Hemoglobin A1C: DCA Vantage vs. Tosoh HPLC

Tascha Stanaitis, MLS(ASCP)CM and Donna J. Spannaus-Martin, PhD, MLS (ASCP)CM

CENTER FOR ALLIED HEALTH PROGRAMS
MEDICAL LABORATORY SCIENCES

Abstract

The Health Partners Specialty Clinic has been sending out hemoglobin A1c tests and wanted to determine if a point of care test would provide results with satisfactory correlation to the current Tosoh Bioscience HPLC send-out method. The point of care instrument could provide results to patients as soon as 10 minutes after sample collection compared to the 3 hour to 2 day turnaround time for the send out method. This study aims to address this inquiry by performing a method validation between the DCA Vantage immunoassay by Siemens and the Tosoh Bioscience HPLC.

For the testing, fifteen proficiency samples were run on the DCA Vantage and all the results were within the acceptable range. Additionally, seventeen patient samples of whole blood in EDTA were collected in duplicate. One sample was sent to the Central Laboratory to be run on the Tosoh HPLC instrument. The other sample remained at the Specialty Clinic where the blood had been collected, to be run on the DCA Vantage immunoassay instrument. The patient values of the new instrument were compared to the current method using regression statistics. Using EP Evaluator software, a Two Instrument Comparison report was generated. The hemoglobin A1c values of the seventeen samples ranged from 5.5% to 10.6% using the Tosoh method. The correlation coefficient for the DCA Vantage compared to the Tosoh method was 0.9920, and all values were within the designated total allowable error of 10%. This confirms that the DCA Vantage hemoglobin A1c results correlate well to the values obtained by the Tosoh method and can be used as a suitable substitute for the monitoring of hemoglobin A1c in diabetic patients at the Health Partners Specialty Clinic at Hudson.

Introduction and Background

According to the CDC, the prevalence of diabetes in U.S. population is 9.4% and continues to rise. They estimate that around 7.2 million people with diabetes are undiagnosed and untreated. With the multitude of health complications and lost work associated with diabetes, the estimated cost associated with the disease in the U.S. in 2012 was $245 billion dollars[1].

While there are many different tests for monitoring, screening, and diagnosing diabetes, hemoglobin A1c (HgbA1c) is becoming increasingly prevalent. HgbA1c is hemoglobin A that has been glycated. When high concentrations of glucose are continually present, there is a higher collision rate of glucose with hemoglobin. This causes spontaneous, irreversible binding, or glycosylation, to occur. Red blood cells have an average life span of 120 days. For this reason, measuring the HgbA1c found in the circulating red blood cells can be used to determine the average plasma glucose concentration during a 2-3 month period[2]. Diabetics can be treated or counseled on the control of their blood glucose levels based on these findings. Testing for HgbA1c can be performed on various analyzers using a variety of methods like: borate affinity, immunoassay, enzymatic, ion-exchange high-performance liquid chromatography (HPLC), and capillary electrophoresis[3].

Point of care tests have become available for evaluating HgbA1c and can provide faster results with the patient present. The largest benefit is to the patient who can have immediate feedback, whether adjustments in treatment need to be made or they can be validated for their efforts. Point of care tests that are classified as waived tests by the FDA can be performed on-site, which makes them more accessible to facilities without a full clinical laboratory. Acceptable quality controls and management oversight are still required as they would be with the reference method[4]. When replacing a method, point of care testing must be validated[5,6]. This can be done by comparing point of care results to the reference method currently in place. This study gives the results of such validation testing. The purpose of this study was to compare a new point of care immunoassay, DCA Vantage, to a reference method, Tosoh G8 HPLC, and evaluate the result reliability.

