EFFECT OF LONG-TERM OPIOIDS ADMINISTRATIONON THE ULTRASTRUCTURE OF THE RETINA IN AN EXPERIMENT

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Relevance: The management of consequences of long-term use of opioid medications for medical indications and uncontrolled use of psychotropic and highly potent medications without medical indications is still an important problem. The use of opioids under combat conditions is a particularly contentious issue.

Background: Currently, the issue of structural reorganization in the layers of the rat retina and disruption of its blood supply processes during subchronic and chronic periods of experimental opioid exposure remains unclear.

Purpose: to find out the features of the ultrastructural reorganization of the rat retina at the end of the fourth and sixth weeks after experimental opioid exposure.

Material and Methods: The material of the study was sexually mature, purebred, white male rats, in the number of 48 animals, weighing 200-250 g, aged 4.5 months.

Animals were injected with the drug nalbuphine (active substance: nalbuphine hydrochloride); intramuscularly, daily 1 time a day in one period of time (10–11 am) for 42 days. The initial dose of nalbuphine during the first 2 weeks was 0.212 mg/kg, during the next 2 weeks (II - IV weeks) - 0.225 mg/kg, and during (IV - VI weeks) -

0.252 mg/kg. Thus, conditions for chronic opioid exposure were created. Experimental animals were divided into groups: 1 group (19 animals) received nalbuphine for 28 days, followed by material sampling (the end of the 4th week of experimental opioid exposure); Group 2 (19 animals) received nalbuphine for 42 days, followed by sampling (the end of the 6th week of experimental opioid exposure); The 3rd group was the control (10 animals), of which 5 animals received injections of 0.22 ml/kg of 0.9% physiological solution for 28 days intramuscularly, the remaining 5 animals for 42 days in one period of time (10 – 11 o'clock in the morning), received an identical dose of 0.9% physiological solution. Transmission electron microscopic examination of the retina of rats was carried out according to the generally accepted method.

Results: As a result of our study of the retina of rats, at the end of the fourth week of experimental opioid exposure, an increase in the number of retinal vessels with signs of hyperemia and degenerative changes in the cells of the pigment epithelium, increased destruction of the membranes of the discs of the outer segments of photoreceptors, necrobiotic changes in the nuclei of individual photoreceptors, degeneration of axons of the outer and inner retina were revealed. layers, degenerative changes in horizontal neurons, the appearance of degenerative and necrotic changes in the cytoplasm of bipolar and amacrine cells. At the end of the sixth week, the phenomena of hyperemia of retinal vessels continued to progress, degenerative and necrotic changes of individual cells of the pigment epithelium, outer segments of photoreceptors increased, shortening and fragmentation of mitochondrial cristae of inner segments of photoreceptors, necrotic changes in the nuclei of individual photoreceptors, degeneration of axons of the outer and inner retinal layers, degenerative and necrotic changes of bipolar and amacrine cells, hypertrophy of processes of Müller cells, degeneration of ganglion cells, hyperemia and moderate perivascular edema of the vessels of the outer and inner reticular layers.

Conclusion:

