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Morphometric Changes in the Pancreas of Rats of Reproductive Age Under Experimental Nicotine-Alcohol Intoxication and Methods of Correction

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Abstract **Background.** In recent years, the incidence of pathological conditions associated with the combined toxic effects of nicotine and alcohol on the pancreas has been increasing. These factors exert a synergistic effect, inducing inflammatory, dystrophic, and degenerative changes at both cellular and tissue levels. However, effective approaches for correcting such damage, particularly through phytotherapeutic agents, remain insufficiently studied. **Objective.** To investigate morphological and morphometric changes in the pancreas under experimental nicotine-alcohol intoxication and to evaluate the corrective efficacy of a turmeric (Curcuma)-based phytopreparation. **Materials and methods.** The study was conducted on 60 three-month-old outbred white rats. The animals were divided into three groups: control (n=20), experimental (n=20), and correction group (n=20). Intoxication was induced using standard experimental models. The phytopreparation was administered intragastrically at a dose of 2 ml using a gastric tube. At the end of the experiment, the animals were euthanized under ether anesthesia. Pancreatic tissue samples were stained with hematoxylin–eosin and Van Gieson methods and subjected to morphological and morphometric analysis. **Results.** Nicotine-alcohol intoxication caused significant structural alterations in the pancreas. In the exocrine component, acinar cells exhibited vacuolization, granular degeneration, a reduction in secretory granules, and decreased acinar size. Morphometric analysis showed a decrease in acinar diameter, acinar area, and epithelial height. Stromal expansion and accumulation of collagen fibers indicated early fibrotic changes. In the endocrine component, the changes were more pronounced, including a reduction in the number and size of the islets of Langerhans, decreased endocrinocyte density, and increased signs of apoptosis. Administration of the phytopreparation resulted in partial restoration of pancreatic structure, reduction of dystrophic changes, and a significant decrease in collagen content, indicating its antifibrotic and cytoprotective effects. **Conclusion.** Combined nicotine-alcohol exposure leads to profound morphofunctional disturbances in the pancreas and activates fibrogenesis at early stages. The turmeric-based phytopreparation effectively reduces these pathological changes and improves structural and morphometric parameters of the pancreas. It may be considered a promising pathogenetic therapeutic agent in toxic pancreatic injury.

Keywords Pancreas, Nicotine-alcohol intoxication, Morphometry, Acinar structures, Islets of Langerhans, Endocrinocytes, Turmeric

1. Introduction

In recent decades, a steady increase has been observed in the prevalence of toxic lesions of the digestive system organs caused by the combined effects of nicotine and alcohol. These exogenous factors are considered major inducers of inflammatory processes at both tissue and cellular levels in the pancreas [5,20]. Particularly under conditions of combined intoxication, the study of morphological and morphometric changes is of great importance, as their pathogenetic effects are synergistic, leading to profound damage to both the exocrine apparatus and islet components [22,26].

The pancreas, as an organ with high metabolic activity, is extremely sensitive to toxic factors. This manifests as disruption of acinar architectonics, vacuolization of the cytoplasm of pancreatocytes, destruction of the rough endoplasmic reticulum, and a decrease in the density of secretory granules [2,12]. Nicotine exerts a vasoconstrictive effect, leading to ischemia and hypoxia in tissues, which results in reduced acinar parameters and expansion of the interstitial space [7,24]. Ethanol activates enzymatic autolysis,

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enhances oxidative stress, and stimulates apoptotic processes in exocrine cells [3,19].

Morphometric studies show that under chronic nicotine-alcohol intoxication, the average diameter of acini decreases by 15-25%, the nuclear area of pancreatocytes decreases by 10-18%, and the nuclear-cytoplasmic ratio increases, indicating the development of dystrophic changes [6,23]. In addition, a reduction in the number of β-cells in the islets of Langerhans and a decrease in their secretory activity are observed, leading to impaired endocrine function of the gland [15,27].

Given the above, the search for effective methods to correct structurally identified changes remains a relevant task in modern morphology. In this regard, phytopreparations with antioxidant, anti-inflammatory, and cytoprotective properties are of particular interest [1,8]. Turmeric-based preparations are especially noteworthy due to curcumin, a biologically active compound capable of inhibiting free radical processes and stabilizing cell membranes [4,21].

It should be noted that the comprehensive evaluation of morphological and morphometric changes in the pancreas under combined nicotine and alcohol intoxication in relation to phytocorrection remains insufficiently studied. This determines the relevance of the present study, aimed at an in-depth investigation of structural changes in the pancreas of laboratory animals and evaluation of their correction using a turmeric-based phytopreparation.

Aim of the study. To investigate morphological and morphometric changes in the pancreas of three-month-old outbred rats under experimentally induced nicotine-alcohol intoxication and to determine the corrective properties of a turmeric-based phytopreparation.

