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CLINICAL ASPECTS OF ENDOGENOUS INTOXICATION IN VIRAL HEPATITIS C

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Relevance: Viral hepatitis C (HCV) remains a critical global health challenge, affecting over 58 million people worldwide according to recent WHO estimates. Chronic hepatitis C is often asymptomatic in its early stages but can progress to cirrhosis and hepatocellular carcinoma if left untreated. One of the key pathophysiological features is the phenomenon of endogenous intoxication — the accumulation of toxic metabolites resulting from impaired liver function and ongoing inflammatory processes. Monitoring and managing endogenous intoxication in HCV patients is essential for slowing disease progression, improving quality of life, and ultimately reducing the overall burden of chronic liver disease.

Keywords: Viral hepatitis C (HCV), Endogenous intoxication, Hepatocellular damage, Inflammatory markers, Liver function, Cytokines, Oxidative stress

INTRODUCTION

Hepatitis C virus (HCV) primarily targets hepatocytes, leading to chronic liver inflammation, fibrosis, and cirrhosis over time. The pathogenesis of HCV-induced liver injury involves both direct viral replication within hepatocytes and immune-mediated damage. Endogenous intoxication refers to the buildup of a wide range of toxic byproducts (e.g., bilirubin, ammonia, reactive oxygen species) and pro-inflammatory mediators that accumulate due to impaired liver detoxification and ongoing inflammatory responses.

These toxic compounds can further aggravate liver injury, induce oxidative stress, and disrupt metabolic pathways. Consequently, the degree of endogenous intoxication is not only a reflection of the severity of hepatic dysfunction but also a contributor to disease progression. A better understanding of the clinical aspects of endogenous intoxication in HCV can guide therapeutic decision-making, including antiviral therapy, antioxidant strategies, and supportive measures to preserve liver function.

Objectives - To evaluate the clinical manifestation of endogenous intoxication in patients with chronic HCV infection.

To analyze the correlation between serum markers of endogenous intoxication and disease severity.

To assess the impact of antiviral therapy on the dynamics of endogenous intoxication markers.

MATERIALS AND METHODS

Study Design and Population - A prospective, observational study was conducted at the Department of Infectious Diseases in a tertiary care hospital. Patients diagnosed with chronic hepatitis C, confirmed

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by the presence of anti-HCV antibodies and HCV RNA (by PCR), were enrolled between January 2023 and December 2024.

Inclusion Criteria: Age ≥ 18 years; Positive HCV serology (anti-HCV) and detectable HCV RNA; No evidence of co-infection with hepatitis B virus (HBV) or HIV; Informed consent provided

Exclusion Criteria: Pregnant or lactating women; Patients with decompensated liver cirrhosis (Child-Pugh C); Patients with active substance abuse or severe comorbid conditions (e.g., congestive heart failure, advanced renal disease).

Data Collection - Clinical Assessment: A thorough history (symptoms such as fatigue, right upper quadrant discomfort, and any signs of encephalopathy), physical examination (jaundice, hepatomegaly, splenomegaly), and demographic information were recorded.

Laboratory Investigations: Complete blood count (CBC); Liver function tests (ALT, AST, ALP, GGT, bilirubin); Coagulation profile (PT, INR); Albumin, total protein.

Serum markers of endogenous intoxication, including medium-weight molecules (MWM) measured by spectrophotometric methods, ammonia levels, and lactate. Inflammatory and oxidative stress markers (e.g., CRP, TNF-α, IL-6, and malondialdehyde [MDA]).

Imaging: Abdominal ultrasound to assess liver structure, portal vein diameter, and the presence of splenomegaly or ascites.

Histopathology (if indicated): Liver biopsy or non-invasive fibrosis assessment (e.g., FibroScan) was performed to stage liver fibrosis.

Treatment and Follow-up - Antiviral Therapy: Eligible patients received direct-acting antiviral (DAA) regimens according to national guidelines (e.g., sofosbuvir/velpatasvir), with treatment duration ranging from 8 to 12 weeks based on baseline viral load and fibrosis stage.

Supportive Therapy: Patients with elevated ammonia or clinical signs of encephalopathy received lactulose or rifaximin. Those with high oxidative stress markers were advised antioxidant supplementation (vitamin E, silymarin) as per physician discretion.

Follow-up: Patients were monitored monthly during antiviral therapy and at 12 weeks post-treatment for: Clinical evaluation and side effects; Laboratory tests to measure changes in endogenous intoxication markers; HCV RNA to determine virological response.

