Performance Evaluation of LUMIPULSE G1200 Autoimmunoanalyzer for the Detection of Serum Hepatitis B Virus Markers

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Background: We evaluated recently introduced automated immunoassay analyzer LUMIPULSE G1200 (Fujirebio, Inc., Tokyo, Japan) for detecting serologic hepatitis B virus (HBV) markers by comparison with the results by ARCHITECT i4000SR (Abbott, Abbott Park, IL). **Methods:** Precision performance was evaluated over 20 days. HBV surface antigen (HBsAg), HBV e antigen (HBeAg), antibodies to HBV core antigen (anti-HBc), antibodies to HBeAg (anti-HBe), and antibodies to HBsAg (anti-HBs) in a total of 1,000 serum samples were assessed by the two analyzers. Discrepant results were retested by COBAS e411 (Roche Diagnostics, Mannheim, Germany). **Results:** LUMIPULSE showed excellent precision performance of total imprecision less than 3.5% coefficient of variation. The qualitative results between the two analyzers were agreed with each other

in 92.0–99.8% of the specimens according to the different HBV markers. The degrees of reactions for HBeAg were moderately correlated between the two analyzers ($r = 0.60$), and those of other HBV markers were well correlated ($r = 0.80$ or greater). However, there were 183 discrepancies among 1,000 cases, and most of them showed degree of reaction around the cutoff values. **Conclusions:** LUMIPULSE G1200 showed well-concordant results with ARCHITECT for hepatitis B serologic tests. However, results near the cutoff values would need to be retested with other immunoassay or molecular methods, when the serological profiles of HBV markers are unusual or are not correlated to the clinical conditions of the patient, due to discrepancies between the immunoassay analyzers. J. Clin. Lab. Anal. 27:204–206, 2013. © 2013 Wiley Periodicals, Inc.

Key words: hepatitis B virus marker; automated analyzer; hepatitis B; LUMIPULSE G1200; immunoassay

Hepatitis B virus (HBV) infection is one of the major global public health problems. In worldwide, two billion people have been infected with HBV, and more than 350 million of infected patients are chronic carriers of HBV (1). Many automated immunoassay analyzers with high sensitivity, specificity, and throughput have been developed. However, there are not many reports that have compared the performance of automated immunoassay analyzers for serological markers of HBV infection. Therefore, we compared the results of serum HBV markers measured by two automated immunoassay analyzers, LUMIPULSE G1200 (Fujirebio, Inc., Tokyo, Japan) and ARCHITECT i4000SR (Abbott Diagnostics, Abbott Park, IL).

Five serologic markers were selected for comparison: HBV surface antigen (HBsAg), antibodies to HBV core

antigen (anti-HBc), antibodies to HBsAg (anti-HBs), HBV e antigen (HBeAg), and antibodies to HBeAg (anti-HBe). A total of 1,000 serum samples from patients were tested by using the two automated immunoassay analyzers in parallel. The samples that showed discrepant results were tested by another automated immunoassay analyzer, COBAS e411 (Roche Diagnostics, Mannheim, Germany). For the evaluation of precision performances, two pooled

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Received 10 February 2012; Accepted 7 January 2013

DOI 10.1002/jcla.21584

Published online in Wiley Online Library (wileyonlinelibrary.com).

sera, with positive and negative for each serologic marker assay, were assayed in duplicate at two separate times daily for 20 days. Mean, standard deviation (SD), and coefficient of variation (CV) of cutoff index (COI), inhibition rate (INH), or IU/l were calculated. To compare the qualitative results between serum HBV markers for LUMIPULSE G1200 and ARCHITECT i4000SR, the percent agreements and kappa coefficients were calculated. Correlation coefficients between the reaction degrees as COI, INH, relative light unit (RLU), or IU/l for the two analyzers were calculated by Spearman's rank test.

