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Short Communication

Performance evaluation of SD A1cCare as a HbA1c analyzer for point-of-care testing

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ABSTRACT

Objectives: Some studies have shown that a rapid feedback of HbA_{1c} results is helpful for controlling plasma glucose levels. Point-of-care (POC) instruments that are fast, portable, and easy to use are suitable for rapid determination of HbA_{1c} levels. Here, we evaluated the analytical performance of a newly developed POC HbA_{1c} analyzer, SD A1cCare (SD Biosensor, Inc.).

Design and methods: The precision, linearity, and correlation with the Variant II Turbo instrument (Bio-Rad Laboratories, Inc.) were evaluated according to CLSI guidelines for SD A1cCare. All tests were performed according to the manufacturer instructions, and statistical analyses, including linear regression and Passing-Bablok regression, were performed. Bias from the IFCC reference targets was also evaluated with 12 duplicate specimens ($n = 24$ in total).

Results: The coefficients of variation based on EP9-A2 protocol were 2.6% in SI unit and 1.8% in NGSP unit. The calibration curve was linear, with $R^2 = 0.9911$ in the range of 23.5 to 125.1 mmol/mol in SI units (4.3% to 13.6% in NGSP units). The results of the SD A1cCare correlated with those of the Variant II Turbo ($r = 0.986$). Deviations from IFCC targets at 30, 60, and 90 mmol/mol IFCC levels were −1.95, −1.85, and −1.74 mmol/mol, respectively.

Conclusions: The SD A1cCare analyzer showed excellent precision, linearity, correlation with the Variant II Turbo analyzer, and accuracy with IFCC targets. Therefore, it may be suitable for HbA_{1c} assays in the POC setting and in small laboratories.

Introduction

Glycated hemoglobin (hemoglobin A1c, HbA_{1c}) levels, which reflect the average plasma glucose concentration over the preceding 3 months, play a pivotal role in the diagnosis, assessment, and monitoring of diabetes [1]. Standardization of HbA_{1c} levels are recognized worldwide, allowing the development of well-defined reference measurement procedures and primary reference materials [2]. These efforts, spearheaded by programs such as the National Glycohemoglobin Standardization Program (NGSP) HbA_{1c} harmonization program and the IFCC Working Group on HbA_{1c} standardization, have further supported the role of HbA_{1c} in the management of diabetes. In addition, studies have shown that immediate feedback of HbA_{1c} levels is highly effective for controlling plasma glucose levels [3–5]. Thus, point-of-care (POC) instruments, characterized as fast, portable, and easy-to-use, have been shown to be suitable for providing rapid feedback of HbA_{1c} levels.

However, although POC HbA_{1c} measurement offers convenience in some clinical settings, the performance of some POC methods may not be sufficient to meet clinical needs [6]. In Korea, the Korean Association of External Quality Assessment Service (KAEQAS) began using accuracy-based proficiency testing (PT) for HbA_{1c} in 2009. Since then, the overall bias from reference targets and method-specific interlaboratory variability has decreased steadily. However, some POC testing methods have an unusually large bias and variability. Therefore, there is a continuous need for development of a POC HbA_{1c} analyzer with enhanced performance.

In this study, we assessed the analytical performance of the newly developed POC HbA_{1c} analyzer, SD A1cCare (SD Biosensor, Inc., Suwon, Korea), including analysis of the precision, linearity, correlation with the Variant II Turbo analyzer (Bio-Rad Laboratories, Inc., Hercules, CA, USA), and bias from the IFCC reference targets of this instrument.

Materials and Methods

The SD A1cCare analyzer, which utilizes an immunochromatography assay, provides results in 3 min. The SD A1cCare Test kit uses an anti-

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HbA_{1c} antibody that is specific for the first few amino acid residues of the glycated N-terminus of the β-chain of hemoglobin A_0. Fresh whole blood is added to the lysis buffer solution and mixed with a latex tablet that contains blue-dyed conjugates. The sample mixture then forms a complex between released HbA_{1c}, and the conjugate is loaded onto the sample port of the test panel and migrates to the detection zone, immobilizing the capture antibody to form a blue-colored line. The SD A1cCare analyzer measures total hemoglobin and HbA_{1c} levels via its optical system and calculates the percentage HbA_{1c}.

