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P. Popyk

Danylo Halytsky Lviv National
Medical University 79010, Lviv,
Ukraine

L. Mateshuk-Vatseba

Danylo Halytsky Lviv National
Medical University 79010, Lviv,
Ukraine

Dynamics of ultrastructural changes exocrine part of rat pancreas under the influence of opioid

P. Popyk, L. Mateshuk-Vatseba

Abstract

The article is devoted to the study of ultrastructural organization of exocrine part of a white rat pancreas under the conditions of long-term influence of opioid. The paper describes the new data changes in ultrastructure after 2, 4 and 6 weeks of nalbuphine induction. First changes of ultrastructural organization of some exocrine pancreocyte is observed after 2 weeks of nalbuphine induction and grow during next terms of the experiment. Long-lasting influence of opioids causes deep dystrophic changes of exocrine pancreocyte, including loss of regular form, karyopyknosis and karyorrhexis of nuclei, swelling and enlightenment of cytoplasm, the development of microcystic degeneration of the cells, loosening and disorganization of basal membrane which may lead to the disturbance of exocrine function of pancreas and difficulties of the process of elimination of secretory granules into the lumen of the inserted ducts. The work is a base for further researches of morphologists and clinicians to develop new diagnostic methods in the future, prevention and treatment of the pancreas diseases of drug addicts and patients who had to take opioids for a long time.

Keywords: exocrine part of the pancreas, ultrastructure, rat, opioid.

1. Introduction

The research of structural changes organs in the conditions of long-term use of opioids is one of the urgent problems of modern medicine [5, 6]. The widespread use of narcotic drugs in clinical practice in terms to obtain painkillers and anti-inflammatory effects requires immediate comprehensive study of morphological features of structural organization organs under the influence of opiates and opioids [3, 7, 8]. However, the information professional literature gives on the problems mentioned above is insufficient and often contradictory. A negative influence of narcotic drugs on the pancreas is obvious, but only a few works are devoted to the structural organization of the pancreas in normal and harmful conditions [1, 2]. The aim of this research is to define ultrastructural features of exocrine part of the pancreas in the dynamics influence of opioid.

2. Material and Methods.

The research was made on 24 mature white male rats aged 4.5-5.5 months and weight 150-170 g. Experimental animals are divided into 3 series: in the first (5 rats) the structure of exocrine part of white rat pancreas after two weeks nalbuphine induction is studied, in the second (5 rats) the changes of ultrastructural exocrine part of white rat pancreas after 4 weeks duration of the experiment is studied, in the third serious of the research (5 rats) the reconstruction of exocrine part of white rat pancreas after 6 weeks nalbuphine induction is defined. Nine white rats which were physiological solutions inducted served as control.

Intramuscular nalbuphine infusion was conducted as follows: I week - 8 mg/kg, II week - 15 mg/kg, III week - 20 mg/kg, IV week - 25 mg/kg, V week - 30 mg/kg, week VI - 35 mg/kg [4]. The method of electron microscopy was used in this work. The animal was withdrawn from the experiment by intraperitoneal overdose of anesthesia using thiopental sodium (rate of 25 mg/kg). Right after the animal death the standard procedure of material for electron microscopy was made. Ultrathin cuts were prepared on ultramicrotome UZHTP-3 with the help of glass knives. Tape cuts of silver or pale lemon colours were selected for the research. The cuts were contrasted first in 2% uranylacetate solution, and then in lead citrate. The study and photography of the material were performed using a microscope UEMV-100 K at 75 kV accelerating voltage and expanse microscope screen 4000-15000s. All the animals were kept in the vivarium conditions of Danylo Halytsky Lviv National Medical University, the experiments were made according to the principles of the European Convention for the

Correspondence:

P. Popyk

Danylo Halytsky Lviv National
Medical University 79010, Lviv,
Ukraine

protection of vertebrate animals used for experimental and other scientific aims (Strasbourg, 1986), European Council Directive 86/609 / EEC (1986), Law of Ukraine № 3447 – IV “On protection of animals from cruelty”, general ethical principles of animal experiments adopted the First national congress of Ukraine on bioethics (2001).

3. Results and Discussion

After 2 weeks nalbuphine induction to rats the ultrastructure of the exocrine part of the pancreas is mainly preserved (fig. 1).