2. Materials and Methods

The study was conducted on three-month-old outbred rats. A total of 60 experimental animals were selected and divided into three groups: control group (n=20), experimental group exposed to nicotine-alcohol intoxication (n=20), and correction group (n=20).

The animals were maintained under standard vivarium conditions for one month [9,11]. All experimental animals met representativeness requirements in terms of age, body weight, diet, and housing conditions. Animals in both control and experimental groups had free access to food, with a daily diet consisting mainly of grains and vegetables.

Nicotine intoxication was induced using the model proposed by Solomina A.S. (2011). Alcohol intoxication was modeled using methods described by Sidorov P.I. (2002) and Knyshova L.P. (2016). The phytopreparation was administered intragastrically via a probe at a dose of 2 ml.

At the end of the experiment, animals were euthanized in the morning on an empty stomach. Euthanasia was performed in accordance with bioethical standards using rapid decapitation under ether anesthesia [14,16,17]. Pancreatic tissue was collected, processed for histological analysis, and stained with hematoxylin-eosin and Van Gieson stains.

3. Results

In control animals, the exocrine part of the pancreas showed relatively large acini, with abundant granules in the cytoplasm of acinar cells. The pancreatic duct system showed no deformation, the epithelial lining remained intact, and no vascular congestion or spasm was observed. Morphometrically, the acinar diameter was 31.2 ± 0.7 μm, area 960.0 ± 35.0 μm², epithelial height 12.7 ± 0.4 μm. The area of exocrinocytes was 130.0 ± 6.0 μm², nuclear area 20.2 ± 0.8 μm², cytoplasmic area 110.0 ± 5.0 μm², with a nuclear-cytoplasmic ratio of 0.18 ±0.01. The number of cells per acinus was 7.2 ± 0.2. The relative area of exocrine parenchyma was 74.0 ± 1.6%, stroma 24.0 ± 1.0%, with a stroma-parenchyma index of 0.32 ±0.06.

In the endocrine apparatus, islet area was 12.8 ±0.5 $\times 10^3$ μm², diameter 113.0 ± 7.0 μm, number of endocrinocytes per islet 98.0 ± 4.0, cell density 7.7 ± 0.3 $\times 10^{-3}$ cells/μm², average endocrinocyte area 68.0 ± 3.0 μm², relative endocrine area 2.1 ±0.1%, and number of islets 1.50 ±0.10.

In the experimental group, significant reactive and dystrophic changes were identified. These included vacuolar and granular dystrophy in acinar cells, decreased basophilia, reduced secretory granules, interstitial edema, and ductal epithelial desquamation. Morphometric parameters showed a decrease in acinar diameter, area, epithelial height, and cellular components, along with an increase in stromal proportion.

Endocrine changes were more pronounced, with reduced islet size, decreased endocrinocyte number and density, cytoplasmic vacuolization, nuclear pyknosis, and apoptosis.

Collagen fibers in the stroma significantly increased, indicating early fibrotic changes.

In the phytocorrection group, a decrease in collagen density, reduction of sclerosis, partial restoration of acinar and endocrine structures, and normalization of morphometric parameters were observed.

4. Discussion

The findings confirm that nicotine-alcohol intoxication induces significant morphological and morphometric alterations in the pancreas. These results are consistent with literature data demonstrating synergistic toxic effects leading to enhanced dystrophic and degenerative processes.

Observed acinar cell damage corresponds to toxic pancreatopathy described by Alekseev (2020). Microcirculatory disturbances align with findings by Zhukova (2019), while ethanol-induced oxidative stress and apoptosis correspond to Vasilyev (2021).

Reduction in β-cell population is consistent with studies by Kuznetsov (2020) and O'Connor (2021). Increased collagen deposition supports fibrogenesis activation as described by Nelson (2020).

Positive effects of phytocorrection are explained by antioxidant and cytoprotective properties of curcumin (Gusev, 2022; Zhang, 2022), as well as antifibrotic effects (Miller, 2019).

5. Conclusions

Experimental nicotine-alcohol intoxication in three-month -old rats leads to profound morphological and morphometric changes in the pancreas, affecting both exocrine and endocrine components. These changes include acinar reduction, dystrophic processes, decreased secretory activity, interstitial edema, fibrosis, disruption of islet architecture, reduction in endocrinocyte number, and apoptosis.

Increased stromal collagen and sclerosis indicate early activation of fibrogenesis.

Administration of a turmeric-based phytopreparation significantly reduced pathological changes, promoted partial structural recovery, improved morphometric parameters, and demonstrated antifibrotic, antioxidant, and cytoprotective effects.

Thus, turmeric-based phytopreparations may serve as a promising pathogenetic approach for correcting pancreatic damage induced by nicotine-alcohol intoxication.

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