ORIGINAL ARTICLE

CONTENTS

Microscopic changes in the pancreas at late stages after experimental exposure to monosodium glutamate

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ABSTRACT

Aim: To determine the structural reorganization of the pancreas at late stages after experimental MSG exposure.

Materials and Methods: The study was performed on 20 sexually mature male rats. The experimental group received MSG orally at 70 mg/kg of body weight daily for 8 weeks. The control group was fed a standard diet without MSG. Decapitation was performed at week 18. Pancreatic tissues were collected for histological analysis and processed by standard methods**.**

Results: Ten weeks after MSG withdrawal, atrophic areas were detected in the exocrine parenchyma. Acini and pancreatocytes decreased in size. In the ductal epithelium, dystrophic and destructive changes were observed, including cytoplasmic metachromasia, nuclear pyknosis, eccentric localization, and karyorrhexis. Periductal sclerosis and pancreatic lipomatosis were recorded. Vascular walls were thickened and homogeneous due to edema and mucoid swelling. Capillaries were plethoric with stasis and occasional perivascular hemorrhages.

Conclusions: At late stages after MSG exposure, marked alterations in pancreatic structure were revealed. Irreversible atrophic changes of exocrinocytes led to dysfunction of the gland, indicating the toxic effect of monosodium glutamate.

KEY WORDS: monosodium glutamate, pancreas, histological changes

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INTRODUCTION

The issue of nutrition and food quality in Ukraine and globally has become particularly relevant, especially nowadays [1-3]. This is associated with the extensive use of a wide range of preservatives, sweeteners, flavor enhancers, and other food additives, the consumption of which can lead to structural changes in various tissues, particularly those of the digestive system [4-6]. The pancreas exhibits high vulnerability to various exogenous and endogenous factors, among which monosodium glutamate occupies a significant place. This food additive affects the physiological function of the pancreas. Receptors for glutamate and transporters have been identified in the islets of Langerhans, ductal cells, and acini [7,8]. Accumulation of monosodium glutamate in pancreatic juice has been proven[7]. Morphological studies in this area allow for the identification of certain links in the structural disturbances of this vital organ under conditions of increased and prolonged exposure to monosodium glutamate [9,10]. The presence of receptors and transporters in the pancreas indicates that this gland is also a target organ for monosodium glutamate action [11-13].

AIM

To establish the features of structural and morphological reorganization of the pancreas at late stages of monosodium glutamate exposure.

MATERIALS AND METHODS

The studies were conducted on 20 sexually mature male Wistar rats weighing 200–250 g, which were housed in the vivarium of Danylo Halytsky Lviv National Medical University [14]. The object of the study included the exocrine and endocrine parts of the pancreas. Animal care and experimental procedures adhered to international rules and principles of the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Strasbourg, 1986) and

