Study of hepatitis E virus infection of genotype 1 and 3 in mice with humanised liver


Abstract:

ABSTRACT Objective The hepatitis E virus (HEV) is responsible for approximately 20 million infections per year worldwide. Although most infected people can spontaneously clear an HEV infection, immune-compromised individuals may evolve towards chronicity. Chronic HEV infection can be cured using ribavirin, but viral isolates with low ribavirin sensitivity have recently been identified. Although some HEV isolates can be cultured in vitro, in vivo studies are essentially limited to primates and pigs. Since the use of these animals is hampered by financial, practical and/or ethical concerns, we evaluated if human liver chimeric mice could serve as an alternative. Design Humanised mice were inoculated with different HEV-containing preparations. Results Chronic HEV infection was observed after intrasplenic injection of cell culture-derived HEV, a filtered chimpanzee stool suspension and a patient-derived stool suspension. The viral load was significantly higher in the stool compared with the plasma. Overall, the viral titre in genotype 3-infected mice was lower than that in genotype 1-infected mice. Analysis of liver tissue of infected mice showed the presence of viral RNA and protein, and alterations in host gene expression. Intrasplenic injection of HEV-positive patient plasma and oral inoculation of filtered stool suspensions did not result in robust infection. Finally, we validated our model for the evaluation of novel antiviral compounds against HEV using ribavirin. Conclusions Human liver chimeric mice can be infected with HEV of different genotypes. This small animal model will be a valuable tool for the in vivo study of HEV infection and the evaluation of novel antiviral molecules

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