

Hepatitis E Virus and Renal Transplantation

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ARTICLE INFO

Article Type: Editorial

Article history: Received: 17 Aug 2011 Revised: 20 Aug 2011 Accepted: 24 Aug 2011

Keywords: Hepatitis E virus Renal transplantation • Implication for health policy/practice/research/medical education:

Hepatitis E is a significant health concern in endemic area. During graft transplantation it can affect the recovery process and may increase chronicity. This study is recommended to the internal and infectious specialists, graft transplantation surgeons and virologists.

▶ Please cite this paper as:

Hosseini Moghaddam SM. Hepatitis E Virus and RenalTransplantation. *Hepat Mon.* 2011;**11**(8):599-600.

[DOI: 10.5812/kowsar.1735143X.770]

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Sepehrvand et al. demonstrated a considerable seroprevalence rate of anti-HEV in Iranian kidney transplant recipients (1). The impact of HEV infection on renal transplantation and the risk of chronic HEV infection in this group are debated-issues that I would like to discuss. Hepatitis E virus (HEV) was first discovered in New Delhi, India, in 1955 (2). The virus is transmitted via the oral-fecal route (3). Other possible routes of transmission include blood transfusions, drug vertical transmission, person-to-person contact, and zoonotic transmission (4, 5). The frequency of HEV transmission by non-fecal-oral routes remains unknown (2, 6). In endemic areas, exposure occurs in childhood (7, 8). In high-income countries, most cases of hepatitis E appear to be acquired locally and are not imported from endemic regions. In these areas, it likely has a zoonotic origin (9). In immunocompetent individuals, hepatitis E is a self-limited disease. However, HEV can cause chronic infection in solid organ transplants (10, 11), patients who receive chemotherapy (12), and HIV-infected persons (13). HEV infection causes chronic hepatitis in more than

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DOI: 10.5812/kowsar.1735143X.770

60% of recipients of solid organ transplants. Factors that increase the risk of chronic hepatitis in solid organ transplant recipients are shorter interval since the transplant, lower levels of liver enzymes and serum creatinine, lower platelet counts, and tacrolimus-based immunosuppression (compared with cyclosporin A), the most significant of which are tacrolimus use and low platelet count (11, 14, 15).

In otherwise healthy kidney transplant recipients, HEV might be considered the etiological agent for the development of hepatitis in those who live in endemic regions (16). Viral hepatitis E may progress rapidly to cirrhosis in renal transplant recipients (17). Although occult infection of HEV may be transferred to the recipient via liver graft (18), other allograft organs appear to be clear for transmission of the virus. As a result, screening for HEV at the time of transplantation is only recommended in liver transplant donors and recipients in endemic areas (19). Such a screen is not recommended for patients with renal failure who are waiting for renal transplantation. Rising liver enzyme levels is a nonspecific finding following solid organ transplantation. Renal transplant patients may experience such increases, due primarily to drug reactions, sepsis, and hepatotropic virus-related infectious diseases. The diagnosis of viral hepatitis E in renal transplant recipients is usually made by ELISA. In renal transplant recipients, the seroprevalence of anti-

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HEV IgG is 6% to 16% (10). Other immunocompromised hosts, such as patients with hematological malignancies, might avoid forming HEV IgG following an infection. Moreover, viremia may exist for more than 6 months after an acute infection (20). In addition, the development of HEV IgG in renal transplant patients does not appear to be universal. The presentation of chronic hepatitis in renal transplant patients may be associated with normal liver enzymes and a negative serological assay (21). This phenomenon underscores the need for molecular studies in suspected subjects.

Decreasing the numbers and doses of immunosuppressive drugs remains the first approach toward controlling viral hepatitis E in renal transplant recipients. A prolonged follow-up period might be required to assess the eventual outcome (14). In addition, pegylated interferon alpha-2b may be useful in the management of chronic HEV infections in solid organ recipientsinwhomareductionoftheimmunosuppressive regimen is insufficient (22). Interestingly, 3-month Peg- IFN- -2a therapy was shown to be efficacious in a hemodialysis patient with chronic HEV infection following renal transplantation (23). In 2010, the efficacy of ribavirin 12 mg/kg of body weight daily for 12 weeks was reported in kidney transplant patients with chronic HEV infection. However, due to the short term follow-up (3 months), eradication of the virus could not be claimed (24). In 2011, another report demonstrated that a 3-month course of oral ribavirin (17 mg/kg/day) in solid organ transplant patients with chronic HEV infection induced a sustained virological response for more than 4 months after cessation of ribavirin (25). A long follow-up is always required to evaluate the outcome of HEV infection in solid organ transplant patients. HEV infection may cause cirrhosis in renal transplant individuals. As a result, close follow-up is required after the diagnosis. In addition, HEV infection may result in nonhepatic complications in kidney transplant recipients. Neurological diseases that affect the peripheral or central nervous system have been demonstrated in renal transplants with chronic HEV infection. Surprisingly, HEV was isolated from the cerebrospinal fluid in such patients (26).

Financial Disclosures

None declared.

References

- Sepehrvand N, Khameneh ZR, Masudi S. Seroprevalence of Hepatitis E among Iranian Renal Transplant Recipients. *Hepat* Mon. 2011;11(8):[Epub a head of print].
- Chandra V, Taneja S, Kalia M, Jameel S. Molecular biology and pathogenesis of hepatitis E virus. J Biosci. 2008;33(4):451-64.
- Ghorbani GA, Alavian SM, Esfahani AA, Assari S. Seroepidemiology of hepatitis E virus in Iranian soldiers. *Hepat Mon*. 2007;7(3):121-4.
- Somi MH, Farhang S, Majidi G, Shavakhi A, Pouri AA. Seroprevalence of hepatitis E in patients with chronic liver disease from East Azerbaijan, Iran. *Hepat Mon.* 2007;7(3):125-8.
- 5. Pourahmad M, Sotoodeh A, Nasiri H. Hepatitis E virus infection in hemodialysis patients: a seroepidemiological survey in

Jahrom, Southern Iran. Hepat Mon. 2009;9(3):232-5.