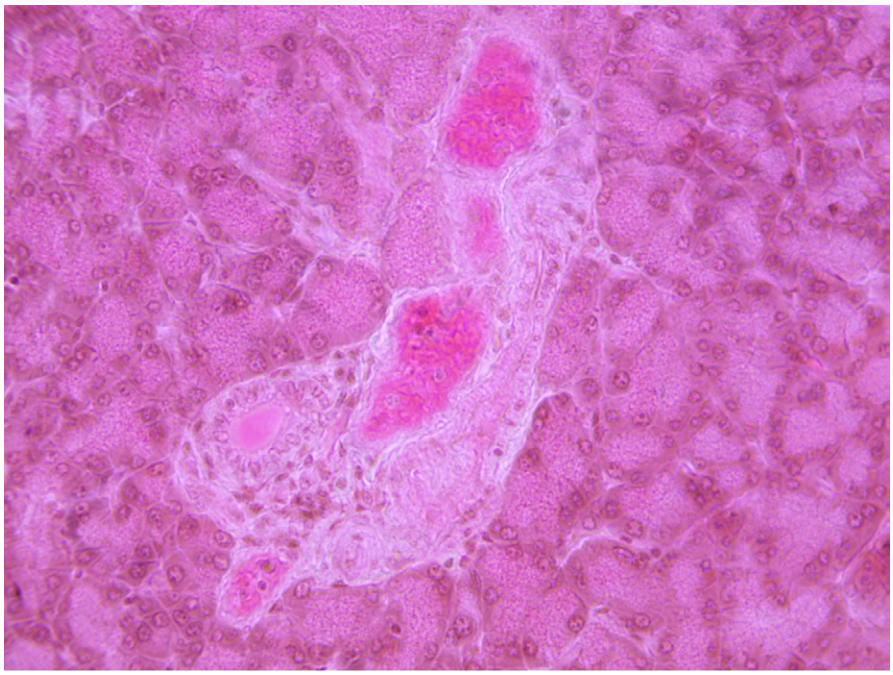

Fig. 1. Histological changes in the pancreas 10 weeks after monosodium glutamate withdrawal. Staining with hematoxylin and eosin (magnification x200). Disorganization of pancreatic acini, dystrophic and destructive changes in acinar exocrinocytes, karyopyknosis, and vacuolization of nuclei. Slight periductal lymphocytic infiltration
Picture taken by the authors

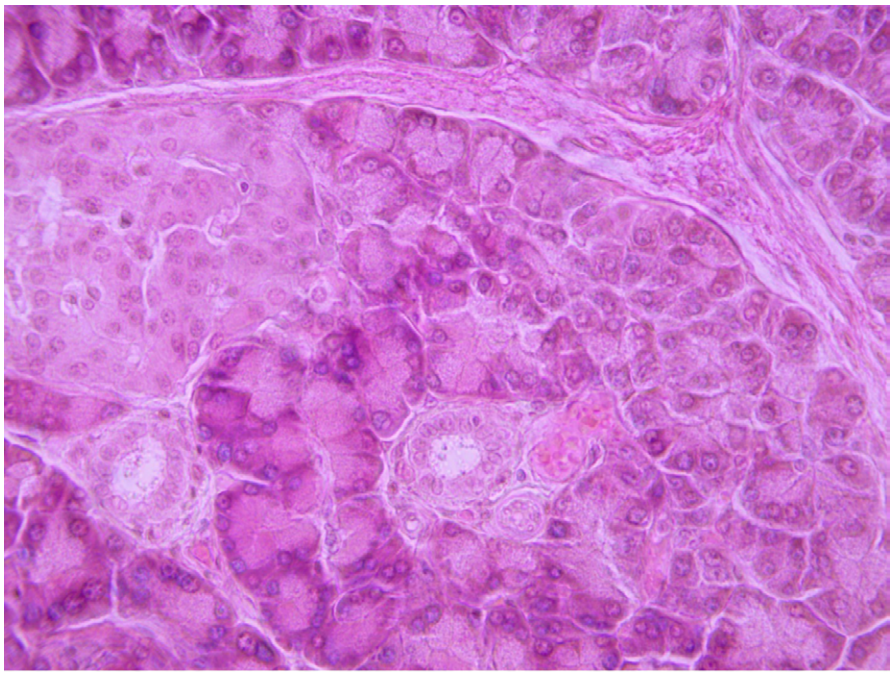

Fig. 2. Histological changes in the pancreas 10 weeks after monosodium glutamate withdrawal. Staining with hematoxylin and eosin (magnification x200). Dystrophic changes in the epithelium of intralobular excretory ducts. Increased volume of collagen fibers and edema of connective tissue in the interlobular spaces of the pancreas
Picture taken by the authors

«On the Protection of Animals from Cruel Treatment, General Principles of Work on Animals (Kyiv, 2001)». This study was approved by the Bioethics Committee of Uzhhorod National University, Bioethics Protocol. Monosodium glutamate was administered orally daily to rats in the experimental group at a dose of 70 mg/kg of body weight for 8 weeks. The control group of animals received a standard diet without the addition of monosodium glutamate. Animals were withdrawn from the experiment at 2, 3, 4, 5, 6, 7, 8 weeks with the addition of the food additive to the diet, and after withdrawal of monosodium glutamate from the diet, animals were withdrawn from the experiment at 10 weeks.

Material collection was performed according to generally accepted methods. For histological examination, collected pancreatic tissue samples were fixed in a neutral 10% formalin solution, followed by dehydration in increasing concentrations of alcohol and embedding in paraffin blocks. Histological sections 4–6 μm thick, obtained with a sliding microtome Tesla BS-500 (Швеція). were stained with hematoxylin and eosin and Azan [15]. Sections were examined and photographed using a MICROmed SEO SCAN light microscope (objectives x10, x20, x40) and a Vision CCD Camera. The photographs of histological micropreparations were saved in .jpg format.

