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CORRESPONDENCE

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Hepatitis E virus infection in hemodialysis patients: A prospective analysis

To the Editor,

Hepatitis E virus (HEV) infection is a major cause of enterically transmitted hepatitis worldwide. While HEV typically causes an acute self-limited infection, genotypes 3 and 4 have been associated with chronic hepatitis in immunosuppressed individuals.[1,2] Several studies have shown that patients undergoing hemodialysis (HD) have a higher seroprevalence of HEV than the general population.[3-5] The dynamics of HEV infection in this population, such as the incidence of new and chronic infections as well as temporal variations in seropositivity, are poorly understood. To assess the dynamics of HEV infection in this population, we prospectively evaluated individuals with end-stage renal disease (ESRD) undergoing HD at a private hospital in Córdoba, Argentina, between November 2014 and November 2017.

Seventy-six individuals who were negative for anti-HEV IgG, IgM, and HEV RNA, were included in our analysis. Patients underwent reassessment for HEV every 6 months during different periods of time (30 patients underwent a total of 4 evaluations, up to 36 months), with a median follow-up period of 480 days (interquartile range: 365-1080 days). Detection of anti-HEV IgG and IgM was performed by ELISA (Dia.Pro, Italy). HEV RNA was amplified by RT-nested-PCR targeting ORF-2 genomic region.[6] Cumulative incidence was calculated to estimate the cumulative risk of HEV infection using the Fine and Gray's method. Transplantation, change to other HD center, or death were considered as a competing risk. Statistical analysis was performed using EZR (R version 2.13.0) statistical package. This study was approved by the Ethics Committee of Hospital Privado de Córdoba, according to the regulations of the Ministry of Health of the Province of Córdoba (protocol HP 4-231/14).

Among reevaluated individuals who were initially negative for anti-HEV IgG, IgM, and HEV RNA, 5 underwent seroconversion for specific IgG antibodies during the follow-up; the cumulative incidence was 9.6% (95% CI 3.4%-19.5%). Interestingly, of the 5 patients who underwent seroconversion, 3 reverted back to a negative anti-HEV IgG status at their subsequent serological reassessment ≥6 months later, 1 showed positivity for anti-HEV IgG in the last sample taken (therefore, is unclear if it maintained seropositivity over time), and only 1 remained seropositive throughout the course of the study. All samples, including those that were positive for anti-HEV IgG, were negative for anti-HEV IgM. No subjects tested positive for HEV RNA during the entire study period. None of the patients with HEV seropositivity reported symptoms of acute or chronic infection at any point in the study.

Our results demonstrate alternating seropositivity for HEV in our HD patient population. These findings suggest that either these patients cannot sustain immune-memory for HEV, that is, their immune system fails to express IgG specific for HEV, or that they do not produce high antibody titers, possibly due to ESRD-related deficiencies in humoral and cellular immunity.[3,7] None of the individuals with anti-HEV IgG seropositivity expressed anti-HEV IgM, and serological analyses were ≥6 months apart, suggesting that our HD patients experienced a rapid decline in IgM antibody titers or, as with IgG, that their immune response was suppressed to a point that anti-HEV IgM antibodies did not reach detectable levels. None of the patients showed evidence of chronic HEV infection, which is consistent with previous reports in other parts of the world.[8] No acute symptomatic infections were registered either.

This study highlights variations in HEV serological status in patients with ESRD undergoing HD. Larger studies are needed to confirm these results. However, until more evidence emerges about the course of HEV in these patients, caution should be used when evaluating these individuals for liver disease, as previous positivity for anti-HEV IgG may not indicate persistent immunity to the virus.

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