All assays by LUMIPULSE G1200 showed excellent reproducibility with within-run CVs of 1.0%, 0.1%, 2.1%, 2.7%, and 0.7%, and total CVs of 1.3%, 0.1%, 2.5%, 3.4%, and 0.9% for positive pooled serum samples of HBsAg (mean COI 629.6), anti-HBc (mean INH 98.2%), anti-HBs (mean 614.4 IU/l), HBeAg (mean COI 419.6), and anti-HBe (mean INH 76.9%), respectively. In addition, those for negative samples (as mean values; HBsAg, COI 0.10; anti-HBc, INH 24.22%; anti-HBs, 0.34 IU/l; HBeAg, COI 0.13; anti-HBe, INH 0.10%) also presented precision performances as within-run SDs of 0.00, 1.00, 0.09, 0.05, and 0.00, and total SDs of 0.00, 1.60, 0.13, 0.07, and 0.00, respectively. Thus, the newly introduced autoanalyzer LUMIPULSE G1200 showed excellent total precision for both positive and negative specimens. The concordance rates between the qualitative results of HBsAg, anti-HBc, anti-HBs, HBeAg, and anti-HBe assays by LUMIPULSE G1200 and ARCHITECT i4000SR were 99.8% ($k = 1.00$), 95.8% ($k = 0.91$), 92.0% ($k = 0.84$), 98.8% ($k = 0.95$), and 95.3% ($k = 0.88$), respectively ($P < 0.0001$ for all kappa coefficients; Table 1). The overall agreement between the results of the panel consisting of the five HBV serologic markers for each specimen by the two analyzers was 83.1% (831/1,000), and the total agreement between the results of all five serum HBV markers was 96.3% (4,817/5,000). The degrees of reac-

tions (COI for HBsAg and HBeAg, INH for anti-HBc and anti-HBe, and IU/l for anti-HBs) among the specimens, which were measured by LUMIPULSE G1200, were well correlated with those (IU/l for anti-HBs and RLU for others) by ARCHITECT i4000SR (HBsAg, $r = 0.80$; anti-HBc, $r = 0.95$; anti-HBs, $r = 0.94$; and anti-HBe, $r = -0.90$; $P < 0.0001$ for all), and COIs for HBeAg of LUMIPULSE G1200 were moderately correlated with RLUs for HBeAg of ARCHITECT i4000SR ($r = 0.60$, $P < 0.0001$). The results of anti-HBe assays between the two analyzers were inversely correlated because the method for the determination of anti-HBe by ARCHITECT i4000SR was a competitive immunoassay.

A total of 183 serum HBV markers from the 169 serum samples, which showed discrepant results between LUMIPULSE G1200 and ARCHITECT i4000SR, were tested by COBAS e411. The results of LUMIPULSE G1200 and ARCHITECT i4000SR, which also showed discrepant results with COBAS e411 were regarded as false-positive or false-negative. Consequently, 91 results tested by LUMIPULSE G1200 and 92 assayed by ARCHITECT i4000SR were regarded as either false-positive or false-negative results. A total of 33 results from LUMIPULSE G1200 including 17 for anti-HBc (median INH 54.4%, cutoff 50.0%), 15 for anti-HBs (median 13.9 IU/l, cutoff 10 IU/l), and 1 for HBeAg (COI = 1.1, cutoff 1.0) were false-positive, and there were 58 false-negative results by LUMIPULSE G1200 (19 for anti-HBc, median INH 42.0%; 7 for anti-HBs, median 4.2 IU/l; 32 for anti-HBe, median INH 44.0%). On the other hand, there were 17 cases of false-positive results from ARCHITECT i4000SR including one for HBsAg (RLU 551.15), 3 for anti-HBs (median 13.12 IU/l), 11 for HBeAg (median RLU 1.264, cutoff 1.0), and 2 for anti-HBe (median RLU 0.88, cutoff 1.0). There were also 75 false-negative results tested by ARCHITECT i4000SR (1 for HBsAg with 0.31 RLU; 6 for anti-HBc, median RLU 0.485; 55 for

TABLE 1. Agreements of Serum HBV Markers Between the Qualitative Results of LUMIPULSE G1200 and ARCHITECT i4000SR

Markers	ARCHITECT	LUMIPULSE		Agreement (%)	k (95% CI) ^a	P value
		Positive	Negative			
HBsAg	Positive	314	1	99.8	1.00 (0.99–1.00)	<0.0001
	Negative	1	684			
Anti-HBc	Positive	620	19	95.8	0.91 (0.88–0.94)	<0.0001
	Negative	23	338			
Anti-HBs	Positive	451	10	92.0	0.84 (0.81–0.87)	<0.0001
	Negative	70	469			
HBeAg	Positive	132	11	98.8	0.95 (0.92–0.98)	<0.0001
	Negative	1	856			
Anti-HBe	Positive	261	34	95.3	0.88 (0.85–0.92)	<0.0001
	Negative	13	692			

^aKappa coefficient and its 95% confidence interval.

anti-HBs, median 5.75 IU/l; 13 for anti-HBe, median RLU 1.17).