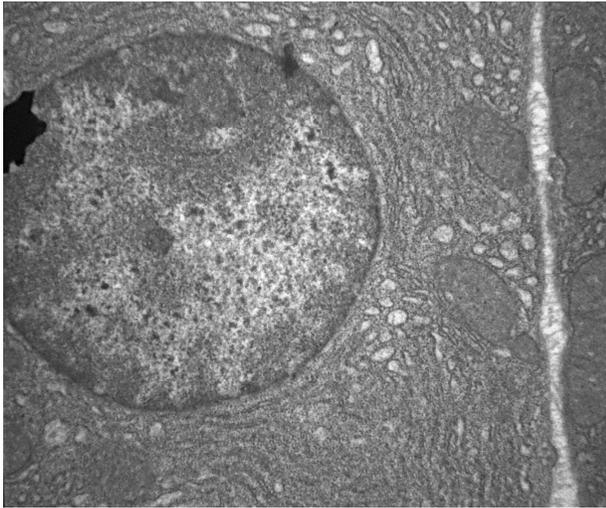


Fig 1: Ultrastructural organization of rat exocrine pancreocyte after 2 weeks of nalbuphine induction. Electron. x 8000

As in the control, pancreatic acinus is formed by 8-12 large secretory cells – exocrine pancreocyte conical shape with a narrower top and a broad base, which fits closely to the basal membrane. Sell membrane of the basal cell surface is wrinkled but the apical makes micrivilli. At this stage of the experiment, as in the control, the contacts on the side surfaces of the sells in the form of locking plates and desmosomes are situated. The nuclei rich in chromatin, contain 1-2 nucleolus, are mostly located in the basal part of the cell. The basal part of the cell contains a well-developed granular endoplasmic reticulum and numerous ribosomes. Apical part contains many secretory granules. Golgi apparatus was found at the epic of nucleus sell, mitochondria are scattered throughout the whole cytoplasm. The wall of the inserted ducts is formed by several tiny cells flat or cubic form, which lie on the basal membrane. Centroacinar sells of inserted ducts are irregular flat form, have oval nucleus, light and organelles poor cytoplasm. However, after 2 weeks of nalbuphine induction a few changed exocrine pancreocyte are detected, their cytoplasm is enlightened in comparison to control, canaliculi of endoplasmic reticulum and Golgi apparatus tanks are expand. Mitochondria are located smoothly and keep spherical or oval form, but an insignificant swell is observed, cristas are particular destructed.

After 4 weeks of the experiment a sell membrane of some exocrine pancreocyte is destroyed, the desquamation of cytoplasm into interstitial tissue is observed, vacuoles and lipid inclusions are noticed in the cytoplasm of many sells. Nuclei are enlarged, of irregular form, nulcollem has uneven contours, which makes numerous invaginations, heterochromatin is peripheral (fig. 2).

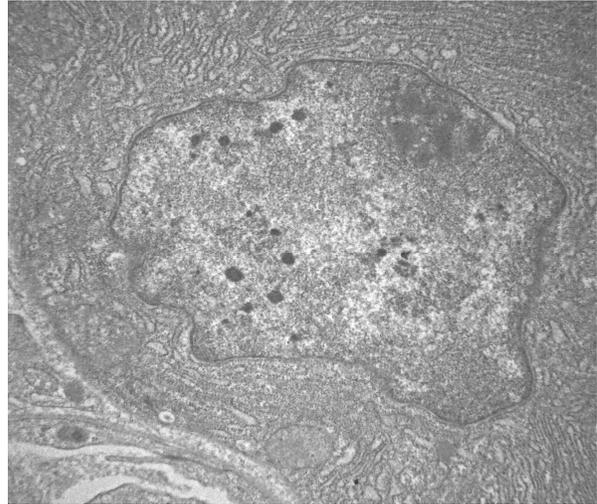


Fig 2: Ultrastructural organization of rat exocrine pancreocyte after 4 weeks of nalbuphine induction. Electron. x 4000

Mitochondria are swollen, membranes of some mitochondria are destroyed and not solid, crysts are destructed, matrix is electro-transparent. Canaliculi of endoplasmic reticulum and Golgi apparatus tanks are expand. In some acynocytes the amount of ribosomes, which are centred on the membranes of endoplasmic reticulum, grows that shows the development of the compensatory process. The concentration of glycogen in the sells decreases, the amount of lipid drops in cytoplasm increases.

