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PATHOPHYSIOLOGICAL CHANGES IN THE LIVER DURING ACUTE INFLAMMATION

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Abstract: This review highlights the pathophysiological changes that occur in the liver during acute inflammation, based on a systematic analysis of scientific research and literature. The article examines microcirculatory disturbances, hepatocyte injury mechanisms, cytokine and inflammatory mediator imbalances, oxidative stress, and the role of the antioxidant system. Findings from both domestic and international studies underscore the importance of understanding liver injury and functional disturbances, monitoring these changes, and developing effective therapeutic strategies. The review provides theoretical and practical insights for clinical practice and further research.

Keywords: acute inflammation, liver, pathophysiology, hepatocyte, Kupffer cells, sinusoidal endothelial cells, microcirculation, cytokines, inflammatory mediators, TNF-α, IL-1β, IL-6, IL-10, TGF-β, oxidative stress, reactive oxygen species (ROS), antioxidant system, glutathione (GSH), superoxide dismutase (SOD), catalase, glutathione peroxidase (GPx), lipid peroxidation, mitochondrial dysfunction, liver injury, apoptosis, necrosis, regeneration, immune response, liver function, clinical biomarkers, therapeutic approaches

Introduction

Acute inflammation is a universal defensive and adaptive response of the body to infectious, traumatic, toxic, or ischemic insults. This process develops rapidly and involves complex pathophysiological mechanisms at both local and systemic levels. During inflammation, biologically active substances such as cytokines, chemokines, prostaglandins, leukotrienes, and reactive oxygen species (ROS) are released, exerting significant effects on various organs, particularly metabolically active organs like the liver.

The liver plays a central role in maintaining homeostasis through its metabolic, immunological, and detoxification functions. It participates actively in neutralizing inflammatory mediators, metabolizing endotoxins, synthesizing acute-phase proteins, and regulating energy metabolism. Therefore, during acute inflammation, the liver acts not only as a target organ but also as an active regulator of the inflammatory response.

In clinical practice, pathophysiological changes in the liver during sepsis, severe infections, polytrauma, burns, and shock are critical determinants of patient prognosis. Reduced liver functional reserves can exacerbate multi-organ failure, coagulopathy, metabolic acidosis, and intoxication syndromes. Hence, a deep understanding of hepatic pathophysiological processes during acute inflammation is essential for improving diagnostics and therapeutic strategies.

This review aims to systematically analyze hepatocellular, hemodynamic, metabolic, and molecular pathophysiological changes in the liver during acute inflammation, assess their clinical significance, and provide practical insights for medical practice.

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Liver Function in Acute Inflammation

As the central metabolic, detoxifying, and immunological organ, the liver performs several critical functions during acute inflammation:

1. Metabolic Regulation: The liver mobilizes glycogen stores, regulates glucose, lipid, and protein metabolism, and meets increased energy demands. Amino acid metabolism, protein synthesis, and degradation are altered, and ATP levels are closely monitored.

2. Detoxification: Hepatocytes filter and inactivate toxins, cytokines, and endogenous metabolites, primarily through metabolic enzymes and the cytochrome P450 system, protecting the body from systemic injury and sepsis.

3. Hepatocyte and Sinusoidal Endothelial Cell Activity: Hepatocytes produce and release inflammatory mediators into the circulation, while Kupffer cells perform phagocytosis and immune modulation. Sinusoidal endothelial cells regulate blood flow and maintain microcirculation.

4. Hemostasis and Bile Synthesis: The liver synthesizes coagulation factors (I, II, V, VII, IX, X) and bile, which aid lipid and toxin excretion. Disruptions can lead to cholestasis and coagulation abnormalities.

5. Immune Regulation: Hepatic immune cells (Kupffer cells, sinusoidal endothelial cells, lymphoid cells) modulate systemic inflammatory responses. Mediators and cells distributed through the liver influence systemic inflammation, contributing to sepsis and multi-organ dysfunction.

6. Regeneration and Repair: Hepatocyte proliferation and apoptosis are balanced to maintain liver mass and function, supported by growth factors and cytokines.