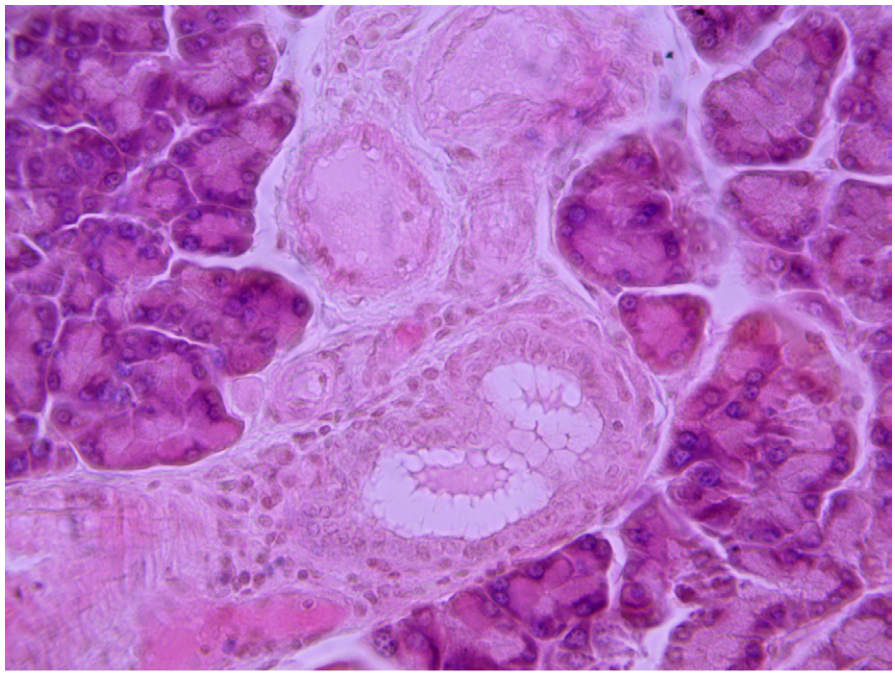

Fig. 3. Histological changes in the epithelium of the interlobular excretory duct wall of the pancreas 10 weeks after monosodium glutamate withdrawal. Staining with hematoxylin and eosin (magnification x200). Deformation and dilation of interlobular pancreatic ducts with secretory stasis in their lumen. Dystrophy and desquamation of the epithelium of interlobular pancreatic ducts
Picture taken by the authors

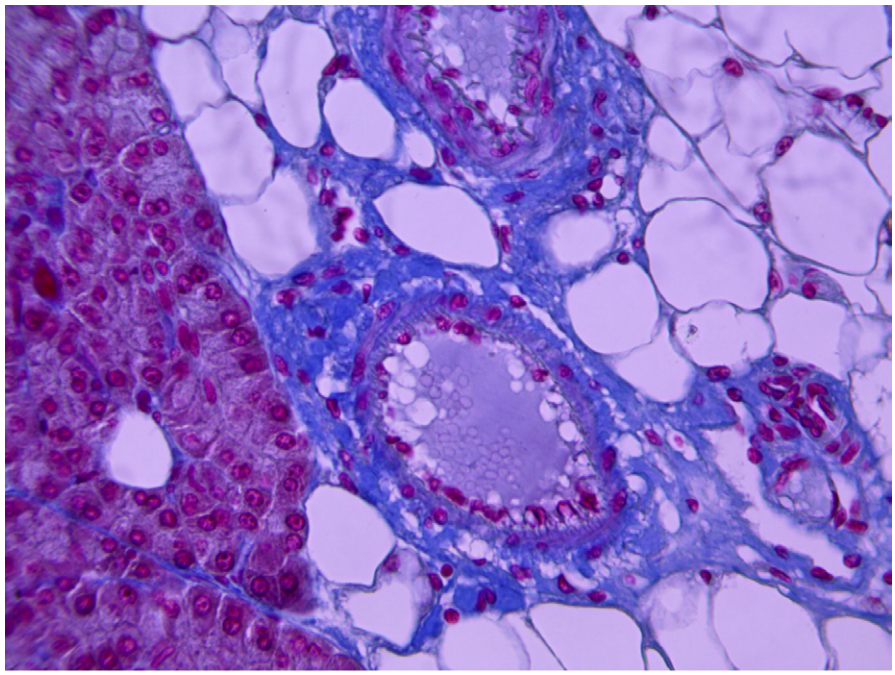

Fig. 4. Late changes in the pancreas 10 weeks after monosodium glutamate withdrawal. Azan staining (magnification x400). Proliferation of adipose tissue in the interlobular connective tissue and around the interlobular excretory ducts of the pancreas
Picture taken by the authors

RESULTS

Histological studies of the exocrine portion of the pancreas at 10 weeks after withdrawal of the MSG food additive revealed edema and an increase in the area of the connective tissue component of the gland. Areas of atrophy of the exocrine part of the organ's parenchyma were evident, along with a chaotic arrangement of exocrinocytes. The area of acini, and consequently pancreatocytes, visually decreased. The most characteristic signs included the loss of apical eosinophilia and basal basophilia of the cytoplasm, pyknosis of the nuclei of pancreatic parenchymal cells, vacuolization of nuclei, and disruption of their intracellular localization (Fig. 1).