After 6 weeks a sell membrane of exocrine pancreocyte is not solid, nuclei are not homogeneous in form and electron density, hyperchromatic, with condensed chromatin at the edges, nucleoli mostly are not detected, nuclear envelope has uneven contours and expanded edge and makes invaginations (fig. 3). Perinuclear space is expanded and enlightened, which indicates the development of the perinuclear swell. Pancreocyte with pyknotic nuclei is found.

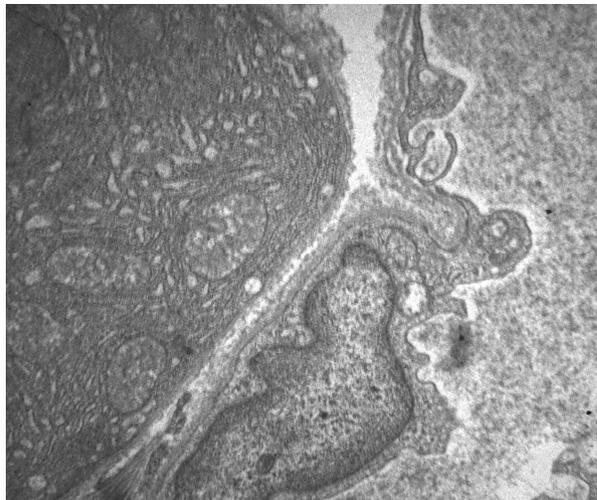


Fig 3: Ultrastructural organization of rat exocrine pancreocyte after 6 weeks of nalbuphine induction. Electron. x 8000

The number of fatty inclusions, large vacuoles and lysosomes in the sell cytoplasm increases. Mitochondria are with the swollen matrix and with a few crysts located irregularly, mitochondrial membrane is affected. Endoplasmic reticulum is hypertrophied, its tanks are expanded and sometimes fused,

forming a structureless areas with missing ribosomes in them. In other cells canaliculi of endoplasmic reticulum and Golgi apparatus are fragmented. The accumulation of intensely painted granules located at the apical pole of acinocytes, which adjoins the ducts, is found, that indicates a delay of the elimination of secretion into the lumen of inserted ducts (free of secretion vacuoles occupy the central area near the cell nucleus). The lumen of the duct doesn't contain any secretory material or can contain 1-2 granules. Intercellular spaces are expanded, the edge spaces are also expanded, where there is accretion of collagen fibers, hypertrophy and hyperplasia of fibroblasts.

The lumens of the inserted ducts are expanded, the walls are scleroid and thickened (fig. 4).



Fig 4: Ultrastructural organization of the inserted duct of rat exocrine pancreocyte after 6 weeks of opioid induction. Electron. x 4000

The cytoplasm of epithelial cells of inserted ducts is of weak electron density, with a great number of vesicles and vacuoles, crystals of mitochondria are destructed. Luminal surface of the membrane of these cells forms cytoplasmic outgrowths which protrude into the lumen of the duct, there is a great amount of homogeneous osmophilic material in the duct. The nuclei of epithelial cells are large, of irregular form, with nucleolar invaginations and irregularly placed chromatin and light nucleoplasm.

4. Conclusions

First insignificant changes of ultrastructural organization of exocrine part pancreocyte is observed right after 2 weeks of nalbuphine induction to rats and grow during next terms of the experiment. Long-lasting influence of opioids causes deep dystrophic changes of exocrine pancreocyte, including loss of regular form, karyopyknosis and karyorrhexis of nuclei, swelling and enlightenment of cytoplasm, the development of microcystic degeneration of the cells, loosening and disorganization of basal membrane which may lead to the disturbance of exocrine function of pancreas and difficulties of the process of elimination of secretory granules into the lumen of inserted ducts.

5. Prospects for further research

The work is a base for further researches of morphologists and clinicians to develop new diagnostic methods in the future, prevention and treatment of the pancreas diseases of drug addicts and patients who had to take opioids for a long time.

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