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RESEARCH ARTICLE

Comparative Analysis of Morphological and Morphometric Changes in The Pancreas Of 15-Month-Old Rats Induced by Modeling Nicotine Intoxication Versus the Control Group

Akhtamov Azizbek Avaz ugli
PhD., Associate professor, Department of Anatomy, Clinical Anatomy, Bukhara State Medical Institute named after Abu Ali ibn Sino, City of Bukhara, 200118, Gijduvan street, 23, Uzbekistan

Radjabov Akhtam Boltaevich
DSc., Professor, Head of the Department of Anatomy, Clinical Anatomy, Bukhara State Medical Institute named after Abu Ali ibn Sino, City of Bukhara, 200118, Gijduvan street, 23, Uzbekistan

Abstract: Background: The pancreas is a morphologically complex parenchymal organ composed of closely integrated exocrine and endocrine components responsible for digestive enzyme secretion and hormonal regulation of metabolism. Nicotine is a well-known toxic agent with cytotoxic, pro-oxidant, and vasoactive properties that can disrupt cellular homeostasis and induce structural damage in various organs, including the pancreas. Oxidative stress, apoptosis, and stromal remodeling are considered key mechanisms underlying nicotine-induced tissue injury. However, age-related morphofunctional changes in the pancreas under nicotine exposure remain insufficiently studied. Objective: To compare morphological and morphometric changes in the pancreas of 15-month-old rats under modeled nicotine intoxication with those of the control group. Materials and methods: The experimental study was conducted on 30 outbred white rats divided into two groups: control (n=15) and nicotine-exposed (n=15). Nicotine intoxication was modeled using passive tobacco smoke exposure in a 0.3 m^3 glass chamber based on A.S. Solomin (2011) for 30 days, twice daily for 30 minutes. Histological examination of pancreatic tissue was performed using Hematoxylin-Eosin and Van Gieson staining. Morphometric analysis included assessment of exocrine and endocrine parenchymal areas, acinar dimensions, duct diameter, islet size, and cellular characteristics. Results: Nicotine exposure caused significant structural alterations in both exocrine and endocrine components of the pancreas. The relative area of exocrine parenchyma decreased, along with reductions in acinar diameter, epithelial height, and exocrinocyte size and number. The nucleus-to-cytoplasm ratio increased, indicating cellular stress and functional impairment. In the endocrine portion, reductions in islet number, size, endocrinocyte density, and cellular area were observed, reflecting decreased hormonal activity. Histological analysis revealed epithelial desquamation, nuclear swelling, chromatin dispersion, cytoplasmic shrinkage, connective tissue hypertrophy, and interstitial space formation. Van Gieson staining confirmed stromal fibrosis and tissue degeneration. Conclusion: One-month nicotine intoxication in 15-month-old rats induces pronounced morphological and morphometric alterations in the pancreas. These changes include suppression of exocrine and endocrine activity, structural disorganization, connective tissue remodeling, and cellular degeneration. The findings indicate that nicotine significantly impairs pancreatic structure and function through mechanisms associated with oxidative stress, apoptosis, and stromal fibrosis.

Key words: Nicotine intoxication, pancreas, morphology, morphometry, exocrine part, endocrine part.

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INTRODUCTION

The pancreas is a morphologically complex parenchymal organ characterized by structural heterogeneity; it contains closely integrated exocrine and endocrine components that are both morphologically and functionally interconnected [1]. The exocrine portion is responsible for the synthesis and secretion of digestive enzymes, while the endocrine apparatus regulates carbohydrate metabolism through the islets of Langerhans, primarily via the production of insulin and glucagon [5].

Research indicates that the pancreas is highly sensitive to external toxic factors, including nicotine, which possesses strong cytotoxic, pro-oxidant, and vasoactive properties [2, 3]. Nicotine easily penetrates biological membranes, interacts with nicotinic acetylcholine receptors, and leads to disturbances in intracellular homeostasis [4].

One of the key pathogenetic mechanisms of nicotine intoxication is the development of oxidative stress, characterized by excessive generation of reactive oxygen species and subsequent damage to lipid membranes, proteins, and nucleic acids [10, 12]. In pancreatic tissue, this manifests as cellular destruction, disruption of mitochondrial and endoplasmic reticulum structures, and activation of apoptotic processes [9].

Morphological changes induced by nicotine include disorganization of acinar architecture, interstitial edema, stromal fibrosis, and infiltration of tissue elements [1, 15]. Particularly significant is the damage to the endocrine apparatus of the gland, manifested by a reduction in the size and number of islets of Langerhans, β-cell depletion, and impaired islet vascularization [13].