The epithelium of the pancreatic ducts also underwent significant dystrophic and necrobiotic changes. Cells of the intercalated ducts were disorganized, largely losing their shape. Some centroacinar ducts had a narrow lumen without secretory content. The epithelium of the intralobular and interlobular ducts was thinned; in places, there was destruction of the epithelial layer, with single desquamated epithelial cells in the lumen. Secretory stasis was observed; the ducts' own connective tissue lamina propria was edematous and thickened. At the 10th week of the experiment, histological changes in the exocrine portion of the pancreas intensified and were characterized by destructive-degenerative and moderate chronic inflam-

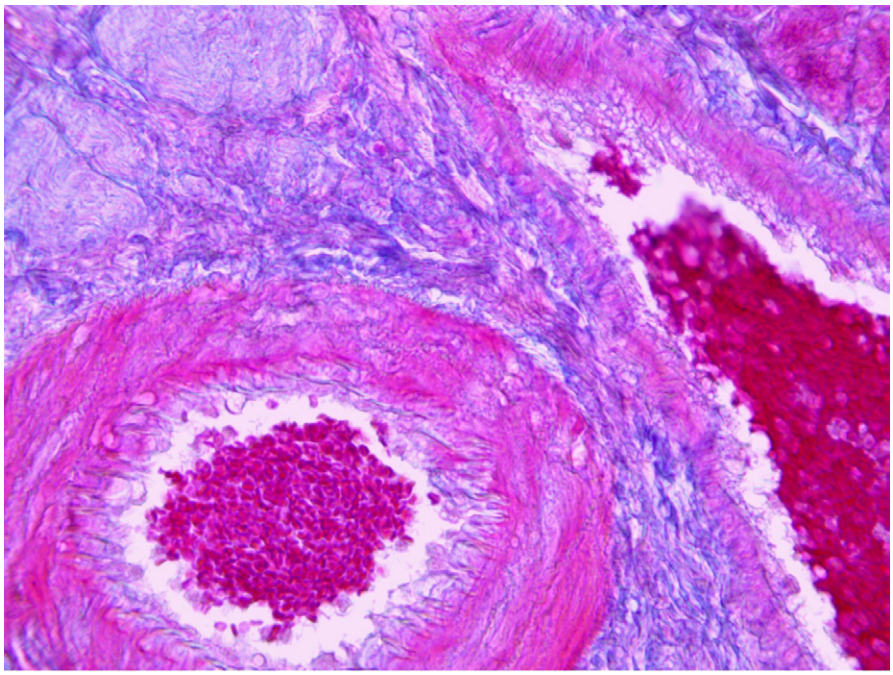

Fig. 5. Microscopic changes in pancreatic vessels 10 weeks after monosodium glutamate withdrawal. Azan staining (magnification x400). Vessel walls are thickened and homogenized due to edema and mucoid degeneration. Vacuolization and desquamation of endothelial cells. Sludge phenomenon of erythrocytes in the vessel lumen
Picture taken by the authors

matory changes in the structural components of the organ. Edema of the connective tissue with numerous collagen fibers was found in the interacinar and, especially, in the interlobular connective tissue; a slight monocytic-lymphocytic infiltration was determined. The diameter of the acini decreased, and polygonal pancreatocytes showed signs of focal dystrophy with intensely basophilic nuclei exhibiting vacuolization and pyknosis (Fig. 2).

Interlobular ducts were deformed, with destruction and fragmentation of the ductal epithelium. Destruction of the ductal epithelium and its detachment from the basement membrane were observed. Numerous desquamated epithelial cells and secretory stasis were present in the ductal lumen (Fig. 3). Accumulation of a large number of adipocytes was noted around the interlobular pancreatic ducts, characteristic of the development of pancreatic lipomatosis (Fig. 4).

