Proof Source Summary
HbA1c

Multicenter assessment of a hemoglobin A1c point-of-care device for diagnosis of diabetes mellitus

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Background

Point-of-care (POC) testing is becoming increasingly valuable in health care delivery, and it is important that the devices used meet the same quality criteria as main laboratory analyzers. Historically HbA1c POC devices demonstrated significant bias and variability when compared to non-POC assays, which led to clinical guideline recommendations against utilization for diagnostic purposes. Nevertheless, POC HbA1c measurements can expedite diagnostic decisions and medical interventions provided they meet performance standards. Due to challenges in obtaining a fasting plasma glucose specimen, an FDA cleared POC HbA1c device that demonstrates comparable accuracy and precision to common laboratory platforms with claims for diagnosis of diabetes has considerable clinical utility.

Study Purpose

1) To evaluate the analytical performance of HbA1c using the Afinion™ AS100 POC analyzer between multiple sites.
2) To compare the performance characteristics of the Afinion™ AS100 POC analyzer to other frequently used automated HbA1c assays and a National Glycohemoglobin Standardization Program (NGSP) reference method.

Methods

Analytical performance of the Afinion™ AS100 POC analyzer was compared to three clinical laboratory HbA1c platforms (turbidimetric immunoassays - Roche Tina-quant® HbA1c Gen. 3, Siemens Dimension Vista or cation-exchange HPLC- Bio-Rad Variant II Turbo) across five clinical laboratories, and with an NGSP reference laboratory (cation-exchange HPLC- Tosoh G8 Automated Glycohemoglobin Analyzer).

De-identified, remnant EDTA anti-coagulated whole blood specimens with clinical orders and indications for HbA1c testing were utilized for this study.

Specimens that had Afinion™ HbA1c Dx values that differed by>10% from the reference method were reflexed for confirmatory testing using alternative NGSP certified boronate affinity methods (Ultra2 and Premier Hb9210 HbA1c Analyzers, Trinity Biotech).

A total of 618 patient specimens were analyzed between the POC and all laboratory methods. Specimens were excluded from POC and routine laboratory measurements if they were previously frozen or were known to have >5% Hemoglobin F (HbF) present.

The accuracy of the Afinion™ HbA1c Dx test was assessed at each site by evaluating a minimum of 120 specimens evenly distributed across the low (4.00–6.00% HbA1c), mid (6.01–7.00% HbA1c) and high (7.01–15.00% HbA1c) range for HbA1c.

Precision of the POC device relative to each laboratory method was conducted and evaluated independently at each site using three EDTA whole blood specimens (one specimen at each target HbA1c value). Each site independently created their own pools for low, medium, and high HbA1c at similar nominal concentrations. Each specimen was analyzed in duplicate twice a day, for a total of 4 measurements per day by each laboratory's and POC methods over 8–10 consecutive days.

Findings

- The Deming regression demonstrated a strong correlation (Pearson R=0.994) between the Afinion™ HbA1c values and the Tosoh G8 reference method values. The mean of laboratory sites HbA1c also displayed a strong correlation (Pearson R=0.989) with the reference method values.

- 600 of 618 Afinion™ AS100 results (97.1%) and 584 of 618 laboratory results (94.5%) were within ±6% TAE when compared to the NGSP reference method. (NGSP certification requires that across the measurement range 37/40 (92.5%) of results must be within ±6% of the NGSP reference method.)

- Three specimens tested by the Afinion™ AS100 had HbA1c results (mean A1c of 4.4%, 8.6% and 13.4%) that differed by>10% relative to the NGSP reference method (mean A1c of 3.9%, 7.4%, and 11.6%). Repeat analysis of these specimens using an NGSP certified boronate affinity method yielded results that were in close agreement (within 3%, e.g. 0.3% HbA1c at an HbA1c of 8.6%) to the Afinion™ AS100 HbA1c results.

- At the HbA1c diagnostic decision point of 6.5%, the Afinion™ AS100 results exhibited a total bias of −0.6% (e.g. an absolute bias of −0.04 % HbA1c) compared to the reference method while the aggregate of laboratory methods displayed a total bias of −0.9% (e.g. an absolute bias of −0.06% HbA1c).

- Total imprecision for each HbA1c method.

Lab Method	Mean %HbA1c	Total CV (%)	# of Labs	# of Replicates
Afinion™ AS100	5.3 6.5 9.8	1.46 1.35 0.85	5 5 5	359 363 368
Variant II Turbo	5.4 6.6 11.5	2.39 1.87 0.83	2 2 2	136 140 140
Tina Quant Gen 3	5.2 6.2 9.2	1.89 1.28 1.55	2 2 2	152 152 152
Dimension Vista	5.1 6.7 8.5	3.23 1.96 1.44	1 1 1	72 72 72

Interpretation/Key Points

- This multicenter analytical trial demonstrates equivalent or superior performance of the Alere Afinion™ POC HbA1c device compared to routine clinical laboratory HbA1c assays currently employed in the diagnosis of diabetes.

- The discrepancies in HbA1c values between POC and the reference measurements in the three outliers were likely due to differences in methodologies as the two methods based on boronate gave near identical results. For these three specimens the differences in results appears to be due to differences between boronate affinity and the direct measurement of HbA1c via ion-exchange chromatography and is not specific to the POC method.

- The data demonstrates that the analytical performance of the Afinion™ POC HbA1c device is equivalent to a variety of common laboratory methods across multiple laboratories and supports the recent FDA decision clearing the Afinion™ HbA1c Dx device as substantially equivalent to routine clinical laboratory methods allowing it to be used in the diagnosis of diabetes.

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