MORPHOMETRIC CHARACTERISTICS OF THE RAT LIVER IN NORMAL CONDITIONS AND UNDER POLYPHARMACY: EFFECTS OF TWO DIFFERENT ANTI-INFLAMMATORY DRUGS

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Abstract

The effectiveness of treatment in humans and the desire to eliminate all coexisting diseases often inevitably lead to the prescription of multiple drugs, which, in turn, causes polypharmacy. Polypharmacy is a serious problem in healthcare because it clinically manifests as reduced pharmacotherapy efficacy, an increased risk of adverse reactions, and a significant rise in healthcare expenditures. Although the term “polypharmacy” is widely used in the medical literature, a universally accepted definition does not exist. The present study aimed to compare morphometric parameters of the liver in normal conditions and under polypharmacy when exposed to anti-inflammatory drugs, thereby contributing additional data on morphological and morphometric alterations in hepatic tissue.

Keywords: polypharmacy, morphometry, morphology, inflammation

Introduction

In modern medicine, the rapid growth in the development and introduction of pharmaceuticals has improved patient outcomes but has also resulted in significant health risks. In Russian medical literature, polypharmacy is described as the simultaneous administration of multiple drugs, including those used without sufficient indication, while in foreign literature, the equivalent term *polypharmacy* (from the Greek *poly*, many, and *pharmakon*, drug) is applied. Medical dictionaries

define polypharmacy as prescribing several medications within a single prescription or using multiple drugs for one or more diseases. This phenomenon is most common in elderly patients, and over 24 definitions are reported in scientific publications.

Objectives

Adverse drug effects, particularly in renal and cardiovascular pathology, represent a pressing global concern. Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most widely used medications and play a leading role in the development of these complications. While histological analysis is a key tool in diagnosing and differentiating liver pathologies of various etiologies, its findings do not always reflect the full spectrum of structural damage at the organ level. Therefore, the present study was designed to investigate macroscopically and microscopically the effects of polypharmacy on rat livers when administered NSAIDs, specifically aspirin and paracetamol. In total, 64 rat livers were examined for morphometric and morphological alterations.

Materials and Methods

The study included 40 liver tissue samples, divided into two groups. Macroscopic and microscopic analyses were performed using sections of 1.5 × 1.5 cm from the central and major lobes, which were fixed in 10% neutral buffered formalin. Following washing in running water, the tissues were dehydrated in graded ethanol solutions, cleared in xylene, and embedded in paraffin. Sections of 5–8 μm thickness were cut and stained with hematoxylin and eosin. The experimental group of rats received aspirin (5 mg/kg) and paracetamol (15 mg/kg), administered intragastrically in aqueous solution for 10 days, while the control group was given 0.5 ml of distilled water under similar conditions. Morphometric analysis was conducted using a trinocular microscope (DN-107t/Model NLCd-307b, Roman, China) with ocular micrometry to measure hepatocyte size and parenchymal structures. Statistical analysis was performed with Microsoft Excel 7.0 and STTGRAPH 5.1 software, using parametric statistics, Student's *t*-test, Fisher's criterion, and kurtosis measures to determine normal distribution and variance equality. The statistical significance threshold was set at $p < 0.05$.

Results and Discussion

Administration of NSAIDs under polypharmacy conditions resulted in multiple pathological changes in the hepatic parenchyma of white rats. These included disorganization of lobular architecture, degenerative alterations in hepatocytes, and lysis of some hepatocyte nuclei. The control group exhibited normal histological structures, with preserved central veins, intact lobules, and hepatocytes of typical morphology. Morphometric evaluation confirmed statistically significant differences in hepatocyte size and parenchymal parameters between groups. These findings highlight that prolonged NSAID exposure in polypharmacy can trigger hepatotoxic effects and structural liver damage. Considering the chronic course of many diseases

requiring long-term therapy, the inclusion of hepatoprotective agents into treatment regimens is strongly recommended to prevent toxic liver pathologies.