Materials and Methods

In this study, seventeen patient samples and fifteen proficiency samples were used in the validation process. The patient samples were from known diabetic patients without hemoglobin variants. Duplicate whole blood samples were collected in EDTA vacutainer tubes from each patient. One sample was tested on the DCA Vantage at the collection site while the other sample was sent to the central laboratory to be run on the reference method, the Tosoh G8. The DCA Vantage is an immunoassay that uses a traditional ferricyanide method for total hemoglobin determination. This is coupled with an inhibition latex agglutination which uses latex beads coated with monoclonal mouse anti-HgbA1c antibodies to measure the HgbA1c present. The instrument then calculates the percent HbA1c by taking the HgbA1c divided by the total hemoglobin x 100[7,8]. The Tosoh G8 uses a non-porous ion-exchange HPLC column to determine HgbA1c. HgbA1c is separated from most other hemoglobin variants based on charge. The chromatograph is used to determine the percent HgbA1c[9].

Results obtained were analyzed using regression statistics calculated on EP Evaluator's Two Method Comparison[10]. The correlation coefficient, slope and the allowable total error (Tea) were used to evaluate the statistical equivalence of the two methods. While the correlation coefficient and slope were used to demonstrate the correlation between the two methods, the TEa was set per the laboratory's policy as 10% of the concentration as determined by the Tosoh HPLC reference method. It was used to provide an upper limit of variation between methods.

Results and Statistics

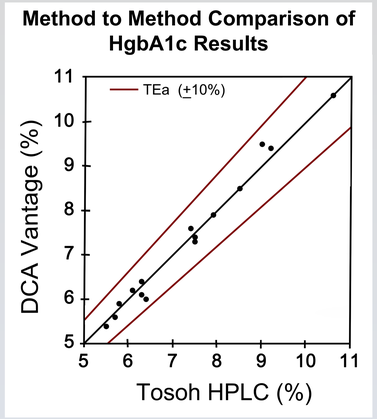

Figure 1. Regression analysis of DCA Vantage HGbA1c patient results vs. results obtained using the Tosoh HPLC reference method. Correlation coefficient = 0.9920; Slope = 1.069; Intercept = -0.49.

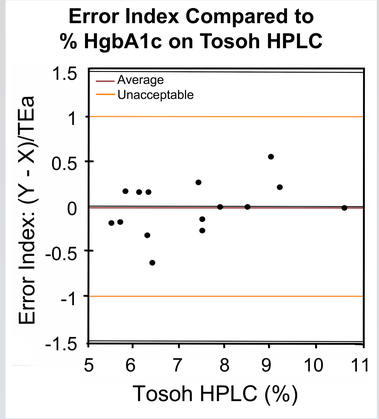

Figure 2. Scatter Plot of Error Index compared to the reference method. All values are within the allowable range between -1 and 1 (corresponds to ±10% Allowable Total Error).

Seventeen specimens were compared over a HgbA1c range of 5.5% to 10.6% obtained by the Tosoh HPLC reference method. All of the sample values were within the total allowable error range when comparing the difference between the two methods. The range of the error index ([Y-X]/Tea) was -0.63 to 0.56 with the average being -0.01. The largest error index was at a concentration of 6.4%[10].

Discussion and Conclusion

Hemoglobin A1c is very useful in monitoring how well a patient's blood glucose is being controlled. It is a powerful tool that can be used by physicians to recognize the need to adjust treatment or counsel patients on better diabetes management.

This study was able to provide statistically relevant data showing that the DCA Vantage by Siemens provides clinical results for HgbA1c that have acceptable correlation to the reference method, Tosoh G8 HPLC. With the DCA Vantage on site, the sample can be drawn and put directly onto the instrument which only takes 7 minutes to run. The reference method requires send out to the Central Laboratory, which is only open Mon- Fri and not 24 hours a day, therefore; results can take from 3 hours up to 2 days if the sample is drawn on a weekend. The DCA Vantage provides faster and equally reliable results that can improve patient care.

Some limitations of the study include the patient demographics for the samples used in the instrument testing. Patients did not suffer from hemoglobinopathies or other diseases that affect red blood cell turnover rate which can cause inaccurate HgbA1c results. Data from the National Glycohemoglobin Standardization Program (NGSP) states the DCA Vantage Method does not exhibit interference from hemoglobins C,S,E, D, or from concentrations of less than 10% hemoglobin F, whereas the Tosoh G8 system does show interference by these hemoglobin variants in versions other than the Tosoh G8 5.24[11]. Additional studies will be needed to determine correlations in patients with hemoglobin variants.

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