Comparison of the Abbott Architect i2000 Assay, the Roche Modular Analytics E170 Assay, and an Immunoradiometric Assay for Serum Hepatitis B Virus Markers

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Abstract. Serum hepatitis B virus (HBV) markers are the most important data for epidemiological screening and clinical diagnosis of HBV infection, especially in endemic areas. We compared the results of the Roche Modular Analytics E170 assay, the Abbott Architect i2000 assay, and an immunoradiometric assay (IRMA) for HBV surface antigen (HBsAg), anti-HBV surface antigen (anti-HBs), HBV e antigen (HBeAg), and anti-HBV e antigen (anti-HBe). A number of serum samples (264, 263, 224, and 202 for HBsAg, anti-HBs, HBeAg, and anti-HBe, respectively) were studied. For samples giving discrepant results for HBeAg between methods, real-time PCR assays were performed. The concordance rates among the three methods were high for HBsAg (100%) and HBeAg (94.6), but low for anti-HBs (91.6%) and anti-HBe (82.2%). For anti-HBs, which could be measured quantitatively by the Modular E170 and Architect i2000 procedures, discrepant results were observed at low levels of anti-HBs. For anti-HBe, the positive rate was highest with Modular E170 (60.9%) followed by the IRMA kit (54.1%) and Architect i2000 (51.0%). This study shows substantial differences between the assay results by the three methods, which should be taken into account in determinations of serum HBV markers.

Keywords: automated analyzers, hepatitis B viral markers; immunoradiometric assay

Introduction

Hepatitis B virus (HBV) infection is a major global public health problem. Of the approximately 2 billion people who have been infected worldwide, more than 350 million are chronic carriers of HBV. Approximately 15 to 40% of infected patients will develop cirrhosis, liver failure, or hepatocellular carcinoma (HCC) [1]. In particular the HBsAg seroprevalence in the Western Pacific (China, South Korea, and Taiwan) ranges between 10 and 12% [2]. Determination of serum HBV markers is crucial for rapid screening and clinical diagnosis of HBV infection, particularly in regions with high prevalence. Recently, automated analyzers, such as Roche Modular Analytics E170 (Modular E170) and Abbott Architect i2000 (Architect i2000) have been developed. However, there are few reports that have assessed the performance of these analyzers. In this study, we compared the test results of HBV serologic markers as measured by an immunoradiometric assay (IRMA), the Modular E170 assay, and the Architect i2000 assay.

Materials and Methods

Four serologic markers were selected for comparison: HBV surface antigen (HBsAg), anti-HBsAg (anti-HBs), HBV e antigen (HBeAg), and anti-HBeAg (anti-HBe). From July to August 2006, 264, 263, 224, and 202 samples were submitted for routine testing for HBsAg, anti-HBs, HBeAg, and anti-HBe, respectively. Samples were tested using IRMA and two automated immunoassay analyzers (Modular E170, Architect i2000) in parallel.

Measurement of four serum HBV markers. The IRMA kit (North Institute of Biological Technology, Beijing, China), a
For samples showing discrepant results for HBeAg among the IRMA and two automated analyzers, a real-time PCR assay was performed using HBV PCR kits (Abbott Diagnostics, Hamburg, Germany) and an ABI PRISM 7000 HT Sequence Detection Systems (Applied Biosystems, Foster City, CA, USA). DNA extraction was performed using the Abbott DNA Sample Preparation System (Abbott Diagnostics, Wiesbaden, Germany) following the manufacturer’s instructions. The prepared DNA samples were stored at -20°C until use.

Statistics. For comparison of anti-HBs titers by the Modular E170 and Architect i2000 assay, the correlation coefficient was calculated by the Excel 2000 program (Microsoft, Seattle, WA, USA).

Results

The concordance rates among the three analyzers were 100%, 91.6%, 94.6%, and 82.2% for HBsAg, anti-HBs, HBeAg, and anti-HBe, respectively (Table 1). The positive rates and concordance rates between analyzers are shown in Tables 2 and 3.

For anti-HBs, the 22 cases that showed discrepancy among the three analyzers were low in anti-HBs level (<100 IU/L). However, the concordance rate of Modular E170 and Architect i2000 was significantly higher (97.3%) than that of IRMA and Modular E170 (92.4%), or that of IRMA and Architect i2000 (93.5%) (Table 3). The correlation between the serum anti-HBs levels measured quantitatively by Modular E170 and Architect i2000 was high (r = 0.918) (Fig. 1).

