



**DEVELOPMENT OF A NAFLD MODEL UNDER CONDITIONS OF HYPOKINESIA
AND HIGH-FAT DIET**

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Abstract: In this experimental study, histostructural changes in the liver tissue were examined using a rat model fed with a high-fat diet. The observed histostructural alterations correspond to the main stages of non-alcoholic fatty liver disease (NAFLD), including steatosis (fat accumulation in the hepatic parenchyma), inflammation, and fibrosis, each demonstrating distinct developmental features. These findings provide an opportunity to assess the mechanisms of NAFLD progression under experimental conditions and reveal the clinical-morphological correlations of the disease.

Keywords: NAFLD, high-fat diet, liver, experimental model, histostructure, steatosis, fibrosis, ballooning degeneration.

Introduction

Non-alcoholic fatty liver disease (NAFLD) is a pathological condition that develops against the background of metabolic syndrome, characterized by lipid accumulation in the hepatic parenchyma, inflammation, and progressive fibrosis. Today, it is recognized as one of the major global health issues, especially associated with obesity and insulin resistance. To investigate this condition under experimental conditions, animal models based on high-fat diet feeding are commonly used. In clinical practice, NAFLD frequently manifests as histostructural alterations in the liver of laboratory animals exposed to high-calorie fatty nutrition, closely resembling those observed in humans. The aim of this study was to investigate the histostructural changes in the liver of rats fed a high-fat diet and to correlate these alterations with the clinical features of NAFLD.

Materials and Methods

A total of 120 healthy male albino rats (weighing 150–160 g) were selected and divided into three groups:

1. Control group – kept under standard vivarium conditions, provided with normal food and drinking water.
2. Experimental group 1 – kept under vivarium conditions and fed with a high-fat diet and water.
3. Experimental group 2 – kept under hypokinetic conditions (in specially designed narrow cages) and fed with a high-fat diet containing animal fats and unsaturated fatty acids, with free access to water.

The experiment lasted up to 60 days to assess the dynamic development of histostructural changes in the hepatic parenchyma. At experimental days 3, 7, 15, 30, and 60, animals were euthanized under anesthesia, and liver samples were collected. Tissues were fixed in 10%



formalin, embedded in paraffin, and sectioned at 5–7 μm thickness. General histological, histochemical, and morphometric methods were applied to evaluate steatosis, ballooning degeneration, and the degree of fibrosis in accordance with the stages of NAFLD.

Results

Histological examination of liver tissues in the experimental groups revealed the following changes:

- Macrovesicular steatosis of hepatocytes;
- Ballooning degeneration characterized by perinuclear vacuolization and cytoplasmic swelling;
- Mild portal and perisinusoidal fibrosis confirmed by Masson's trichrome staining.

Biochemical analyses demonstrated increased levels of ALT and AST. The observed histological features corresponded to typical changes seen at various stages of NAFLD progression. High-fat diet feeding induced metabolic dysfunction, lipotoxic effects, and oxidative stress in the hepatic parenchyma. Steatosis represents the initial stage of NAFLD, while ballooning degeneration and fibrosis are indicators of its progression. The histostructural alterations observed in this study are consistent with clinical manifestations of NAFLD, such as right upper quadrant pain, fatigue, heaviness, and elevated ALT/AST levels. This experimental model can therefore be used to assess early stages of NAFLD and to evaluate the efficacy of hepatoprotective agents.

Conclusion

The histomorphological changes observed in the liver of rats fed a high-fat diet under hypokinetic conditions can serve as a reliable experimental model of NAFLD. This model contributes to a deeper understanding of the pathogenesis of NAFLD from a morphological perspective and is of significant importance for the development of preventive and therapeutic strategies in clinical practice.

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