Studies also demonstrate degenerative changes such as vacuolization, pyknosis, karyorrhexis, and karyolysis, indicating the development of necrobiotic and apoptotic processes [8, 19]. Alterations in the nucleus-to-cytoplasm ratio reflect cellular stress and adaptive-compensatory responses [14].

Morphometric analysis is an important tool for the objective assessment of cellular changes, allowing quantitative evaluation of acinar area, islet volume, duct diameter, and cellular density [7]. Researchers have shown that nicotine exposure leads to a reliable decrease in morphometric parameters of parenchymal structures, while indicators associated with inflammation and fibrosis increase [15].

Age significantly influences tissue adaptive capacity. In older organisms, reduced regenerative potential, increased sclerosis, and heightened sensitivity to toxic agents are observed [6, 18]. Therefore, studying morphological changes in the pancreas of 15-month-old rats, corresponding to mature age, is of particular scientific importance.

Despite the large number of studies on nicotine toxicity, comprehensive comparative analyses of age-related morphological and morphometric changes in the pancreas remain insufficiently developed [11, 16]. The lack of systematic data limits a full understanding of pancreatic injury mechanisms and restricts the development of preventive and pathogenetically justified corrective approaches.

Thus, in-depth morphological and morphometric investigation of the pancreas under nicotine intoxication in age-related experimental animals represents one of the relevant directions in modern morphology and pathological anatomy.

Aim of the study

To compare morphological and morphometric changes in the pancreas of 15-month-old rats under modeled nicotine intoxication with those of the control group.

METHODS

The experimental study was conducted on 3-month-old outbred white rats. A total of 30 animals were included, divided into two groups: Group 1-control (n=15); Group 2-nicotine-exposed (n=15).

During the experiment, animals in the experimental group were exposed to tobacco

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smoke for 30 days, twice daily, for 30 minutes per session.

A model proposed by A.S. Solomin (2011) was used. A 0.3 m^3 glass chamber was employed for exposure. Smoke generation was achieved using a device designed for holding cigarettes and an electronic smoking apparatus. Each cigarette was replaced immediately after complete combustion, ensuring a continuous flow of tobacco smoke in the chamber.

On average, one person smokes 20 cigarettes per day, receiving approximately 20 mg of nicotine. Based on this, the equivalent daily nicotine dose for a rat, adjusted for a 70 kg human, was determined to be 0.043 mg.

To standardize experimental conditions, 15 animals were placed in each chamber. Smoke exposure lasted 30 minutes, during which two cigarettes were burned. The experimental animals were exposed to "passive smoking" twice daily.

According to calculations, each animal received a maximum of 0.048 mg of nicotine per day, which corresponds to the estimated human daily intake.

After each 30-minute exposure, animals were removed from the chamber and kept under standard vivarium sanitary conditions. At the end of the experiment (day 30), animals were euthanized under light ether anesthesia. The obtained tissue samples were stained using Hematoxylin-Eosin and Van Gieson methods.

RESULTS

The study revealed that one-month nicotine intoxication in 15-month-old outbred white rats led to significant morphological changes in the pancreas. After preparation of histological specimens stained with Hematoxylin–Eosin and Van Gieson, morphological alterations in both exocrine and endocrine compartments, as well as morphometric parameters, were identified and analyzed.

The relative area of the exocrine parenchyma decreased from 71.5 ± 1.4% in the control group to 63.2 ± 1.6% under nicotine exposure, indicating reduced density and functional activity of the parenchyma. The diameter of acini decreased from 29.0 ± 0.7 μm to 25.4 ± 0.8 μm, and their area from 860.0 ± 30.0 μm^2 to 720.0 ± 28.0 μm^2. A reduction in epithelial height from 11.6 ± 0.4 μm to 9.8 ± 0.3 μm reflected a decline in the secretory activity of exocrinocytes. The average area of exocrinocytes decreased from 120.0 ± 5.0 μm^2 to 105.0 ± 4.0 μm^2, and nuclear area from 18.7 ± 0.7 μm^2 to 16.2 ± 0.6 μm^2, resulting in an increase in the nucleus-to-cytoplasm ratio from 0.18 ± 0.01 to 0.22 ± 0.02. The number of exocrinocytes per acinus decreased from 6.7 ± 0.2 to 5.4 ± 0.2, and the diameter of intralobular ducts from 13.0 ± 0.6 μm to 11.5 ± 0.5 μm. These findings confirm the direct toxic effect of nicotine on the exocrine portion of the pancreas.

