

How accurate and reliable are point-of-care A1c tests?

July 3, 2013

Glycosylated hemoglobin A1c testing has traditionally been limited to clinical/laboratory settings. However, point-of-care (POC) A1c monitoring devices have been available since 1997.¹ Records of 9 devices were found on the Food and Drug Administration (FDA) website

(<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cflVD/Search.cfm>). They include the following:

Table 1. A1c Testing Devices.¹

Device Name	OTC or Professional Use	Approval Date
Bayer A1c Now SelfCheck	OTC	5/30/12
Bayer A1c Now +	Professional Use	5/30/12
Metrika INVIEW Multi-Test A1c Monitor	OTC	6/15/05
Metrika INVIEW Multi-Test A1c Monitor	Professional Use	6/15/05
Osborn Group Hemocek A1c sample collection kit	Not specified	12/21/99
Medisense Precision A1c Home HbA1c sample collection kit	Not specified	11/20/98
Boehringer Mannheim Accu-check A1c hemoglobin test	Not specified	5/13/98
Flexsite Diagnostics, EZchek Hgb A1c blood collection kit	Not specified	9/5/97

OTC=over the counter

Of note, all of these devices were approved for monitoring of A1c but not as diagnostic aids.¹ It is also important to note that the use of A1c to aid in diagnosis of diabetes was also a recent change in practice guidelines, as evidenced by the revisions to the recommendations outlined in the standards issued by the American Diabetes Association (ADA) in January 2010.²

In May 2013, the FDA announced marketing of the first A1c test that may be used for A1c testing and for diagnosis of diabetes by health care professionals.³ The device, COBAS INTEGRA 800 Tina-quant HbA1cDx assay (Tina-quant HbA1cDx assay), is available by prescription but for use specifically in laboratories. Interestingly, the FDA asserts in this announcement that over-the-counter (OTC) A1c tests should not be used by patients to diagnose diabetes.

While the ADA recognizes the importance of A1c testing, the organization states that A1c testing does not replace daily self monitoring of blood glucose.⁴ The A1c serves as a measure of blood glucose control over a period of a few months and will not match an individual, daily glucose measurement,⁵ nor will it reflect

changes in blood glucose control achieved in the past few weeks. Since A1c does not measure acute changes in blood glucose, insulin therapy should not be adjusted based on A1c results. Additionally, though A1c (laboratory) results may be used as a diagnostic tool, this method should be avoided in certain populations, including pregnant women, patients with recent severe bleeding or blood transfusions, patients with chronic kidney or liver disease, and patients with blood dyscrasias (e.g., anemia).

The accuracy of POC A1c tests is questionable. While the FDA has published criteria for assessment of A1c in-vitro diagnostic devices,⁶ organizations such as the American Association for Clinical Chemistry (AACC) state that POC tests, even those administered at a doctor's office, are not accurate enough for use in diagnosis but may be used to monitor treatment (both lifestyle modifications and pharmacotherapy).⁵ In observation of the FDA device review criteria, devices are approved as "substantially equivalent" if compared to an FDA-cleared device or a reference method (e.g., those of the National Committee for Clinical Laboratory Standards).⁶ Results must be analyzed using linear regression methods and meet the FDA criteria for equivalence. The FDA also recommends reporting of these statistical results in the "Performance Characteristics" of the device package insert.

In contrast, laboratory testing of A1c is typically certified by the National Glycohemoglobin Standardization Program (NGSP), initiated in 1996 to implement recommendations of the AACC⁷ – the AACC goal was to develop a plan allowing for clinical laboratories to relate their A1c results to those of landmark trials such as the Diabetes Control and Complications Trial.⁸ The NGSP offers laboratory certification and manufacturer method certification based on a 40 sample comparison with a secondary reference laboratory.⁷ The A1c results of the majority of these samples (37 or 38 of the 40) must be within $\pm 7\%$ of each other. The NGSP lists certified laboratories and asserts that these facilities have "documented traceability to the Diabetes Control and Complications Trial reference method." Per Holmes et al, virtually all laboratory A1c assays in the US are certified by the NGSP.⁹

From a search of the literature, several articles have been published describing the accuracy of POC A1c tests.¹⁰⁻¹⁶ In 2003, 5 POC tests supplied by 4 different manufacturers were evaluated.¹⁰ The investigators found that the tests varied substantially in their use and administration. For example, 1 test was intended for single use in a clinical setting, and another test was a batch analyzer designed for low-to-moderate volume laboratory testing of up to 15 samples.

