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Short communication

Performance of rapid diagnostic tests for the detection of anti-HBs in various patient populations

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ABSTRACT

Background: Rapid diagnostic tests (RDTs) represent an attractive alternative method to conventional diagnosis of hepatitis B virus (HBV) infection.
Objective: The aim of the present study was to evaluate the diagnostic performance of commercially available RDTs for the detection of anti-HBs in various patient populations.
Study design: A total of 347 individuals, 198 positive and 149 negative for anti-HBs, were studied.
Results: The specificity of RDT detection of anti-HBs in serum was 98.0%, 96.0% and 97.3% with TOYO® HBsAb Test, QuickProfile™ HBsAb test and QuickProfile™ HBV-3 Panel test, respectively. The diagnostic sensitivity varied between 60.4% and 69.5%. The sensitivity of the three RDTs was markedly better when testing serum samples with an anti-HBs titer higher than 100 IU/L, and reached 90% or more for an anti-HBs titer above 150 IU/L.
Conclusions: This performance was disappointing because the assays were not sensitive enough to detect low antibody titers. Thus, these tests require further improvement before they can be widely used in clinical practice.

1. Background

Hepatitis B virus (HBV) infection is a major cause of chronic liver disease that affects approximately 240 million people worldwide [1]. Each year, nearly 700,000 people die from HBV-related chronic liver disease through end-stage cirrhosis, liver failure or hepatocellular carcinoma [2]. Despite the availability of an effective vaccine against HBV and of potent and safe antiviral drugs, chronic hepatitis B remains a global health problem with its prevalence varying geographically. The World Health Organization (WHO) recommended that the first vaccine dose be administered in all infants as early as possible after birth. This measure resulted in a profound reduction of mother-to-infant HBV transmission in the regions where it was implemented. The vast majority of HBV-infected patients are unaware of their infection and related liver disease. In low- to middle-income areas, the vast majority of infected patients have not been diagnosed.

Hepatitis B surface antigen (HBsAg) is a key marker for screening and laboratory diagnosis of HBV infection. The presence of anti-HBs reveals both immunity associated with resolved infection and induced by vaccine. A number of rapid diagnostic tests (RDTs) have been developed for the detection of HBsAg. Most of these assays meet the WHO-recommended analytical sensitivity of 0.13 international units (IU)/L or 4 IU/L, depending on the targeted population [3]. However, in recent evaluations, the analytical sensitivity of individual RDTs varied widely, while the specificity of most of them appeared to be satisfactory [4,5]. RDTs for anti-HBs detection are currently used in some parts of the world and only one has received product license in Europe, but not in the US.

2. Objectives

The aim of the present study was to evaluate the diagnostic performance of commercially available RDTs for the detection of anti-HBs in various patient populations.

3. Study design

A total of 347 serum samples were obtained from anti-HBs positive

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(n = 198) and negative (n = 149) individuals with various conditions.

Group A was comprised of 231 subjects recruited in the Department of Hepatology of the Henri Mondor Hospital between September 2012 and November 2013 with various HBV serological profiles, HBV seronegative individuals (n = 73), HBsAg-positive patients (n = 14), subjects with isolated anti-HBc (n = 3), individuals with markers of resolved infection, characterized by the presence of both anti-HBc and anti-HBs (n = 28), and subjects with a vaccination profile, i.e. isolated anti-HBs (n = 114). Anti-HBs positive patients had various titers of anti-HBs. Among the patients from Group A, 52 were HCV-seropositive and all were HIV-seronegative.

Group B was comprised of 115 consecutive organ, tissue and cell donors tested for viral markers in the Viral Emergency and Organ, Tissue and Cell Donor Screening Laboratory of the Henri Mondor Hospital in 2008. They included HBV-seronegative individuals (n = 61), and subjects with markers of resolved infection (n = 8) or a vaccination profile (n = 46) with various titers of anti-HBs. All of them were HCV- and HIV-seronegative.

HBV markers (HBsAg, anti-HBc and anti-HBs) were systematically checked in blood samples by means of automated EIAs using the VITROS ECi/ECiQ immunodiagnostic system (Ortho-Clinical Diagnostics, Raritan, New Jersey). When anti-HBs titers were below 100 UI/L, another test, VIDAS® Anti-HBs Total II (bioMérieux, Marcy-l'Etoile, France) was used. The HCV and HIV statuses were determined by means of commercial EIAs (aHCV VITROS ECi™, Ortho-Clinical Diagnostics, and HIV Ag/Ab Combo, Abbott Diagnostics, Chicago, Illinois, respectively).

Three RDTs were tested for their ability to detect anti-HBs in serum. They were TOYO® Anti-HBs test (Türklab Medical Devices, Izmir, Turkey), which is CE-marked, QuickProfile™ HBsAb test (LumiQuick Diagnostics, Inc, Santa Clara, California), and QuickProfile™ HBV-3 Panel test (LumiQuick Diagnostics, Inc). The latter test allows for qualitative detection of HBsAg and total anti-HBc in addition to anti-HBs.

4. Results

As shown in Table 1, the three RDTs had a high specificity for the detection of anti-HBs, between 97.3% and 98.0%. Only three, six and four HBV-seronegative participants tested anti-HBs positive with the TOYO® Anti-HBs test, QuickProfile™ HBsAb test, and QuickProfile™ HBV-3 Panel test, respectively. The overall sensitivity, as compared to EIA, was low for the three RDTs used, regardless of the anti-HBs titers (range: 10 UI/L to more than 1000 UI/L): 60.4% for the TOYO® Anti-HBs test, 69.5% for the QuickProfile™ HBsAb test, and 65.5% for the QuickProfile™ HBV-3 Panel test. The positive and negative likelihood ratios of the three tested RDTs are shown in Table 1. Statistical analysis showed no significant difference between performance of the three RDTs.