For HBeAg, the concordance rate between the two automated analyzers was higher than for each with the IRMA (Table 3). Of 224 samples, 7 were
negative only by the IRMA, 2 were positive only by IRMA, and for these 9 cases real time PCR was performed. Six of 9 samples showed positive results in real-time PCR. For these 6 samples, IRMA was positive in only 1, whereas with Modular E170/Architect i2000, 5 gave positive results (Table 4). Of the 3 real-time PCR negative samples, IRMA gave 2 negative results and Modular E170/Architect i2000 gave 1 negative result. Concordance rates of IRMA and Modular E170/Architect i2000 assays with real-time PCR were 33.3% (3/9) and 66.6% (6/9), respectively.

For anti-HBe, the positive rate was highest with Modular E170 (60.9%) followed by IRMA kit (54.1%) and Architect i2000 (51.0%). In 16 cases positive results were obtained only by Modular E170, and 15 of them were HBeAg-positive with all three analyzers.

Discussion

Determination of serum HBV markers is crucial for rapid screening and clinical diagnosis of HBV infection, particularly in regions with high prevalence. However, in determination of serum HBV markers, discrepancies among test results from different types of immunoassay analyzers, which could affect the accuracy of epidemic screening and clinical diagnosis, have been reported [3]. In this study, we compared the results for HBsAg, anti-HBs, HBeAg, and anti-HBe among two automated immunoassay analyzers (Modular E170, Architect i2000) and an IRMA assay.

Table 4. Cases showing HBeAg and Anti-HBe discrepancies among the three methods.

<table>
<thead>
<tr>
<th>Sample No.</th>
<th>HBe Ag</th>
<th>PCR</th>
<th>Anti-HBe</th>
</tr>
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<tbody>
<tr>
<td>IRMA E170</td>
<td>i2000</td>
<td>IRMA E170</td>
<td>i2000</td>
</tr>
<tr>
<td>[data not available]</td>
<td>[data not available]</td>
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In determination of HBsAg, the concordance rate of the three methods was 100%, but only Architect i2000 could perform quantitative analysis. This quantitative measurement of HBs titers may be an easy and economical reference for HBV replication, because the change in HBsAg concentration correlates well with the changes in HBeAg and HBV DNA levels [4,5]. Serum anti-HBs is important for confirmation of protective immunity after vaccination and recovery after HBV infection. An anti-HBs concentration >10 IU/L, is considered to be protective against HBV infection [6]. Therefore, low titers of anti-HBs must be accurately determined for evaluating the effect of vaccination and booster injections. Modular E170 and Architect i2000 can perform quantitative analysis, and there was good correlation (\( r = 0.918 \), concordance rate = 97.3%) between these two analyzers. These findings are in agreement with another report [3]. For comparison with RIA, Wang et al [7] reported that anti-HBs titers measured by EIA correlated well with the results of RIA. However, inconsistent results have been reported in other studies [3, 8-10]. These differences may be related to the various sources of reagents and to the different HBV vaccines [11].

There are fewer reports comparing serum HBeAg and anti-HBe assays than of HBsAg and anti-HBs assays. HBeAg seroconversion is the short-term goal of antiviral therapy in chronic hepatitis B [12], and the fall of HBeAg levels during early treatment is an important independent predictor of response [13]. In the present study, the
concordance rate of HBeAg with the three analyzers was high (94.6%), and it was higher between Modular E170 and Architect i2000 (98.7%) than for each with IRMA. In addition, although the HBV DNA level does not always correlate with the HBeAg level, the concordance rate of HBeAg results from Modular E170/Architect i2000 with the HBV DNA level was higher than that of IRMA. For anti-HBe, the positive rate was highest with the Modular E170 assay, which is consistent with a previous study [3]. Of the 16 cases positive only by Modular E170, 15 were HBeAg-positive with all three analyzers, suggesting false positive results with the Modular E170 assay.

In conclusion, the concordance rate was highest for HBsAg, followed by HBeAg, anti-HBs, and anti-HBe. The concordance rate was greater between the two automated analyzers than those of each with IRMA for anti-HBs and HBeAg and the positive rates were highest with the Modular E170 assay for anti-HBe. This study shows substantial differences between the assay results by the three methods, which should be taken into account in determinations of serum HBV markers.

Acknowledgments

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References