Accuracy Assessment of the A1cNow

Background and Rationale

The Diabetes Control and Complications Trial (DCCT) convincingly proved that glucose control closer-to-normal range ("tight" glycemic control) reduced the likelihood of the eye, kidney, and nerve complications of diabetes. Hemoglobin A1C testing is an indicator of the average blood glucose control over the past 2–3 months. The American Diabetes Association (ADA) recommends an A1C test every 3 months and, recommends that the patient's A1C level should be below 7%.[(1)] The A1cNow® Monitor (Metrika, Inc., Sunnyvale, CA) was developed as a single-use test for measuring hemoglobin A1c at home.. The device is certified by the National Glycohemoglobin Standardization Program (NGSP), is CLIA waived, and has been cleared by the U.S. Food and Drug Administration (FDA) for home use. The device is the size of a pager and requires one drop of blood to perform the test. Results are displayed in approximately 8 minutes.

The purpose of this study is to determine the accuracy of the device when used by patients and if it differs when used by trained health care providers.

Protocol

1. Thirty subjects will be enrolled in this ancillary study.
2. Subjects participating in another DirecNet protocol are eligible to participate.
3. During the Enrollment visit, subjects will be provided with the A1cNow and a home glucose meter and will be instructed to perform two tests on the day prior to their next study visit or hospital admission. The two tests will be done at the same time. In addition, subjects will also be asked to perform a blood glucose test on the study HGM at the same time.
4. Subjects (parents) will be asked to read the instructions which accompany the device to perform the test. No additional instructions will be provided by the study personnel.
5. One or two days prior to the next visit or hospital admission, the study nurse will contact the family by phone to as a reminder to do the testing.
6. At the time of the visit or admission, the subject's A1c will be tested by the study nurse or investigator using the A1cNow. A second test will be performed by the same person at the same time.
7. At the time of A1cNow testing, the subject's blood glucose will be checked using the study HGM
8. At the time the samples are tested on the A1cNow, a test will be run using the DCA2000 and a sample will be collected to send to the central laboratory.

Benefits

It is possible that an accurate home device which measures hemoglobin A1c may have an important role in the management of diabetes in children. Therefore, the results of this study are likely to be beneficial for children with diabetes.

The subjects will not directly benefit from being a part of this study.

Risks and Discomforts

Testing with the A1cNow requires collection of a blood sample by fingerstick. Fingersticks may produce pain and/or ecchymosis at the site.

The study may include other risks that are unknown at this time.

Analysis Plan

Each A1cNow value will be paired to a central laboratory A1c measurement.

For each of the 4 A1cNow measurements (2 by the subject at home and 2 by nurse/investigator at admission) the following difference measures will be calculated:

- Difference – A1cNow value minus the reference value.
- Absolute Difference – absolute value of the Difference.

- Relative Difference – Difference divided by the reference value.
- Relative Absolute Difference (RAD) – absolute value of the Relative Difference.

Summary statistics including median, mean, quartiles and range will be calculated for each of these difference measures. Results will be stratified by subject vs. staff measurements and additionally by reference A1C, clinical site, gender and age. The bootstrap will be used to generate confidence intervals for each measure and to compare results for subject vs. staff.

A repeated measures regression will be fit with the A1cNow value as the dependent variable and fixed effects for the reference value and subject vs. staff. The hypothesis of a common slope and intercept for subject and staff will be tested. Regression residuals will be examined for normality with any outliers being either truncated or excluded. If residuals show a skewed distribution, a transformation will be used in an attempt to improve the fit of the model. If no transformation can be found to give residuals with an approximate normal distribution, then regression results will not be reported. Scatter plots of A1cNow vs. reference values with Spearman's correlation will be constructed separately for subjects and staff.

Reliability analyses will compare the consistency of the simultaneous A1cNow values (ignoring the lab reference). Four difference measures analogous to those described above will be calculated. The Relative Difference and RAD will use the mean of the two A1cNow values in the denominator. Summary statistics will be given as described above. Separate analyses will be given for subject vs. staff measurements.

Analogous analyses will be done comparing the DCA2000 vs. reference values and the reliability of the two DCA2000 measurements. A QC reliability analysis will be done looking at the consistency of the two laboratory values in an analogous manner.

Sample Size

The chi-square distribution was used to approximate the relative error based on the root mean square assuming a roughly normal distribution.

Estimated Width of 95% Confidence Interval for RAD Assuming Mean Values of 5% or 10%.

Number of Subjects	Mean RAD Value	
	5%	10%
15	(4%, 8%)	(7%, 15%)
20	(4%, 7%)	(8%, 14%)
30	(4%, 7%)	(8%, 13%)
50	(4%, 6%)	(8%, 12%)
75	(4%, 6%)	(9%, 12%)
100	(4%, 6%)	(9%, 12%)

These calculations assume that any subjects dropping out, failing to perform the A1cNow measurements, or for whom laboratory values are unavailable would be replaced. These estimates allow for separate analyses of subject and staff measurements. They may be somewhat conservative because they do not take into consideration the added information from the duplicate A1cNow measurement. If simultaneous values from the same subject are highly correlated (a reasonable expectation), then little is gained from the duplicate and the above numbers apply. Otherwise, if the correlation, ρ, is non-negligibly less than 1, the necessary sample size is scaled by an approximate factor of $(1+\rho)/2$. Confidence intervals will likely be slightly larger for the median RAD.

Reference

1. ADA Clinical Practice Recommendations 2000.