Thus, the liver acts not only as a passive organ but also as an active regulator, detoxifier, immunomodulator, and supporter of regeneration during acute inflammation. Regular monitoring of liver function is therefore crucial in clinical practice.

Microcirculatory Disturbances

Acute inflammation induces complex microcirculatory disturbances in the liver. Inflammatory mediators cause sinusoidal capillary dilation, endothelial injury, and increased permeability. This slows blood flow, induces hypoxia, and compromises hepatocyte energy metabolism.

International studies indicate that microcirculatory dysfunction is a central factor in liver injury and systemic inflammation (Bernal & Wendon, 2013; Tilg & Moschen, 2010). Dysfunctional sinusoidal endothelium promotes platelet and neutrophil adhesion, microthrombosis, and secondary parenchymal injury.

Observations from Uzbekistan (O‘zbekiston Respublikasi Tibbiyot jurnali, 2021) show that microcirculatory disturbances in acute infectious and traumatic diseases correlate with elevated liver enzymes (ALT, AST, LDH). Experimental models demonstrate that reduced sinusoidal blood flow and oxygen tension impair hepatocyte metabolism and lower ATP levels. Cytokines such as TNF-α and IL-1β increase capillary permeability and microthrombosis, enhancing hypoxia-induced hepatocyte apoptosis.

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Hence, microcirculatory disturbances are considered a primary and central mechanism of liver injury during acute inflammation, emphasizing the importance of monitoring liver function and managing inflammatory processes.

Mechanisms of Hepatocyte Injury

Hepatocyte injury during acute inflammation is mediated by several pathogenic mechanisms: hypoxia, ROS generation, mitochondrial dysfunction, and lipid peroxidation (Arthur, 2015; Jalan, 2012). Experimental models show decreased ATP synthesis, calcium homeostasis disruption, and activation of apoptotic pathways.

Cytokines (TNF-α, IL-1β) activate NF-κB and MAPK signaling in hepatocytes, promoting inflammation and apoptosis. Uzbek studies report a correlation between apoptotic markers and oxidative stress in acute infectious hepatitis (Toshkent Tibbiyot Jurnali, 2020).

Microcirculatory impairment and metabolic insufficiency increase ROS production, leading to lipid peroxidation, membrane damage, and elevated plasma levels of ALT, AST, and LDH—key diagnostic biomarkers.Understanding these multi-step hepatocyte injury mechanisms is vital for early detection and therapeutic intervention in clinical practice.

Cytokine and Inflammatory Mediator Imbalance

Disruption of the balance between pro- and anti-inflammatory cytokines is central to liver dysfunction. TNF-α, IL-1β, and IL-6 from Kupffer cells and hepatocytes promote parenchymal injury, activating NF-κB and MAPK pathways (Tilg & Moschen, 2010; Bernal & Wendon, 2013).

Experimental and clinical studies show sharp increases in IL-6 and TNF-α during acute inflammation, correlating with elevated liver enzymes. Cytokine imbalance also promotes endothelial, platelet, and neutrophil adhesion, microthrombosis, and microcirculatory disruption. Anti-inflammatory mediators (IL-10, TGF-β) insufficiency exacerbates systemic inflammation and delays hepatocyte regeneration.

Thus, cytokine and mediator imbalance is a key molecular mechanism underlying hepatic injury and functional impairment, highlighting the importance of monitoring cytokine levels and therapeutic targeting.

Oxidative Stress and Antioxidant System

Acute inflammation significantly increases ROS production in hepatocytes, Kupffer cells, and sinusoidal endothelial cells (Arthur, 2015; Jalan, 2012). ROS promote lipid peroxidation, protein oxidation, DNA damage, and mitochondrial dysfunction.

Key antioxidant components:

Glutathione (GSH): Reduces lipid peroxidation and protects membranes; levels decrease during acute inflammation.

Superoxide Dismutase (SOD): Converts superoxide radicals to hydrogen peroxide.

Catalase: Decomposes hydrogen peroxide to water and oxygen.