In 2005, Sicard and Taylor compared a POC A1c monitor (A1c Now®) to standardized laboratory testing.¹¹ Adult patients with type 1 or type 2 diabetes mellitus were recruited from a pharmacy-run diabetes clinic in Gainesville, Florida, and required to obtain A1c results using the POC test and a local laboratory within 1 week. The primary outcome was accuracy of the POC test, determined by the Spearman's rho correlation coefficient. A total of 23 patients participated, 22 of whom had type 2 diabetes. Laboratory and POC test results were identical for 3 of the patients. The POC test result was lower than the laboratory result for the other 20 patients. In general, A1c Now® was found to have a correlation coefficient of 0.758, indicating "good" accuracy. The most accurate results were obtained for patients with A1c ranging from 6% to 8%. The

authors concluded that this POC test would be beneficial for patients with barriers to laboratory measurement (e.g., transportation/financial issues) but that clinical decision-making should not be based solely on POC test results.

Schwartz et al evaluated the accuracy of POC testing, comparing A1c results from Metrika A1c Now® to those of 4 different laboratories, all NGSP-certified.¹² Adult patients with diabetes were recruited from 5 family medicine centers in Detroit, Michigan. All patients were subjected to a finger prick POC A1c test. Venous samples were also drawn and sent to 1 of 4 laboratories. Physicians were blinded to the POC results and relied on laboratory results for therapeutic decision-making. A total of 99 paired samples were obtained; the mean A1c among POC results was 7.38%, and the mean A1c among laboratory results was 7.53% ($p < 0.0001$). Comparing the 4 laboratory methodologies, correlation coefficients ranged from 0.74 to 0.96. A comparison of all samples combined, between laboratory and POC testing, revealed a significant correlation (Pearson $r = 0.884$, $p < 0.001$). While the POC testing was deemed accurate, its sensitivity and specificity were lower (compared to laboratory measurements) at 81.8% and 93.2%, respectively. Approximately 18% of patients with an A1c result above a certain value (7%) as identified by laboratory results were NOT identified by the POC result. The authors concluded that practitioners consider reviewing the accuracy of a POC A1c test of choice by conducting a similar evaluation (e.g., with a local laboratory) prior to implementation and to repeat this analysis periodically.

Wood et al compared the A1c results of 1 POC test, Afinion™, to another POC test, DCA, as well as results from a central laboratory at the University of Minnesota.¹³ Pediatric patients with diabetes were recruited from 7 clinics; 3 blood samples were obtained from each patient for A1c measurement by both POC methods and the central laboratory. Results from 700 patients were collected. The coefficient of variation was 2% for Afinion™, 3% for DCA, and 1% for the central laboratory. Comparing mean A1c values of POC testing to laboratory testing, Afinion™ had higher results (mean difference +0.15, $p < 0.001$) while DCA had lower results (mean difference -0.19, $p < 0.001$). However, DCA results were found to vary more, particularly at higher A1c levels, while the accuracy of Afinion™ results did not vary by A1c. Still, the authors concluded that the differences in results of the POC tests (compared to laboratory testing) were not clinically significant. They also concluded that the POC tests in their study were similar in accuracy and precision.

In addition to these studies, others were found evaluating the accuracy of POC A1c tests, including the B-D A1c At-Home® test and A1c Now®, with varying results.¹⁴⁻¹⁶ The results of these studies suggest that POC A1c testing may be accurate. However, based on the available literature, use of POC tests for A1c measurement should not replace laboratory testing. While POC A1c testing may be preferable based on ease of use and timeliness of results, several other factors must be considered. These include performance factors (e.g., patient education for OTC tests, training of health care professionals, and feasibility in office operations) and cost. Additionally, per Holmes et al, analytic biases may be concerning in the interpretation of POC A1c test results as compared to laboratory results.⁹

Thus, while POC testing may be convenient and potentially accurate, the clinician is advised not to rely solely on POC A1c tests to guide therapeutic decision-making. If a POC A1c test were to be employed, consultation of the device manufacturer for its performance characteristics as well as periodic comparisons of A1c values (between device and laboratory) are advisable.

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