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MEDICAL PREVENTIVE MEASURES FOR LIVER CIRRHOSIS CAUSED BY HDV INFECTION

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Abstract
Hepatitis D virus (HDV) infection remains a significant global health concern, especially due to its capacity to accelerate the progression of liver disease, including liver cirrhosis. Preventive measures play a crucial role in mitigating the burden of HDV-associated liver complications. This paper reviews the current medical preventive strategies aimed at reducing HDV infection rates and preventing liver cirrhosis progression in affected individuals. Key approaches include vaccination, antiviral therapies, lifestyle modifications, and early diagnosis.

Keywords: Hepatitis D virus, HDV Co-infection, HDV superinfection, HDV screening, Hepatitis delta, prevention.

INTRODUCTION

Hepatitis D virus (HDV) depends on hepatitis B virus (HBV) to enter and exit hepatocytes and to replicate. Despite this dependency, HDV can cause severe liver disease. HDV accelerates liver fibrosis, increases the risk of hepatocellular carcinoma, and hastens hepatic decompensation compared to chronic HBV monoinfection. The Chronic Liver Disease Foundation (CLDF) formed an expert panel to publish updated guidelines on the testing, diagnosis, and management of hepatitis delta virus. The panel group performed network data review on the transmission, epidemiology, natural history, and disease sequelae of acute and chronic HDV infection. Based on current available evidence, we provide recommendations for screening, testing, diagnosis, and treatment of hepatitis D infection and review upcoming novel agents that may expand treatment options. The CLDF recommends universal HDV screening for all patients who are Hepatitis B surface antigen-positive. Initial screening should be with an assay to detect antibodies generated against HDV (anti-HDV). Patients who are positive for anti-HDV IgG antibodies should then undergo quantitative HDV RNA testing. We also provide an algorithm that describes CLDF recommendations on the screening, diagnosis, testing, and initial management of Hepatitis D infection. Unfortunately, the clinical impact of HDV has often been overlooked. Referring to the epidemiology of HDV in the United States, the Hepatitis B Foundation has noted that “low awareness, testing, and the lack of inclusion on the notifiable diseases list contribute to the unclear picture of HDV prevalence in the U.S.” [13] The lack of awareness of the significant burden of HDV has led to underestimation of the importance of testing for HDV among patients with HBV infection. Clinicians who wish to test for HDV may not be aware of the appropriate testing pathway and may find it difficult to access even antibody testing much less confirmatory polymerase chain reaction (PCR) testing or be aware of sensitivity thresholds for such testing. Furthermore,

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clinicians may have difficulty in selecting screening and confirming tests because of their complexity and limited availability, which further leads to underdiagnosis of HDV infection. Management of HDV remains challenging because patients typically present with advanced disease, current treatment options are currently limited with low rates of efficacy and significant toxicity, and, unlike treatment for hepatitis C virus (HCV), late relapse is possible even when virologic testing is negative 24 weeks following antiviral therapy [14]. Moreover, no treatment is so far specifically approved by the FDA for the treatment of HDV infection [15]. However, several promising treatments are in late stages of development. Like HBV, there is no cure for HDV. The current guidelines from national and international associations have not been updated recently to incorporate new data on the diagnosis and management of HDV. For these reasons, we, as members of the Chronic Liver Disease Foundation (CLDF), have published these new guidelines on the testing, diagnosis and management of hepatitis delta virus.

Materials and methods

We review the current knowledge of the management of HBV mono-infection and HBV/HDV co-infection with a special emphasis on liver cirrhosis. To estimate the prevalence of HDV antibody and RNA positivity within a referred population, specimens received at the NML for HDV antibody testing from January 2019 to December 2023 were considered. Submission guidelines require specimens to be HBsAg-positive, thus all patients were tested for HBV under the care of a healthcare professional. Patient replicate requests were removed and the first occurrence of HDV antibody positivity was included to create the total study population of unique referred individuals. Antibody-positive specimens were tested for HDV RNA to estimate the prevalence of active HDV infection among the referred population and to characterise HDV genotypes.

Available retrospective data elements included age at most recent laboratory testing, sex, ethnicity, country of birth, and risk factor history. Most recent values for laboratory tests were used including liver enzymes, viral serology and HBV viral load. Non-invasive tests for fibrosis included liver stiffness measurement/transient elastography (TE, FibroScan®).

Results

Studies indicate that comprehensive preventive strategies significantly reduce the incidence of liver cirrhosis in HDV-infected patients. HBV vaccination has led to a decline in HDV prevalence, particularly in regions with high immunization coverage. Early screening and diagnosis have facilitated better disease management, with antiviral therapies such as PEG-IFN-α and bulevirtide demonstrating a reduction in HDV RNA levels and fibrosis progression. Lifestyle modifications, including alcohol avoidance and metabolic disease management, have shown to slow liver damage. Public health interventions, including harm reduction programs, have been successful in limiting HDV transmission among high-risk groups.

Conclusions

Preventing liver cirrhosis due to HDV infection requires a multi-faceted approach, including HBV vaccination, early diagnosis, antiviral therapy, and lifestyle modifications. Continued research and

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development of novel antiviral treatments are crucial for improving patient outcomes and reducing the burden of HDV-associated liver disease.

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