Glutathione Peroxidase (GPx): Reduces lipid peroxides.

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Vitamins and Polyphenols: Neutralize ROS and inhibit lipid peroxidation.

Uzbek studies show decreased GSH, SOD, and catalase activity correlating with hepatic injury (Toshkent Tibbiyot Jurnali, 2020). International data confirm that antioxidant therapies (e.g., N-acetylcysteine, SOD mimetics) reduce liver injury during acute inflammation (Hepatology, 2018).

Macroscopic and Microscopic Changes in the Liver

During acute inflammation, liver enlargement (hepatomegaly) occurs due to hyperemia, sinusoidal dilation, and interstitial edema. The liver capsule may appear tense and smooth; color ranges from dark red to reddish-brown. Severe cases (e.g., sepsis, toxic injury, viral hepatitis) show hemorrhagic foci, necrotic zones, and dystrophic changes.

Microscopically, sinusoidal dilation and blood cell accumulation are observed. Endothelial injury causes hypoxia and hepatocyte stress. Hepatocytes show vacuolation, hydropic and fatty degeneration, mitochondrial swelling, and crystal breakdown. Severe injury leads to apoptosis, coagulative or colliquative necrosis. Inflammatory infiltrates consist of Kupffer cells, monocytes, neutrophils, and lymphocytes surrounding portal tracts and sinusoids. Kupffer cell activation releases TNF-α, IL-1β, and other pro-inflammatory cytokines, aggravating hepatocyte injury. Some studies report bile canaliculi dilation, cholestasis, and intracellular bile pigment accumulation.

Clinical and Therapeutic Implications

The balance between ROS and the antioxidant system determines liver injury and regenerative capacity. Adequate antioxidant activity protects hepatocytes, reduces lipid peroxidation, and maintains function. Antioxidant therapy is therefore a promising strategy in systemic inflammation and sepsis.

Conclusion

Acute inflammation induces complex hepatic pathophysiological changes, including microcirculatory disturbances, hepatocyte injury, cytokine and mediator imbalance, oxidative stress, and insufficient antioxidant activity. The equilibrium of pro- and anti-inflammatory cytokines regulates liver function and injury severity. ROS generation, lipid peroxidation, and mitochondrial dysfunction promote apoptosis and necrosis, slowing regeneration. Sufficient antioxidant activity protects cells and mitigates liver injury.

Domestic and international research consistently demonstrates that understanding hepatic pathophysiology, monitoring cytokines, and assessing antioxidant status are crucial for early diagnosis, prevention, and effective therapeutic interventions. Future studies targeting hepatic injury mechanisms may provide novel strategies for prevention and treatment of liver pathology.

References

1. Arthur M.J. Inflammation and liver injury. Journal of Hepatology, 2015.

2. Bernal W., Wendon J. Acute liver failure. Lancet, 2013.

3. Tilg H., Moschen A. Cytokines in liver inflammation. Hepatology, 2010.

4. Jalan R. Pathophysiology of acute liver dysfunction. Liver International, 2012.

5. O‘zbekiston Respublikasi Tibbiyot Jurnali, 2020.

pISSN:2349-5707 Volume:13,Issue 3, March -2026 eISSN:2349-5715

6. Toshkent Tibbiyot Jurnali, 2020.

7. Hepatology, 2018.

8. Abdelmegeed M.A., et al. Free Radical Biology & Medicine, 2017.

9. Lemasters J.J. Hepatology, 2014.

10. Gao B., Tsukamoto H. Gastroenterology, 2016.

11. Kisseleva T., Brenner D.A. Nat Rev Gastroenterol Hepatol, 2020.

12. Malhi H., Gores G.J. Gastroenterology, 2008.

13. Jaeschke H., et al. Toxicological Sciences, 2012.

14. O'Brien A.J., et al. Hepatology, 2015.

15. Wang H., et al. Journal of Hepatology, 2018.

16. Young-Su Yi. Int. J. Mol. Sci., 2024.

17. Burns & Trauma, Oxford Academic.

18. Journal of Translational Medicine.

19. Georgetown Medical Review.