Statistical Analysis - All data were compiled and analyzed using SPSS software (version 26.0). Descriptive statistics (mean, standard deviation) were calculated for quantitative variables, and frequencies for categorical variables. Correlation analyses (Pearson or Spearman) were used to evaluate the relationship between endogenous intoxication markers and disease severity indicators. A p-value < 0.05 was considered statistically significant.

ANALYSIS AND RESULTS

Patient Demographics and Clinical Profile - Sample Size: 120 patients with chronic hepatitis C (60 males and 60 females). Mean Age: 42.5 ± 10.2 years. Clinical Staging: Based on non-invasive fibrosis scores (FibroScan), 40% of patients were at F2, 35% at F3, and 25% had compensated cirrhosis (F4, Child-Pugh A/B).

Endogenous Intoxication Markers - Medium-Weight Molecules (MWM): Serum MWM concentrations were significantly elevated in patients with advanced fibrosis (F3/F4) compared to

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those in earlier stages (F2). Mean MWM levels in F4 patients were 0.85 ± 0.15 optical density units, vs. 0.62 ± 0.10 in F2 patients ($p<0.01$).

Serum Ammonia: Elevated in 30% of the total cohort, with notable increases in those exhibiting mild encephalopathy. The mean ammonia level in patients with hepatic encephalopathy was 85 ± 10 µg/dL compared to 55 ± 8 µg/dL in those without encephalopathy ($p<0.01$).

Oxidative Stress Markers: Malondialdehyde (MDA) and inflammatory cytokines (TNF-α, IL-6) were significantly higher in advanced fibrosis stages, indicating ongoing oxidative and inflammatory stress.

Correlation with Liver Damage Indicators - A strong positive correlation ($r=0.72$; $p<0.001$) was observed between MWM levels and ALT, suggesting that rising transaminases parallel an increase in endogenous intoxication.

Serum ammonia showed a moderate correlation ($r=0.55$; $p<0.05$) with bilirubin, underscoring the link between reduced liver clearance capacity and the accumulation of toxic metabolites.

Impact of Antiviral Therapy - Virological Response: Among patients who completed DAA therapy, 90% achieved a sustained virological response (SVR12).

Improvement in Intoxication Markers: SVR12 was associated with a significant reduction in MWM (mean post-treatment level: 0.50 ± 0.08 optical density units) and inflammatory cytokines (TNF-α and IL-6). Serum ammonia levels also decreased in 70% of patients who had been elevated at baseline.

Clinical Outcomes. Patients with marked improvement in endogenous intoxication markers reported fewer symptoms (fatigue, malaise) and improved laboratory parameters (lower bilirubin, decreased ALT/AST).

Those with persistent elevated markers post-therapy often had higher fibrosis scores (F3/F4), suggesting that advanced structural liver damage could limit the extent of metabolic recovery even after viral clearance.

CONCLUSION

Endogenous intoxication is a significant clinical issue in viral hepatitis C, reflecting both the extent of liver injury and the potential for ongoing tissue damage. Elevated levels of toxic metabolites and inflammatory mediators correlate with disease severity, particularly in advanced fibrosis and compensated cirrhosis. Successful antiviral therapy can substantially reduce these markers, indicating that viral eradication helps restore metabolic balance and mitigate intoxication.

RECOMMENDATIONS

Early Diagnosis and Fibrosis Assessment: Implement routine screening for endogenous intoxication markers in patients with HCV, particularly to identify those at higher risk of rapid disease progression.

Comprehensive Monitoring: Track inflammatory and oxidative stress indicators (e.g., MDA, TNF-α, IL-6) alongside standard liver function tests to gain deeper insight into disease activity and response to therapy.

Prompt Antiviral Treatment: Offer direct-acting antiviral (DAA) regimens early to prevent disease progression and reduce the burden of endogenous intoxication, aiming for an SVR in all eligible patients.

Adjunctive Therapies: Consider the use of antioxidants and ammonia-lowering agents (lactulose, rifaximin) in patients with significant oxidative stress or signs of hepatic encephalopathy.

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Lifestyle and Dietary Interventions: Advise patients on balanced nutrition, limiting alcohol, and avoiding hepatotoxic substances to support liver health and reduce additional sources of toxic metabolites.

Long-Term Follow-up: Continue monitoring even after achieving SVR to evaluate the long-term resolution of endogenous intoxication and to manage residual fibrosis-related complications.

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