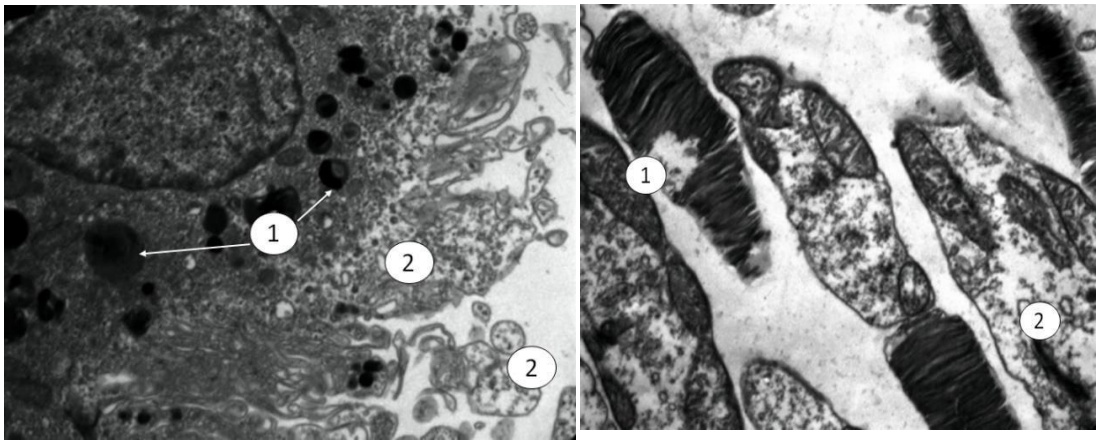

Fig. 1. Electron micrograph. Ultrastructure of the retina of a rat at the end of week 4 of experimental opioid exposure. A. Original magnification x4,500. Note: 1, numerous intensively osmiophilic phagosomes and primary and secondary lysosomes in the apical zone of RPE cells; 2, cytoplasmic edema and focal destruction of apical microvilli. B. Original magnification x7,500. Note: 1, disorganization of membranous discs and destruction of the membranes of photoreceptor outer segments; 2, clear cytoplasmic zones in photoreceptor inner segments and mitochondrial cristae injury

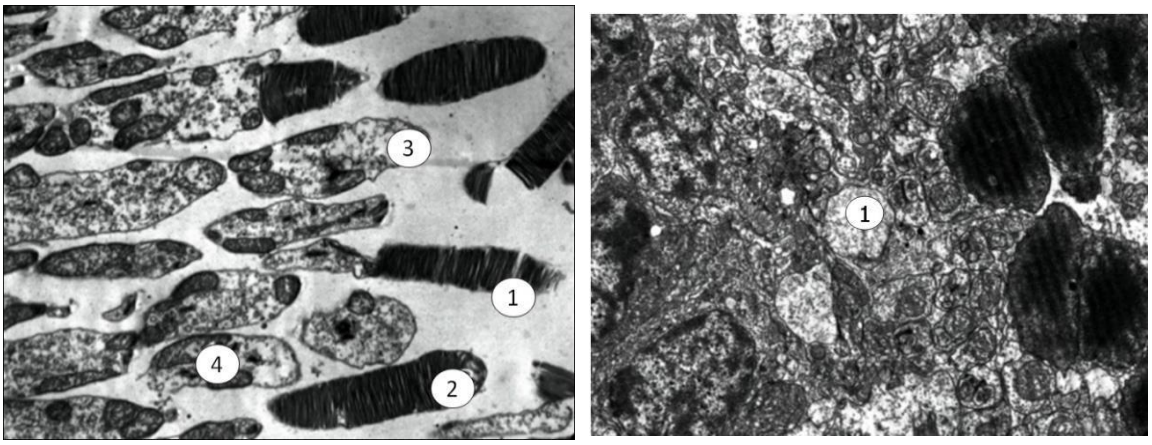

Fig. 2. Electron micrograph. Ultrastructure of the retina of a rat at the end of week 6 of experimental opioid exposure. A. Original magnification x3,800. Note: 1, delaminated membranes in photoreceptor outer segment discs; 2, destruction of the membranes in photoreceptor outer segment discs; 3, edematous cytoplasm of photoreceptor inner segments; 4, destruction and shortening of mitochondrial cristae of photoreceptor inner segments. B. Original magnification x2,200. Note: 1, electron-lucent axoplasm of axons in the outer plexiform layers.

Thus, when nalbuphine was administered to rats in the range of 0.212-0.252 mg/kg for 4 weeks, destructive processes occurred in the structural components of the retina, such as changes in the ultrastructure of the pigment epithelium, outer segments of photosensory neurons, degeneration of axons of the outer and inner retinal layers, degenerative and necrotic changes bipolar and amacrine cells, hypertrophy of processes of Müller cells, degeneration of ganglion cells and hyperemia caused by disturbances in the ultrastructure of the microcirculatory bed. In the 6th week of the experiment, the destructive and degenerative processes in the structural components of the retina intensified.

Key words: eye, retina, rat, Opioid-Related Disorders, electron microscopy.