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CHANGES IN THE EXCRETORY KIDNEY FUNCTION IN THE DYNAMICS OF CHRONIC HYPOXIA DEVELOPMENT

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The consequences of exposure to hypoxia develop in two ways: hypoxia causes pathological changes at the tissue, cellular and molecular levels, while metabolic disorders are observed during the long-term post-hypoxic period. The kidney is an organ with an extremely high rate of oxidative metabolism, which determines its increased sensitivity to changes in oxygen supply as well as its critical role in the development of compensatory reactions during hypoxia. The current research aimed to study the changes in the excretory kidney function in the dynamics of chronic hypoxia development.

The experiments were carried out on 36 white laboratory nonlinear male rats weighing 140-180 g, kept on a standard balanced diet with free access to water. The animals were divided into 5 groups (n=7): the first group - intact animals, the second, third and fourth groups - modeling of chronic hypobaric hypoxia in a modified flow-through pressure chamber imitating the ascent of rats to an altitude of 4000 m above sea level at a speed of 24 km/h. The animals were kept in the chamber for 2 hours daily during 1, 2, 3, or 4 weeks. Animals were withdrawn from the experiment, while blood, urine and kidneys were sampled for biochemical and histopathological assessments. Excretory kidney function was evaluated by diuresis, plasma creatinine level, glomerular filtration rate (GFR), urine protein excretion.

It was found that in animals exposed to chronic hypoxia during one week, diuresis was significantly reduced compared with control (by 1.26 times); after two weeks of the experiment there was a tendency to decrease, but it did not reach significant values, while after three weeks of chronic hypoxia diuresis decreased significantly by 1.27 times. However, the most significant reduction of diuresis was observed after four weeks of exposure to hypoxia (by 1.6 times compared with control). Significant changes in the excretory function of the kidneys during the fourth week of the experiment indicated a possible damaging effect of the chronic hypoxia on both the renal filter and renal tubular apparatus. It was found, that during first and second weeks of the hypoxia influence GFR decreased slightly, but this trend was not significant. While at the end of the third week of the experiment this figure decreased by 1.3 times, and after four weeks of the chronic hypoxia - by 1.9 times, indicating exhaustion of the functional reserve of the kidney at the third week of the experiment. Under the influence of chronic hypoxia, the level and excretion of protein with urine increased gradually and reached the highest levels at the fourth week of experiment (by 10.5 and 6.9 times higher than the control), indicating a combination of damage to the glomerular filter and impaired proximal reabsorption. Along with the significant proteinuria the level of creatinine in urine also gradually increased with prolongation of hypoxia influence: after the first week of experiment - by 1.16 times, after the second and third week of the influence of hypoxia - by 1.3 times and 1.48 times, respectively, and remained significantly high after the fourth week (by 1.28 times compared with control). The plasma creatinine level increased significantly starting from the second week of exposure to hypoxia (by 1.2 times), and during the third and fourth weeks of the experiment reached maximum values (by 1.5 and 1.46 times, respectively, compared with control). A retention azotemia also was most pronounced on the third and fourth weeks of the chronic hypoxia, correlating with the decrease in GFR.

Result of the experimental studies show a significant impairment of the excretory kidney function under the influence of chronic hypobaric hypoxia manifested in the decrease in GFR (corresponding to reduction of diuresis), marked proteinuria and retention azotemia, which reached the highest levels on the fourth week of the experiment.