Detection of acute Hepatitis E and seroprevalences in Germany with new recomWell HEV in comparison to Wantai HEV

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Introduction

Being underdiagnosed for a long time, the Hepatitis E virus (HEV) is now known to be endemic in western countries due to zoonotic transmission, e.g., by raw meat. Seroprevalences in Europe can vary between 0.5% and 52%. Apart from geographic region and study cohort; the sensitivity of the used serological assay has an major impact on the seroprevalence data. In several European countries HEV was described as the most frequent viral cause for acute hepatitis. Furthermore, HEV is associated with several extrahepatic manifestations, like e.g. with neurological diseases. Besides viral RNA detection via PCR, the detection of specific IgM antibodies confirms an acute hepatitis infection. Mikrogen offers its improved versions of recomWell HEV IgG, IgM ELISA assays since 2015 as avenues for epidemiological studies and for acute hepatitis diagnostics. In this study the performance of the new recomWell HEV kits have been compared to Wantai HEV IgG, IgM, which is known for its high sensitivity. Both brands represent the two most commonly used commercial HEV ELISA assays in Europe.

Materials and Methods

In this evaluation recomWell HEV IgG, IgM (Mikrogen, Germany) and Wantai HEV IgG, IgM (via Axiom Diagnostics, Germany or Fortress diagnostics, UK) have been compared. In order to detect seroprevalences in Germany 200 sera from healthy blood donors (Bavarian Red Cross) have been analyzed with recomWell HEV IgG (new & previous version) and Wantai IgG.

Diagnostic sensitivity of recomWell HEV IgM (new version) and Wantai IgM was evaluated using 89 well-defined samples from patients with confirmed acute HEV infection (clinical signs, IgM and IgG positive reactivity confirmed with different ELISA assays). To examine antibody response and detection subsequent follow-up samples from one PCR positive blood donor have been analyzed with both ELISA IgM assays. Diagnostic specificity of recomWell HEV IgM (new version) and Wantai IgM was determined with a HEV seronegative panel consisting of 359 samples (200 sera from blood donors and 159 sera from patients with clinical suspicion of non-E-hepatitis confirmed as HIV, HCV, HAV, Parvovirus B19, EBV, or CMV positive).

Results

Analysis of 200 German blood donors results in similar HEV seroprevalences for recomWell IgG (33%) and Wantai IgG (32%). The clear improvement in sensitivity is demonstrated by the comparison of the present (33%) and previous version (18.5%) of recomWell HEV IgG.

With respect to diagnostic specificity both, recomWell IgG and Wantai IgG, demonstrated a very good and comparable performance (data not shown).

With 98.9% recomWell HEV IgM shows excellent diagnostic sensitivity. Only one serum from a total of 89 was not found positive, whereas Wantai HEV IgM missed 6 sera, reaching a sensitivity of 93.3% (Figure 3). Analysis of paired samples demonstrates that recomWell HEV IgM detects IgM specific antibodies over a long period starting at the end of the viremic phase. Interestingly, Wantai HEV IgM is not able to detect specific antibodies in any sample of this PCR positive patient. IgG seroconversion was confirmed (data not shown).

Both test systems, recomWell HEV IgM and Wantai HEV IgM, show a convincing specificity. Only 5 from 359 sera were found positive by each assays, resulting in a diagnostic specificity of 98.6%.

Conclusion

The new recomWell HEV IgG and IgM assays show an excellent and improved performance. The diagnostic sensitivity for IgG antibodies is similar to Wantai HEV IgG. The finding is also reflected by the determination of comparable seroprevalences (32/33%) for German blood donors. This diagnostic performance needs to be considered when looking at published comparative studies, where mainly the previous version of recomWell HEV IgG has been used (blood donor seroprevalence of around 18%).

Yielding a diagnostic sensitivity of 98.9% recomWell HEV IgM performs better compared to Wantai HEV IgM with 93.9%. Therefore, recomWell HEV IgM is highly suitable for the detection of acute Hepatitis E.