The results of microscopic examinations of blood vessels at this observation period revealed dystrophic-destructive and inflammatory perivascular changes, manifested by slight extravasal macrophagic-lymphocytic infiltration. Vessel walls were moderately edematous, homogenized with signs of mucoid degeneration. The inner lining of the vessels also underwent dystrophic and necrobiotic changes, characterized by vacuolization of endothelial cells, karyopyknosis, and destruction of endothelial cell nuclei with desquamation of endothelial cells into the vessel lumen. Microthrombi and erythrocyte aggregation with the development of sludge phenomenon were found in the lumens of small vessels (Fig. 5).

The structure of medium-caliber vessel walls at the 10th week of the experiment was sharply altered, thickened, with narrowing and deformation of the lumen, which led to a decrease in vascular permeability and, consequently, hypoxic damage to the pancreatic parenchyma, manifested by dystrophic-destructive and atrophic changes in the acini and ducts of the gland. The structure of microvessels also showed characteristic changes: their walls were deformed, thinned, homogenous, with dilated lumens forming thrombi and sludge. Slight monocytic-lymphocytic infiltration of the perivascular connective tissue was observed, with occasional diapedetic hemorrhages. In isolated vessels, lumen obliteration phenomena were observed, leading to a reduction in the pancreatic microvascular bed.

DISCUSSION

Scientific studies by Howell J.A. and Fukushima et al [7]. have demonstrated that the cells of the pancreatic islet apparatus and acini possess trophic receptors for monosodium glutamate (MSG). Consequently, high dietary MSG intake in rats leads to receptor activation, causing damage to the membranes of pancreatic exocrinocytes. This disruption of cellular metabolism results in both superficial and deep dystrophic alterations, including cellular hydropic degeneration, nuclear pyknosis, changes in cytoplasmic staining, and partial necrosis of exocrinocytes. Chronic injury in the pancreatic interstitium provokes a moderate inflammatory response, characterized by lymphocytic–macrophage infiltration.

Structural changes observed in intralobular and interlobular pancreatic ducts are attributable to MSG's ability to enhance pancreatic juice secretion

and its tendency to accumulate therein. This leads to direct epithelial damage via membrane ion-channel dysfunction, manifesting as vacuolar degeneration of cells and nuclei, metachromatic cytoplasmic changes, necrosis, and cell desquamation. Obstruction of duct lumens induces pancreatic juice stasis, resulting in ductal dilation and deformity. Prolonged hypoxia further promotes sclerosis of ductal walls, causing narrowing and partial obliteration, especially of the centroacinar ducts.

Expansion of the interstitial space is associated with toxic injury to capillary endothelium and basement membranes, increasing vascular permeability and leading to interstitial oedema, acinar disorganization, and chaotic arrangement of exocrinocytes. Edema increases the distance between capillaries and exocrinocyte membranes, impairing parenchymal perfusion and inducing hypoxia. This triggers dystrophic and necrobiotic changes in pancreatocytes, eventually culminating in atrophy, fibrosis, reduction of the vascular network, periductal sclerosis, and lipomatosis.

Medium-sized vessels exhibit structural and morphological alterations such as wall thickening and lumen narrowing, driven by mucoid swelling and excessive connective tissue proliferation, both consequences of chronic hypoxia [16].

MSG-induced microcirculatory vascular wall changes include endothelial degeneration (dystrophy, necrosis, desquamation) and basement membrane injury. These changes result in plasmorrhagia and extravasation of blood cellular components into the pancreatic interstitium, causing increased blood viscosity and slowed capillary flow. This leads to thrombosis, a sludging phenomenon in microvessels, and small perivascular hemorrhages in the interstitium [17].

It should be noted that pancreatic structural remodeling in rats was influenced not only by MSG concentration, exposure duration, and withdrawal period, but also by age-related changes. Biological material was collected from sexually mature male rats at the 18th week of the experiment [18].

CONCLUSIONS

The results of microscopic studies of the exocrine part of the pancreas at late stages after monosodium glutamate withdrawal showed that at 10 weeks, destructive-degenerative changes occur, accompanied by sclerosis, inflammation, and atrophy of the investigated area. Proliferation of fibrous structures, atrophy of exocrinocytes, and the walls of the excretory ducts were found. Destruction and breakdown of the vessel walls were observed, and diapedesis with the formation of inflammatory infiltrates was determined. The study showed that even after the cessation of monosodium glutamate consumption, the gland exhibits a low capacity for regenerative processes.

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CONFLICT OF INTEREST
The Authors declare no conflict of interest

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A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

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