Hematoxylin-Eosin-stained sections showed epithelial cell desquamation, swollen nuclei, and chromatin dispersion. Acini were reduced in size and shape, intralobular ducts were narrowed, and ductal epithelial cells exhibited hyperchromasia. Van Gieson staining revealed increased staining intensity of collagen and connective tissue, indicating stromal densification and degeneration. Connective tissue hypertrophy and the formation of interstitial spaces around both endocrine and exocrine cells were also observed.

The relative area of the endocrine portion decreased from 2.30 ± 0.10% to 1.85 ± 0.12%, the number of islets from 1.65 ± 0.10 to 1.42 ± 0.08 units, the islet area from 14.2 ± 0.5 $\times 10^3$ μm^2 to 11.8 ± 0.6 $\times 10^3$ μm^2, and their diameter from 122.0 ± 7.0 μm to 110.0 ± 6.0 μm. The number of endocrinocytes decreased from 108.0 ± 4.0 to 92.0 ± 3.0, their density from 7.2 ± 0.3 $\times 10^{-3}/\mu m^2$ to 6.4 ± 0.2 $\times 10^{-3}/\mu m^2$, and their average area from 71.0 ± 3.0 μm^2 to 64.0 ± 3.0 μm^2. Hematoxylin–Eosin staining showed shrunken endocrinocytes with peripheral nuclei and condensed cytoplasm, while Van Gieson staining demonstrated connective tissue hypertrophy and interstitial space formation around endocrine cells.

DISCUSSION

The results demonstrate that one-month nicotine intoxication in 15-month-old outbred white rats causes pronounced morphological and morphometric alterations in the pancreas.

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Reductions in exocrine parenchymal area, acinar size, and epithelial height indicate a decrease in secretory function. Changes in nuclear and cytoplasmic parameters, as well as an increased nucleus-to-cytoplasm ratio, reflect cellular stress and toxic effects. The decrease in exocrinocyte number and narrowing of intralobular ducts further confirm impaired exocrine secretion. These findings are consistent with previous studies reporting the direct toxic effects of nicotine on exocrine cells (Alekseev, 2020; Baranov & Klimov, 2019).

In the endocrine portion, reductions in islet number and size, as well as decreased endocrinocyte number and density, indicate a weakened hormonal secretory capacity of the islets. Similar observations were reported by Dyakova and Smirnova (2022) in histophysiological analyses. Histological examination revealed swollen nuclei, chromatin dispersion, and cytoplasmic shrinkage in Hematoxylin–Eosin-stained preparations. Van Gieson staining demonstrated connective tissue hypertrophy and interstitial space formation, indicating structural stress and tissue weakening.

The observed morphometric changes are consistent with mechanisms involving apoptosis and oxidative stress (Ivanov & Kuzmina, 2021; Kuznetsov & Orekhova, 2024; Brown & Anderson, 2020). The structural alterations in both exocrine and endocrine components are interrelated and contribute to an overall reduction in pancreatic secretory capacity. These findings align with experimental models described by Miller & Thompson (2025), Patel & Singh (2023), and Smith & Brown (2019).

Furthermore, morphological and morphometric changes observed using Hematoxylin–Eosin and Van Gieson staining highlight epithelial damage, connective tissue hypertrophy, and interstitial expansion, confirming nicotine-induced pancreatic toxicity, in agreement with previous studies (Grigoryev, 2018; Kim & Park, 2024; Lee & Kim, 2021).

CONCLUSION

The study demonstrated that one-month nicotine intoxication in 15-month-old outbred white rats significantly affects the morphological and morphometric characteristics of the pancreas. Decreased exocrine parenchymal area, reduced acinar size, lowered epithelial height, and changes in the nucleus-to-cytoplasm ratio indicate suppressed secretory activity. Narrowing of intralobular ducts and reduced exocrinocyte numbers confirm functional impairment of the exocrine component. Histological findings of nuclear swelling, cytoplasmic shrinkage, connective tissue hypertrophy, and interstitial space formation reflect structural stress and degeneration.

In the endocrine portion, reductions in islet number, size, and endocrinocyte density indicate decreased functional activity of the islets of Langerhans. The morphometric changes are associated with apoptosis and oxidative stress, confirming functional impairment in both pancreatic compartments.

Thus, nicotine intoxication significantly weakens both exocrine and endocrine structures of the pancreas morphologically and morphometrically, reduces its overall secretory capacity, and induces cellular stress.

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