The clinical sensitivity of the three RDTs was markedly better when testing serum samples with an anti-HBs titer higher than 100 IU/L (Table 2). In contrast, the analytical sensitivity was poor in serum specimens containing less than 100 IU/L of anti-HBs. An anti-HBs titer of 150 IU/L is required to reach a sensitivity of at least 90% for all three RDTs. Discrepancies between assays have been repeatedly reported, especially in clinical specimens containing low amounts of anti-HBs [6,7], therefore anti-HBs titers were systematically controlled with VIDAS® Anti-HBs Total II assay, an assay which is accurate in samples containing 10–100 IU/L [6]. The anti-HBs titers in blood samples below 100 UI/L were confirmed in most cases (95.2%, 79/83) using the VIDAS assay.

Table 1
Performance of anti-HBs RDTs in serum, using the EIA result in serum as reference.

Test	Specificity (95%CI)	Sensitivity (95%CI)	LR+	LR-
TOYO® HBsAb Test	98.0% (94.3%–99.6%)	60.4% (53.2%–67.3%)	30.2	0.40
QuickProfile™ HBsAb test	96.0% (91.5%–98.5%)	69.5% (62.6%–75.9%)	24.6	0.35
QuickProfile™ HBV-3 Panel test	97.3% (93.3%–99.3%)	65.5% (58.4%–72.1%)	17.4	0.32

EIA: enzyme immunosorbent assay; LR+: positive likelihood ratio; LR-: negative likelihood ratio, 95%CI: 95% confidence interval determined according to binomial distribution (Stata® 10.0; StataCorp LP, College Station, TX, USA).

Table 2
Performance of anti-HBs RDTs in serum according to the anti-HBs titers using the EIA result in serum as reference.

Test	Sensitivity (95%CI)
Anti-HBs titers < 100 IU/L	
TOYO® HBsAb Test	20.7% (12.6%–31.1%)
QuickProfile™ HBsAb test	40.2% (29.6%–51.7%)
QuickProfile™ HBV-3 Panel test	25.6% (16.6%–36.4%)
Anti-HBs titers ≥100 IU/L	
TOYO® HBsAb Test	88.7% (81.4%–93.8%)
QuickProfile™ HBsAb test	90.4% (83.5%–95.1%)
QuickProfile™ HBV-3 Panel test	93.9% (87.9%–97.1%)

The QuickProfile™ HBV-3 Panel test is capable of detecting HBsAg and total anti-HBc in addition to anti-HBs. Specificity for both markers was excellent [98.8% (95%CI: 97.0%-99.7%) and 100% (95%CI: 98.8%-100%), respectively]. Sensitivity was difficult to interpret due to the small number of positive clinical specimens for these two parameters (13 HBsAg-positive and 52 anti-HBc reactive specimens, respectively). All of the HBsAg-positive individuals were positive for HBsAg detection, whereas only 24 out of 52 anti-HBc reactive specimens were positive for anti-HBc detection. Clinical sensitivities were thus 100% (95%CI: 75.3%-100%) and 46.2% (95%CI: 32.2%-60.5%) for the HBsAg and anti-HBc detection, respectively.

5. Discussion

For the past 20 years, the availability of RDTs has led to their broad use in various fields of medicine. RDTs represent promising alternatives to EIA-based methods. They offer the advantages of simplicity, limited need for instrumentation, minimal training, and rapid performance at room temperature. These assays, therefore, represent a powerful tool for large-scale screening and subsequent appreciation of vaccine status against HBV. In particular, RDTs can be used for anti-HBs detection.

The results of the present study show that RDTs for anti-HBs detection, widely used in some parts of the world, have a satisfactory specificity, but a poor sensitivity (below 70%), essentially due to their inability to detect low antibody titers. These findings are in keeping with previous results with the same [8] or other rapid tests [5,9,10]. A satisfactory sensitivity was found in samples with high anti-HBs titers, indicating that these RDTs can be useful to assess specific populations, such as babies born to HBsAg-positive mothers who benefited from immunization procedures including hepatitis B immune globulin (HBIG) infusion and HBV vaccination, or healthcare workers. Anti-HBs RDTs can also be used to determine HBV vaccine booster by distinguishing vaccine non-responders from vaccinated individuals who have lost their anti-HBs but remain protected against HBV infection.

There are some limitations to our study has. First, only serum specimens have been tested. Further studies will need to assess the performance of RDTs from whole blood specimens. Second, no HIV-seropositive specimens were included. The performance of these rapid tests in HIV-coinfected individuals needs to be evaluated.

In conclusion, this is the first study evaluating the performance of three RDTs for anti-HBs detection. This performance including CE-marked rapid test was disappointing because the assays were not sensitive enough to detect low antibody titers. These tests require further

improvement before they can be widely used in clinical practice. Our findings confirm that careful assessment of the performance of HBV RDTs must be recommended before they can be implemented in clinical practice.

Conflict of interest

The authors have no conflicts of interest to disclose.

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Ethical approval

Patients or their family gave their consent to the use of the leftover samples.

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