinases and their tissue inhibitors, which play an important role in matrix remodeling, cellular migration activity regulation [*Barinov E, Sulayeva O, 2010; Lawson J et al., 2015*].

No specific features of smooth muscle actin expression by myofibroblasts were detected in III group 3 compared to I group. In II and IV groups, compared with I group, marked expression of smooth muscle actin by myofibroblasts was revealed, which may have occurred as a result of proliferation and activation of resident fibroblasts exposed to simulated chronic intrauterine and mixed hypoxia, which change their phenotype (begin to express smooth muscle actin) and secrete matrix proteins [*Strutz F, Zeisberg M, 2006; Lawson J et al., 2015*]. Additionally, the increase in the number of myofibroblasts may occur due to the changes in the phenotype of tubular epithelial cells during epithelial-mesenchymal transformation, which can be explained by the detected clear cytoplasmic staining of some tubular epithelial cells. Epithelial-mesenchymal transformation begins with destruction of the tubular basement membrane exposed to hypoxia and other damaging factors, as well as certain cytokines. The cells

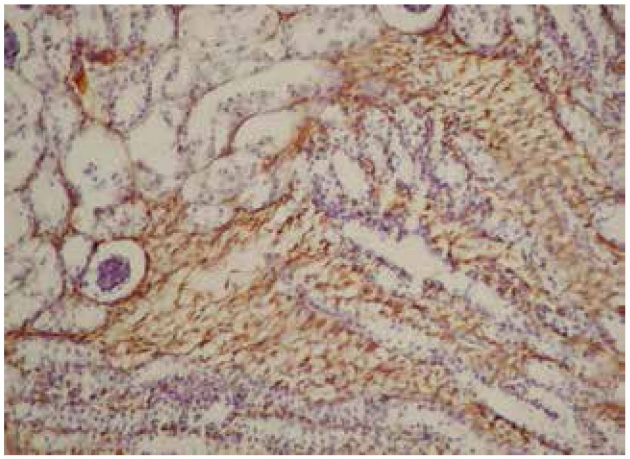

Figure 2. *The expression of smooth muscle actin in the kidney of the newborn exposed to mixed hypoxia. Peroxidase reaction with monoclonal antibodies to smooth muscle actin, ×200*

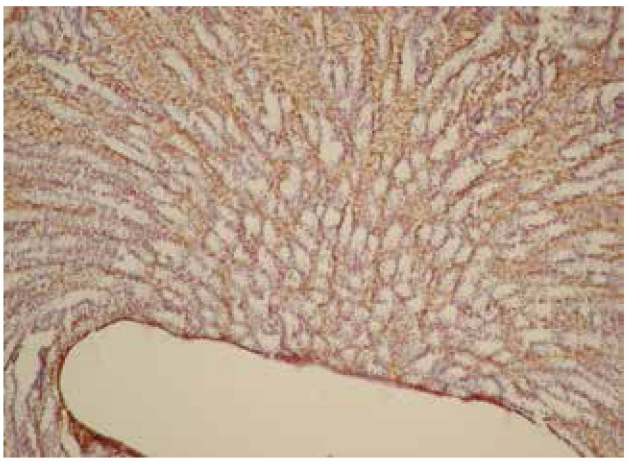

Figure 3. *The expression of smooth muscle actin in the kidney of the newborn exposed to chronic intrauterine hypoxia. Peroxidase reaction with monoclonal antibodies to smooth muscle actin, ×100*

lose apical-basal polarity, begin to express mesenchymal markers and reduce the expression of epithelial markers, then change their shape due to the changes in endogenous cytoskeleton, migrate into the inter-tubal space, turning into activated myofibroblasts [*Barinov E, Sulayeva O, 2010; Puchinskaya M, 2015*].

In I and III groups, some glomeruli demonstrated a small amount of mesangiocytes expressing smooth muscle actin, which has been described by many researchers studying the process of kidney development [*Carey A et al., 1992; Naruse K et al., 2000*]. In II and IV groups, the glomeruli demonstrated moderate to pronounced expression of smooth muscle actin by not only mesangiocytes but also the endothelial cells, possibly, due to the negative effect of chronic intrauterine and mixed hypoxia, which will lead to the future development of sclerotic changes in the urinary system of the child.

Conclusion

In newborns, chronic intrauterine and mixed hypoxia result in significant reduction of mean value of the muscular fiber thickness in the muscular layer of the ureter and bladder, as well as in non-uniform expression of smooth muscle actin by the muscular layer cells of these organs. Acute postnatal hypoxia does not produce a damaging effect on the qualitative and quantitative characteristics of the muscular layer of the ureter and bladder of the newborns.

In infants, acute postnatal hypoxia does not affect the mean value of the muscular fiber thickness in the arterioles and venules of the kidneys, ureters and bladder, while chronic intrauterine and mixed hypoxia result in a significant reduction of these indicators.

Chronic intrauterine hypoxia and mixed hypoxia amplify severity of expression of smooth muscle actin by myofibroblasts in the kidneys, ureters and bladder, as well as by mesangiocytes, glomerular epithelial cells, and epithelial cells of renal tubules, which can lead to the further development of sclerotic changes in these organs in the children at different stages of ontogenesis.

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