HEMATOLOGICAL AND BIOCHEMICAL ALTERATIONS IN PARACETAMOL-INDUCED TOXIC HEPATITIS UNDER CONDITIONS OF WATER DEFICIENCY

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ABSTRACT

Drug-induced liver injury (DILI) remains one of the pressing challenges in modern hepatology due to its high prevalence, variability of clinical manifestations, and potential severity of outcomes. According to recent studies, DILI is one of the leading causes of acute liver failure in developed countries and often necessitates liver transplantation [3]. This issue is of particular importance in the context of the widespread use of medications, including analgesics and nonsteroidal anti-inflammatory drugs, among which paracetamol ranks among the leading causes of hepatotoxic complications [7]..

Relevance: Drug-induced liver injury (DILI) remains one of the pressing challenges in modern hepatology due to its high prevalence, variability of clinical manifestations, and potential severity of outcomes. According to recent studies, DILI is one of the leading causes of acute liver failure in developed countries and often necessitates liver transplantation [3]. This issue is of particular importance in the context of the widespread use of medications, including analgesics and nonsteroidal anti-inflammatory drugs, among which paracetamol ranks among the leading causes of hepatotoxic complications [7].

Recent studies indicate that toxic liver injury is based on complex pathogenetic mechanisms, including oxidative stress, mitochondrial dysfunction, inflammatory responses, and activation of hepatocyte apoptosis [5]. A key role is played by the imbalance between prooxidant and antioxidant systems, leading to cellular membrane damage and impaired liver function. Furthermore, it has been demonstrated that the severity of hepatocellular injury depends not only on the dose of the toxic agent but also on individual characteristics of the organism, including comorbid conditions and metabolic disturbances [2].

Particular attention has been given to the influence of concomitant factors capable of potentiating the toxic effects of drugs. In particular, dehydration is considered a significant modifying factor that contributes to the aggravation of hypoxic and metabolic disturbances in the liver, as well as to the activation of the systemic inflammatory response [4]. Under conditions of water deficiency, tissue perfusion decreases, the production of reactive oxygen species increases, and the detoxification function of the liver is impaired, which collectively leads to more pronounced hepatocellular damage.

Thus, the study of the mechanisms of drug-induced liver injury, as well as the role of associated factors such as dehydration, represents an important area of modern experimental and clinical medicine. The obtained data are essential for the development of effective methods for prevention, early diagnosis, and optimization of therapy for toxic liver injury.

Keywords: toxic hepatitis, paracetamol-induced hepatotoxicity, dehydration, hematological indices, biochemical markers, ALT, ALP, neutrophilia, lymphopenia, thrombocytosis, experimental model.

Aim of the study: To investigate the characteristics of hematological and biochemical blood parameters in paracetamol-induced toxic hepatitis and to assess the effect of dehydration on the severity of the observed changes.

Materials and Methods: The experiment was conducted on laboratory white rats weighing 250–290 g, housed under standard vivarium conditions in accordance with Good Laboratory Practice (GLP) requirements. The animals were divided into four groups: intact (control), dehydration, paracetamol (PCM), and paracetamol combined with dehydration.

The model of toxic hepatitis was induced by intraperitoneal administration of paracetamol at doses of 200, 300, and 600 mg/kg for 3 consecutive days. Dehydration was modeled by restricting access to water throughout the experimental period.

After completion of the exposure, blood and urine samples were collected. Hematological parameters were measured using an automated BIOBASE analyzer, while biochemical parameters were assessed using a HUMALYZER Primus analyzer with evaluation of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), bilirubin, urea, and creatinine levels. Statistical analysis was performed using ANOVA with a significance level of $p \leq 0.05$.

Results: In toxic hepatitis, pronounced changes in the leukocyte formula were observed. In the paracetamol (PCM) group, the relative lymphocyte count decreased to 67.05±3.32% compared to 82.55±1.89% in the control group, whereas neutrophils increased to 19.40±2.12% versus 8.8±0.88%. In the combined PCM + dehydration group, lymphocytes accounted for 78.47±5.33%, and neutrophils for 12.03±3.21%.

The absolute neutrophil count increased from $0.13\pm0.05\times10^9$/L to $0.35\pm0.21\times10^9$/L in the PCM group. Platelet counts rose from $1463.4\pm250.71\times10^9$/L (control) to $2670.33\pm236.55\times10^9$/L in the PCM group, and to 1768.0×10^9/L in the combined PCM + dehydration group. Plateletcrit increased from 1.19±0.26% to 2.12±0.25%.

Red blood cell count, hemoglobin, and hematocrit levels remained stable across all groups. Biochemical analysis demonstrated an increase in alanine aminotransferase (ALT) from 40.47±11.41 U/L (control) to 52.42±15.65 U/L in the PCM group and to 87.94±29.55 U/L in the PCM + dehydration group.

Alkaline phosphatase activity increased to 588.56±69.65 U/L in the PCM group compared to 473.32±354.82 U/L in controls. Urea concentration increased from 3.71±2.16 to 10.8±2.4 in the dehydration group and to 10.18±2.92 under combined exposure. Bilirubin (0.52–0.81 mg/dL) and creatinine (55.22–64.18) levels did not show significant changes. Thus, dehydration enhances the severity of both inflammatory and metabolic disturbances in toxic liver injury.

Conclusions:

Paracetamol-induced toxic hepatitis is associated with the development of a systemic inflammatory response characterized by lymphopenia, neutrophilia, and reactive thrombocytosis, as well as increased activity of liver enzymes reflecting hepatocellular damage.

Dehydration aggravates the severity of toxic liver injury, contributing to a significant increase in ALT and urea levels, which indicates the exacerbation of cytolytic and metabolic disturbances under conditions of water deficiency.

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