The imprecision of the SD A1cCare analyzer was assessed with two controls supplied by the manufacturer for 20 days according to Clinical and Laboratory Standards Institute (CLSI) EP5-A2 protocol and was also calculated on the basis of the duplicates of the fresh patient samples in the EP9-A2 protocol. The linearity of the analyzer was assessed following CLSI EP6-A guidelines by mixing samples from patients with high and low levels of HbA_{1c} at ratios of 4:0, 3:1, 2:2, 1:3, and 0:4 (v/v). In accordance with CLSI EP9-A2 guidelines, 150 residual specimens in the EDTA tube were tested using both the SD A1cCare and the Variant II Turbo (Bio-Rad Laboratories, Inc.) in 14 days. Passing-Bablok regression analysis and Bland-Altman plotting were then carried out.

To investigate the accuracy of the SD A1cCare analyzer, we measured the deviation from the IFCC reference targets using two sets of 12 duplicate fresh venous whole blood specimens (n = 24 in total, range: 33.3–91.3 mmol/mol in SI units, 5.2–10.5% in NSGP units). Each set was measured by using the SD A1Care methods and IFCC reference measurement procedure (RMP) [7]. The IFCC RMP was carried out by Korea Centers for Disease Control and Prevention (KCDC) national medical reference laboratory, one of the laboratories approved by the IFCC HbA_{1c} Network [8].

All statistical analyses were performed with Microsoft Excel 2010 (Microsoft Corporation, Redmond, WA, USA) and MedCalc version 13.2.2.0 (MedCalcSoftware, Mariakerke, Belgium).

This study was approved by the Institutional Review Board of Seoul National University Bundang Hospital (B-1301/186-301).

Results

The results of EP5-A2 protocol and the coefficients of variation (CVs) on the basis of the duplicate patient samples analyzed in EP9-A2 are shown in Table 1. All CVs were below 3.0% in NGSP units.

Linearity was demonstrated between 4.1% and 13.9%. The slope and intercept of the regression equation were 0.973 and 0.533, respectively. The coefficient of determination (R^2) was 0.9911.

Passing-Bablok regression analysis of the data (n = 150) from the comparison between the SD A1cCare and Variant II Turbo showed a slope of 1.025 (95% confidence interval [CI]: 1.0000–1.0625) and an intercept of −0.0863 (95% CI: −0.3375–0.1000) (Fig. 1). The calculated standard error of estimate (Syx) was 0.246. Analysis by Bland-Altman plot showed a mean difference of 0.12% in NGSP units. Among 150 samples, 6 showed the difference of larger than 0.5%.

Deviations from IFCC targets at 30, 60 and 90 mmol/mol HbA_{1c} (4.9%, 7.6 and 10.4% in NGSP units) were −1.95, −1.85, and −1.74 mmol/mol HbA_{1c} (−0.18%, −0.17 and −0.16% in NGSP units), respectively, and the reproducibility of blind duplicate specimens was 1.45%, showing the excellent accuracy and precision of the instrument.

Table 1
Imprecision of the SD A1cCare analyzer and Variant II Turbo based on CLSI EP5-A2 and the duplicates in EP9-A2.

Instruments	HbA1c value			
	SI units (mmol/mol)	CV (%)	NGSP units (%)	CV (%)
SD A1cCare	37	4.5[a]	5.5	2.7[a]
	80	3.2[a]	9.5	2.6[a]
		2.6[b]		1.8[b]
Variant II Turbo		2.3[b]		1.6[b]

[a] Based on EP5-A2.
[b] Based on duplicate in EP9-A2.

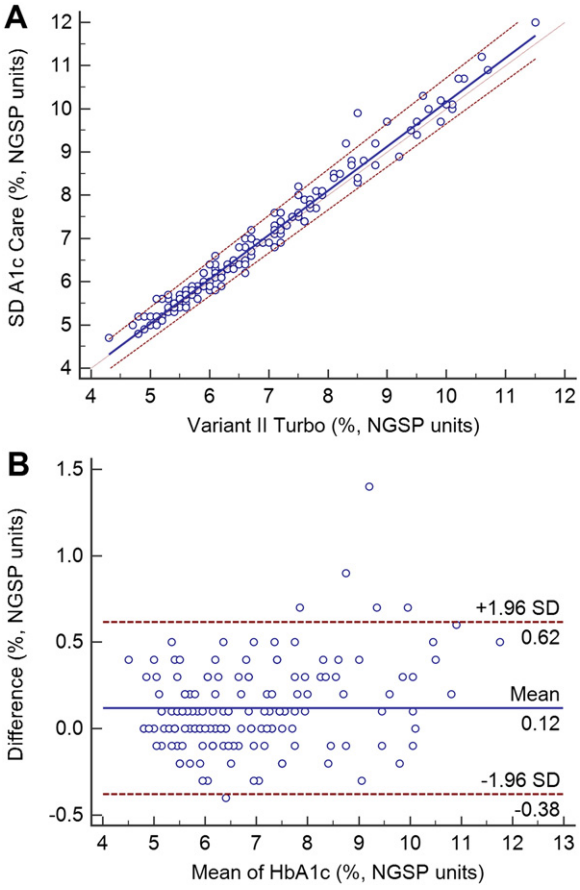

Fig. 1. Comparison of HbA_{1c} levels obtained by the SD A1cCare analyzer (test) and the Variant II Turbo (comparative) by CLSI EP9-A2. Scatter plots with ordinary linear fit with the Passing-Bablok regression analysis (A). Bland–Altman plots (B).