In our study, we tested five serum HBV markers for the comparison of 1,000 serum samples between LUMIPULSE G1200 and ARCHITECT i4000SR. The agreements were high, especially for the results of HBsAg (99.8%) and HBeAg (98.8%). The results of LUMIPULSE G1200 seem to be comparable with those of ARCHITECT i4000SR. The total agreement for all 5,000 results was also high (96.3%), while the agreement between the results of the panel consisting of the five serum HBV markers for all 1,000 study subjects was relatively low (83.1%). Therefore, we retested the 169 discrepant serum samples (183 discrepant results) with another analyzer, COBAS e411, and 91 of 183 results from LUMIPULSE G1200 and 92 of 183 from ARCHITECT i4000SR were discrepant with those from COBAS e411. Therefore, the discrepancies between the results from LUMIPULSE G1200 and ARCHITECT i4000SR could not be attributed to bias or systematic errors from either of the two analyzers.

The greatest number of discrepancies between LUMIPULSE G1200 and ARCHITECT i4000SR was observed in the qualitative results of anti-HBs (80 cases). However, the concentrations of anti-HBs (IU/l) for LUMIPULSE G1200 were well correlated with those of ARCHITECT i4000SR ($r = 0.94$). High rates of discrepancies between the anti-HBs assays have also been reported by other study, which evaluated the performance of nine commercially available analyzers even though all manufacturers use WHO standards for calibrator assignment (2). Although the qualitative results by the two analyzers correlated well with each other in this study, it is not surprising that there were still great number of discrepancies. Almost all of those 80 discrepant results were near the cutoff value of 10 IU/l. This cutoff value for anti-HBs could be clinically significant in certain situations, such as during antiviral therapy for chronic hepatitis, evaluating vaccine responses, and planning schedules for long-term protection (3,4).

In addition, the qualitative results of anti-HBc for LUMIPULSE G1200 well agreed with those of ARCHITECT i4000SR with a percentage agreement of 95.8, and the INH values for LUMIPULSE G1200 were also well correlated with RLUs of ARCHITECT i4000SR ($r = 0.95$). Although 42 qualitative results for anti-HBc showed discrepancy, the INH or RLU values were around the cutoff values. The qualitative or quantitative results of anti-HBe by LUMIPULSE G1200 and ARCHITECT i4000SR were also highly agreed or well correlated, and all the 47 discrepant results were around the cutoff values.

The agreement of qualitative results for HBeAg between the two instruments was high (98.8%), while the COI values of LUMIPULSE G1200 were only moderately cor-

related with RLUs of ARCHITECT i4000SR ($r = 0.60$). In 856 cases, in which the HBeAg were negative for both LUMIPULSE G1200 and ARCHITECT i4000SR, COI values for LUMIPULSE G1200 in 800 cases were less than 0.1. Therefore, the correlation coefficient between the results for the two was relatively low, but it could be considered to be not clinically important. Among the 12 discrepant cases for HBeAg, 11 for LUMIPULSE G1200 were concordant with the results of COBAS e411, and all 12 results were close to the cutoff value.

Consequently, serum HBV markers, particularly around the cutoff values, need to be retested with other methods or analyzers when results of serum HBV markers seem to be aberrant within a panel or are not concordant with the clinical status of the patient. For the diagnosis and monitoring of patients with hepatitis B, detection and quantification of HBV DNA in serum or plasma are considered as important indicators. Many commercial molecular tests for the quantification of HBV DNA have been developed and are routinely used in clinical laboratories (5). Therefore, HBV DNA assays would be helpful to make an accurate diagnosis or to resolve discrepant results among serologic tests, particularly when the results by serologic tests are around the cutoff values.

In conclusion, LUMIPULSE G1200 showed excellent precision performance and highly agreed results with ARCHITECT i4000SR. However, the results between the two analyzers were relatively not well agreed with each other when the results were assessed in the panel consisting of five serum HBV markers. Therefore, we recommend that the results may be needed to be retested by other immunoassays or molecular methods for HBV DNA when they are aberrant for other markers included in the panel or do not correspond to the status of the patients, especially when the results are around the cutoff values.

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