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MORPHO-FUNCTIONAL DISORDERS OF SCIATIC NERVE IN CONDITIONS OF PACLITAXEL-INDUCED PERIPHERAL NEUROPATHY

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Introduction. Chemotherapy-induced peripheral neuropathy (CIPN) is one of the common side effects of anticancer agents. Among this group Paclitaxel (P) – diterpene alkaloid drug is positioned as effective cancer treatment, but although it effectively increases both progression-free survival and overall survival in cancer patients, it also has high neurotoxicity, which most often manifests as peripheral sensory neuropathy. By this time no effective treatment for CIPN is available, so it is important to understand not only pathomorphogenesis, but also peculiarities of physiological revelation of nerve cells injury. Unfortunately, research conducted on this issue do not give a coherent picture of morphological and functional disorders of the nervous system.

The aim of the study: to examine morphological and functional disorders of the sciatic nerve in conditions of paclitaxel-induced peripheral neuropathy.

Material and methods. The study was conducted on 48 white mature male rats weighing 200-250 g. P was administered intraperitoneally at a dose of 2 mg / kg every other day for 4 times (a total dose of 8 mg / kg). As a control, 15 rats were injected isotonic NaCl in equivalent volume. Sampling of experimental and control animals was performed at 1st, 7th, 15th, 28th, 60th, 90th, 120th, 150th day after the last administration. Semi-thin cross sections of blocks for electron microscopy were stained with toluidine blue. Morphometric investigation of myelinated nerve fibers (MNF) was carried out using UTHSCSA Image Tool for Windows (version 2.00) followed by nonparametric statistical analysis. In order to study sensory disturbances von Frey test and "hot plate" test on the eve before every sampling were performed.

Results and discussion. Between the 1st and 90th day of the experiment swelling and progressive degeneration of axial cylinders were observed followed by swelling, deformation and fragmentation of the myelin sheath, the violation of microtubules architectonics and neurofilaments in axial cylinders. Damaged microcapillaries and perineurium, swelling of endoneurium, destruction of axons` mitochondria and degenerative changes of Schwann cells, which display initial reaction to the toxic effects of P were also observed. Starting with 120th day there were clear signs of nerve fibers regeneration and remyelination. According to von Frey test results, the signs of allodynia with decreased pain threshold between the 1st and 90th day of the experiment were noted, followed by subsequent normalization of these parameters. The results of "hot plate" test point to similar decrease of temperature sensitivity threshold.

Conclusion. Paclitaxel-induced peripheral neuropathy is the primary myelopathy and axonopathy followed by sensitive disorders by the 90th day of the experiment with the gradual recovery of morphological and functional parameters starting with 120th day of the experiment.