Discussion

Recently, the Ministry of Health and Welfare of Korea announced that POC testing methods for HbA_{1c} should be certified every year by the NGSP or KCDC national medical reference laboratories for the reimbursement of test fees. However, the NGSP-certified manufacture method is not followed by laboratory medical technologists, but by skillful technologists under ideal circumstances at the site of manufacture, thus not necessarily providing an accurate reflection of the analytical performance of the instruments in the clinic [9]. Therefore, a NGSP manufacturer-certification may not guarantee accuracy of a result produced in the field, and the performance of different reagent lots for POC instruments should be analyzed for optimal clinical use of the test results. For this purpose, we evaluated the analytical performance (including precision, linearity, comparison with an HPLC analyzer, and bias from the IFCC reference targets) of the newly developed POC HbA_{1c} analyzer-SD A1cCare. Our results showed that this POC analyzer provided excellent performance for rapid determination of HbA_{1c} levels.

The performance of POC tests for determination of HbA_{1c} levels is generally assessed by precision and bias. Quality goals can be calculated considering clinical needs, biological variation, and other factors. For optimal clinical monitoring and effective differentiation of small critical differences in HbA_{1c} levels, an imprecision of less than 2% CV is required, assuming an intra-individual biological variation of 2% [10,11]. In terms of POC HbA1c testing, it is recommended that a minimum imprecision goal of 4% is set for this analyte, along

with a desirable goal of 3% and an optimal goal of 2% [12]. Recently, Lenters-Westra and Slingerland performed the second study to evaluate the performance of 7 new POC devices and reported that the CVs of 7 instruments ranged 0.6–2.6% in NGSP units (average, 1.64%) [13]. In this study, the SD A1cCare analyzer showed an optimal precision in the field, having an imprecision of 1.8% in NGSP unit which is similar to the average CV of 7 instruments.

The linearity of the SD A1cCare analyzer was demonstrated over a clinical range of HbA_{1c}, 23.5 to 125.1 mmol/mol in SI units (4.3% to 13.6% in NGSP units). While we attempted to evaluate a more broad range, specimens with below 4.0% HbA_{1c} could not be obtained.

Recently, concerns have been raised about the performance of NGSP-certified POC instruments compared with laboratory-based methods. One study showed that the magnitude of the negative inter-method bias was equal to the POC result minus the central laboratory result [14]. Although our results exhibited positive inter-method bias, the mean difference of 0.12% NGSP units, as observed in our study, was much lesser than that in this previous study (−0.39–0.82% NGSP units) [14]. Moreover, the 95% CI obtained from Passing-Bablok regression analysis for the slope and the intercept were 1 and 0, respectively. The results of the SD A1cCare instrument correlated significantly with those of the Variant II Turbo instrument ($r = 0.986$).

In terms of IFCC manufacturer certification for accuracy, the criteria for excellent, good, and acceptable biases from IFCC reference targets are <2.0, ≥2.0 and <4.0, and ≥4.0 and <7.0 mmol/mol in SI units, respectively. In the present study, deviations of SD A1cCare from IFCC reference targets ranged from −1.74 to −1.95 mmol/mol HbA1c in SI units, showing excellent accuracy for clinical use.

There were a few limitations to our study. First, we did not show that the SD A1cCare analyzer was free of interference from hemoglobin variants because we could not obtained the fresh samples with hemoglobin variants during the evaluation period due to the low prevalence of hemoglobinopathies in Korea. In addition, we did not evaluate the performance of different reagent lots because we could get only one reagent lot during the evaluation period. Lastly, we did not compared the analytical performance study of capillary versus venipunctured specimens.

Conclusions

The SD A1cCare analyzer showed very good performance, including excellent precision, linearity, correlation with the Variant II Turbo analyzer, and accuracy with IFCC reference targets. After further studies to address the limitations listed above, this analyzer may be suitable for HbA_{1c} assays for POC settings and small laboratories, particularly in countries with limited resources.

Conflict of interest

The SD A1cCare analyzer and SD A1cCare Test kits were provided by SD Biosensor, Inc., Korea. The company had no involvement in the design, conduct, or analysis of the trial or in the preparation of the manuscript.

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