- Alavian SM. Hepatitis E Virus Infection: A Neglected Problem in Our Region. *Hepat Mon.* 2007;7(3):119-21.
- Shamsizadeh A, Nikfar R, Makvandi M, Shamsizadeh N. Seroprevalence of Hepatitis E Virus Infection in Children in the Southwest of Iran. *Hepat Mon.* 2009;9(4):261-4.
- Amarapurkar D, Agal S, Baijal R, Gupte P, Patel N, Kamani P, et al. Epidemiology of Hepatitis E Virus Infection in Western India. *Hepat Mon.* 2008;8(4):258-62.
- Pavio N, Mansuy JM. Hepatitis E in high-income countries. Curr Opin Infect Dis. 2010;23(5):521-7.
- 10. Kamar N, Selves J, Mansuy JM, Ouezzani L, Peron JM, Guitard J, et al. Hepatitis E virus and chronic hepatitis in organ-transplant recipients. *N Engl J Med.* 2008;**358**(8):811-7.
- Hosseini-Moghaddam SM, Zarei A, Alavian SM, Mansouri M. Hepatitis E virus infection: a general review with a focus on hemodialysis and kidney transplant patients. *Am J Nephrol.* 2010;31(5):398-407.
- 12. Ollier L, Tieulie N, Sanderson F, Heudier P, Giordanengo V, Fuzibet JG, et al. Chronic hepatitis after hepatitis E virus infection in a patient with non-Hodgkin lymphoma taking rituximab. *Ann Intern Med*. 2009;**150**(6):430.
- Dalton HR, Bendall RP, Keane FE, Tedder RS, Ijaz S. Persistent carriage of hepatitis E virus in patients with HIV infection. NEngl JMed. 2009;361(10):1025-7.
- 14. Kamar N, Garrouste C, Haagsma EB, Garrigue V, Pischke S, Chauvet C, et al. Factors associated with chronic hepatitis in patients with hepatitis E virus infection who have received solid organ transplants. *Gastroenterology*. 2011;**140**(5):1481-9.
- 15. Kamar N, Abravanel F, Selves J, Garrouste C, Esposito L, Lavayssiere L, et al. Influence of immunosuppressive therapy on the natural history of genotype 3 hepatitis-E virus infection after organ transplantation. *Transplantation*. 2010;**89**(3):353-60.
- 16. Kamar N, Mansuy JM, Esposito L, Legrand-Abravanel F, Peron JM, Durand D, et al. Acute hepatitis and renal function impairment related to infection by hepatitis E virus in a renal allograft recipient. Am J Kidney Dis. 2005;45(1):193-6.
- Kamar N, Mansuy JM, Cointault O, Selves J, Abravanel F, Danjoux M, et al. Hepatitis E Virus Related Cirrhosis in Kidney and Kidney-Pancreas Transplant Recipients. *Am J Transplant*. 2008;8(8):1744-8.
- Schlosser B, Stein A, Neuhaus R, Pahl S, Ramez B, Kruger DH, et al. Liver transplant from a donor with occult HEV infection induced chronic hepatitis and cirrhosis in the recipient. J Hepatol. 2011;[Epub ahead of print].
- Pischke S, Wedemeyer H. Chronic hepatitis E in liver transplant recipients: a significant clinical problem? *Minerva Gastroenterol Dietol.* 2010;56(2):121-8.
- 20. Tavitian S, Peron JM, Huynh A, Mansuy JM, Ysebaert L, Huguet F, et al. Hepatitis E virus excretion can be prolonged in patients with hematological malignancies. *J Clin Virol*. 2010;**49**(2):141-4.
- Gerolami R, Moal V, Colson P. Chronic hepatitis E with cirrhosis in a kidney-transplant recipient. N Engl J Med. 2008;358(8):859-60.
- Haagsma EB, Riezebos-Brilman A, van den Berg AP, Porte RJ, Niesters HG. Treatment of chronic hepatitis E in liver transplant recipients with pegylated interferon alpha-2b. *Liver Transpl.* 2010;16(4):474-7.
- Kamar N, Abravanel F, Garrouste C, Cardeau-Desangles I, Mansuy JM, Weclawiak H, et al. Three-month pegylated interferon-alpha-2a therapy for chronic hepatitis E virus infection in a haemodialysis patient. *Nephrol Dial Transplant*. 2010;25(8):2792-5.
- 24. Mallet V, Nicand E, Sultanik P, Chakvetadze C, Tesse S, Thervet E, et al. Brief communication: case reports of ribavirin treatment for chronic hepatitis E. *Ann Intern Med.* 2010;**153**(2):85-9.
- Chaillon A, Sirinelli A, De Muret A, Nicand E, d'Alteroche L, Goudeau A. Sustained virologic response with ribavirin in chronic hepatitis E virus infection in heart transplantation. J Heart Lung Transplant. 2011;30(7):841-3.
- Kamar N, Izopet J, Cintas P, Garrouste C, Uro-Coste E, Cointault O, et al. Hepatitis E virus-induced neurological symptoms in a kidney-transplant patient with chronic hepatitis. *AmJ Transplant*. 2010;**10**(5):1321-4.