Detection of acute Hepatitis E and seroprevalences in Germany with new *recom*Well HEV in comparison to Wantai HEV

F. Struck, T. Lüttich, S. Schulz, E. Eyl, O. Böcher , E. Soutschek; Mikrogen GmbH, 82061 Neuried, Germany

MIKROGEN DIAGNOSTIK

Introduction

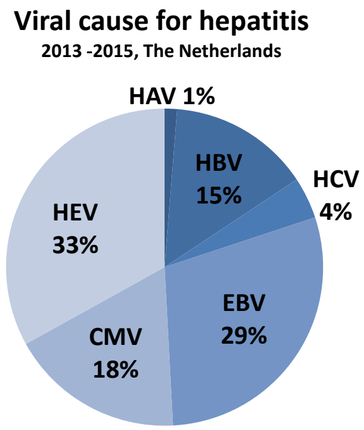

Figure 1: Distribution of viral causes for hepatitis in routine diagnostics, Doting *et al*, Clin Microbiol Infect. 2017

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 HEV infection.

Mikrogen offers its improved versions of *recom*Well 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 *recom*Well 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 *recom*Well 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 *recom*Well HEV IgG (new & previous version) and Wantai IgG.

Diagnostic sensitivity of *recom*Well 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 *recom*Well 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

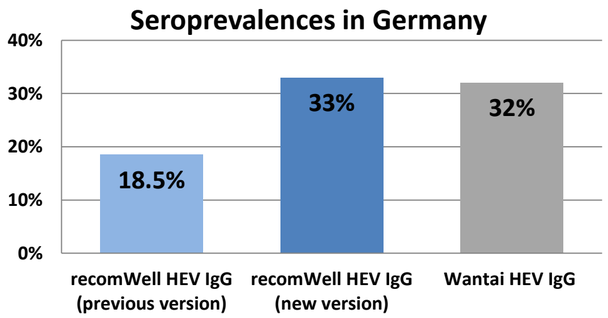

Figure 2: Seroprevalences in Germany (200 sera from healthy German blood donors)

Analysis of 200 German blood donors results in similar HEV seroprevalences for *recom*Well 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 *recom*Well HEV IgG.

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

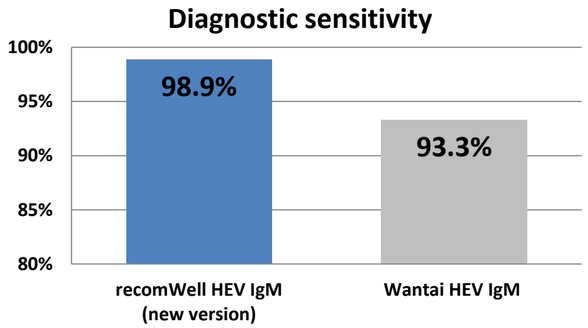

Figure 3: Diagnostic sensitivity of *recom*Well HEV IgM and Wantai HEV IgM (89 preselected sera representing acute HEV infections).

	PCR	*recom*Well HEV IgM (new)		Wantai HEV IgM	
Day	**RNA (IU/ml)**	**OD**	**Eval**	**OD**	**Eval**
0	299	0.071	neg	0.005	neg
6	1,250	0.075	neg	0.005	neg
21	6,650	0.081	neg	0.005	neg
28	47,400	0.068	neg	0.001	neg
42	144	1.155	pos	0.011	neg
48	neg	1.452	pos	0.023	neg
75	neg	1.392	pos	0.013	neg
91	n/a	4.304	pos	0.003	neg
98	n/a	1.026	pos	0.005	neg
104	n/a	0.988	pos	0.002	neg
111	n/a	0.856	pos	0.004	neg
117	neg	0.764	pos	0.002	neg

Table 1: Analysis of follow-up samples from one PCR positive blood donor with *recom*Well HEV IgM and Wantai HEV IgM. neg = negative, pos = positive, highlighted in blue, n/a = not examined

With 98.9% *recom*Well 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 *recom*Well 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).

Specimen characteristics	***recom*Well HEV IgM (new)**	**Wantai HEV IgM**
HIV IgG	0% (0/9)	0% (0/9)
HCV IgG	0% (0/10)	0% (0/10)
HAV IgM	0% (0/29)	0% (0/29)
Parvo B19 IgM	0% (0/30)	3.3% (1/30)
EBV IgM	3.8% (2/52)	3.8% (2/52)
CMV IgM	3.4% (1/29)	3.4% (1/29)
Blood donors	1% (2/200)	0.5% (1/200)
Specificity	**98.6% (5/359)**	**98.6% (5/359)**

Both test systems, *recom*Well 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%.

Table 2: Diagnostic specificity of *recom*Well HEV IgM and Wantai HEV IgM

Conclusion

The new *recom*Well 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 *recom*Well HEV IgG has been used (blood donor seroprevalence of around 18%).

Yielding a diagnostic sensitivity of 98.9% *recom*Well HEV IgM performs better compared to Wantai HEV IgM with 93.3%. Therefore, *recom*Well HEV IgM is highly suitable for the detection of acute Hepatitis E.

5th world congress on Hepatitis & Liver Diseases: August 10-12, 2017 London, UK