The Hepatopathogenesis of Hepatitis E Virus Genotype 3

Mohammad Khalid Parvez1

1 Department of Pharmacognosy, King Saud University College of Pharmacy, Riyadh 11451, Saudi Arabia.

Conflict-of-interest statement: The authors declare that there is no conflict of interest regarding the publication of this paper.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

Correspondence to: Mohammad Khalid Parvez, PhD, Associate Professor, Department of Pharmacognosy, King Saud University College of Pharmacy, P.O. Box 2457, Riyadh 11451, Saudi Arabia. Email: khalid_parvez@yahoo.com. Telephone: +966-14675132. Fax: +966-14677245

Received: April 3, 2019
Revised: May 7, 2019
Accepted: May 10, 2019
Published online: June 21, 2019

ABSTRACT

Of the zoonotic genotypes of hepatitis E virus, the genotype 3 (HEV3) has emerged as the most pathogenic strain causing chronic hepatitis in immunosuppressed patients in industrialized nations. The epidemiology of HEV3 is rather complex because of its hitherto well recognized sources and routes of transmission. Currently, ribavirin is the only effective drug that however, induces mutations in viral polymerase gene leading to drug-resistance or -nonresponse, and teratogenic effects in pregnant women.

Key words: Hepatitis E virus; HEV3; Chronic hepatitis E; Zoonosis; Foodborne hepatitis E

© 2019 The Author(s). Published by ACT Publishing Group Ltd. All rights reserved.
trials. Recently, HEV3 has emerged as the most pathogenic strain to cause chronic hepatitis and liver cirrhosis in immunosuppressed, transplant and transfusion patients in Europe, North America and Japan (10,11). Chemotherapy with immunosuppressive drugs (eg. tacrolimus or FK-506) is considered as the main predictive factor for the development of chronicity where sub-optimal or impaired adaptive immune responses may be a potential reason (11).

HEV3 GENETIC VARIANTS

According to the latest classification, 10 designated subtypes of HEV (HEV3a-HEV3j) and 7 unassigned subtypes are proposed (12,13). Increased virulence associated with HEV3i, HEV3j and HEV3o strains are reported from patients with severe hepatitis in Japan (13). Complete sequencing of HEV3 RNA from acute, fulminant, and chronic patients as well as farmed pigs and wild boar have revealed genetic diversity suggesting its cross-species or host adaptations (12,13).

HEV3 AND PREGNANCY

Pregnant women with acute hepatitis E are at higher risk of morbidity and death than those with chronic hepatitis. Hepatitis E in pregnancy can take a fulminant course, resulting in fulminant hepatic failure, membrane rupture, spontaneous abortions, and stillbirths. Compared to HEV1, there are very few reported cases of HEV3 infection during pregnancy in industrialized countries (20-23). Very recently, cases of HEV3 infections acquired during pregnancy in immunocompetent French women who neither travelled abroad nor consumed raw or undercooked pork are reported (24). Though persistence of HEV has not been reported among patients treated with infliximab or azathioprine, it is observed in a patient receiving azathioprine and oral steroids (25). In another case report of a pregnant woman with chronic hepatitis E who received infliximab and azathioprine without adverse event, spontaneously resolved after delivery (26).

CURRENT TREATMENT AND LIMITATIONS

There is an effective HEV vaccine (HEV239 or Hecolin) available in China that is however, still inaccessible to other countries, including the USA and Europe (27). Ribavirin (RBV) is the only effective treatment of choice in HEV3 infected patients. Although, RBV clears the virus and induces a sustained virological response, emergence of HEV polymerase gene mutants (eg. G1634R/K) lead to drug-resistance or nonresponse to therapy (28,29). Further therapeutic limits of RBV include its teratogenic effects in pregnant women, potential to cause hemolytic anemia, dyspnea, insomnia and irritability (30).

CONCLUSION AND FUTURE PERSPECTIVES

HEV3 has recently evolved as the most pathogenic anthropozoonotic strain causing chronic hepatitis in immunosuppressed population in industrialized nations. Owing to limits of antiviral drugs, prevention of HEV3 relies primarily on avoiding undercooked pork and other products. Pregnant women with liver symptoms should be immediately hospitalized and diagnosed and planned for HEV. In cases of acute liver failure, urgent liver transplant can be a lifesaving option.

REFERENCES

14. Smith DB, Simmonds P, Iozzi J, Oliveira-Filho EF, Ulrich RG,