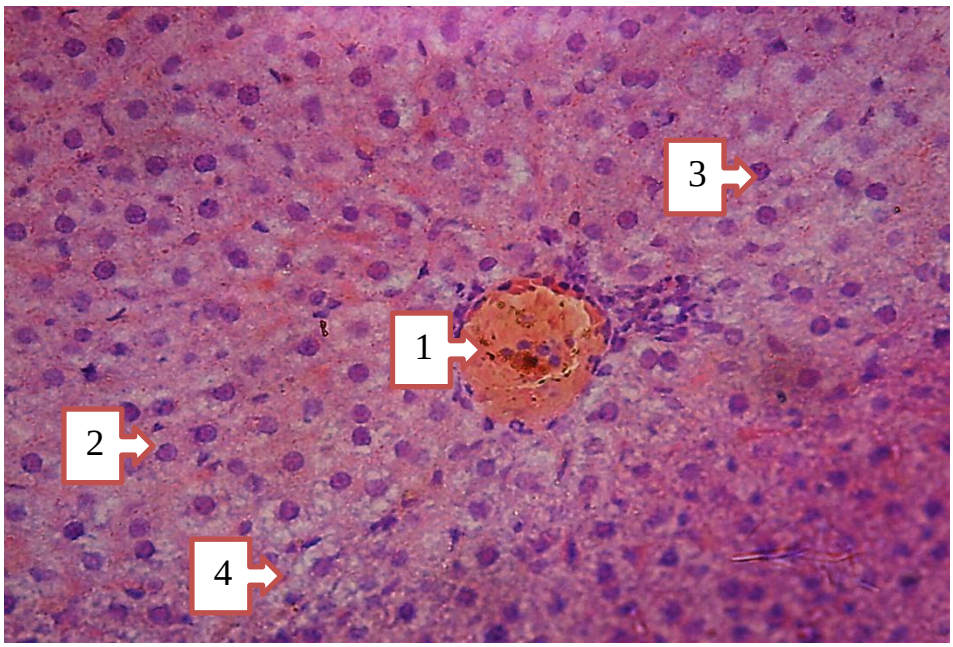

Figure 1. Central vein (1); preserved hepatic lobules (2); normal hepatocytes (3); degenerative hepatocytes (4).

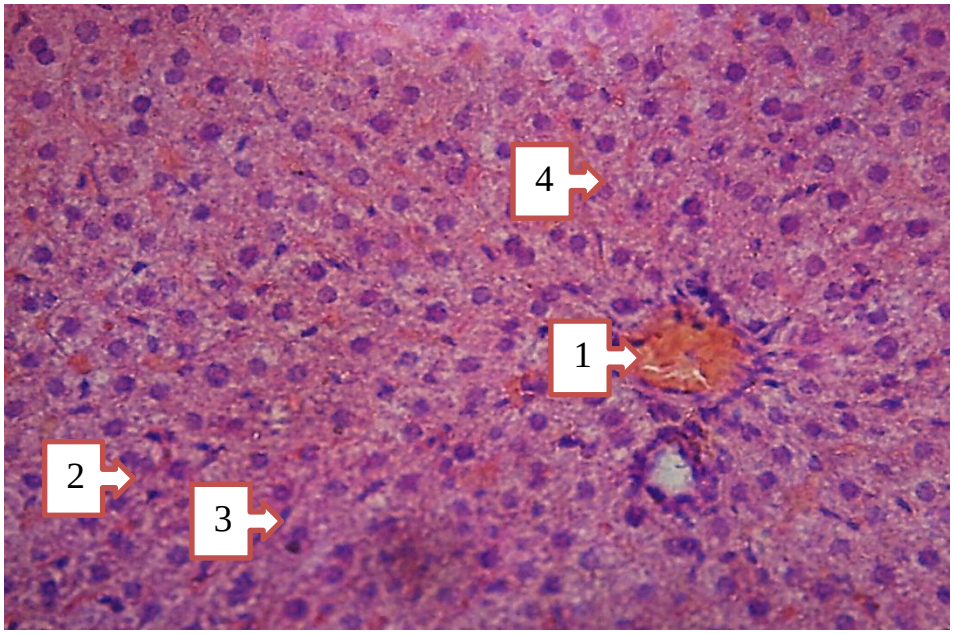

Figure 2. Central vein (1); disorganization of hepatic lobules (2); degenerative hepatocytes (3); lysis of hepatocyte nuclei (4).

Conclusion

Knowledge of normal morphometric liver parameters provides essential guidance for distinguishing pathological changes during microscopic analysis. Histological methods of assessing liver morphofunctional state remain crucial in diagnosing and differentiating hepatic diseases of diverse etiologies. The findings of this study can be applied in medical education at departments of histology and

pathological anatomy to supplement microscopic and macroscopic data for students. Moreover, comparative evaluation of liver morphometric parameters under polypharmacy improves the accuracy of pathohistological diagnosis and underscores the importance of cautious drug prescription.

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