

Assessing the Real-Life Relationship Between Average Capillary Blood Glucose and Hemoglobin A_{1C}: Is the Average Capillary Blood Glucose Value Clinically Useful?

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Abstract

Previous short-term studies have demonstrated a strong relationship between average capillary blood glucose and hemoglobin A_{1C} in a controlled setting. Whether this relationship is maintained in clinical practice over a long period is unknown. This study was designed to assess the predictive value of capillary for hemoglobin A_{1C} in subjects with intensively controlled insulin dependent diabetes mellitus for up to 5 years. Over a 5-year period, monthly determination of HbA_{1C} and average preprandial and bedtime capillary blood glucose was made in 14 subjects with insulin dependent diabetes mellitus who were receiving intensified therapy as a component of their participation in the Diabetes Control and Complications Trial. The predictive value of average capillary blood glucose for hemoglobin A_{1C} was determined by univariate regression analysis on 439 data points. In contrast to the results of previous studies, average capillary blood glucose was found to be a weak predictor of hemoglobin A_{1C} in this population. The relationship between average capillary blood glucose and hemoglobin A_{1C} is described by the following linear regression equation: $HbA_{1C} = 4.826 + (0.018)$ (average CBG [mg dl⁻¹]). Despite the low correlation coefficient, some individuals demonstrated a much stronger relationship between these variables than did others. We conclude that a statistically significant relationship between average capillary blood glucose and hemoglobin A_{1C} exists, but the long-term relationship between these variables is weaker than reported in previous short-term studies. Thus, clinical application of average capillary blood glucose to assess glycemic control is useful in the management of insulin dependent diabetes mellitus but requires clinical validation for each individual patient.

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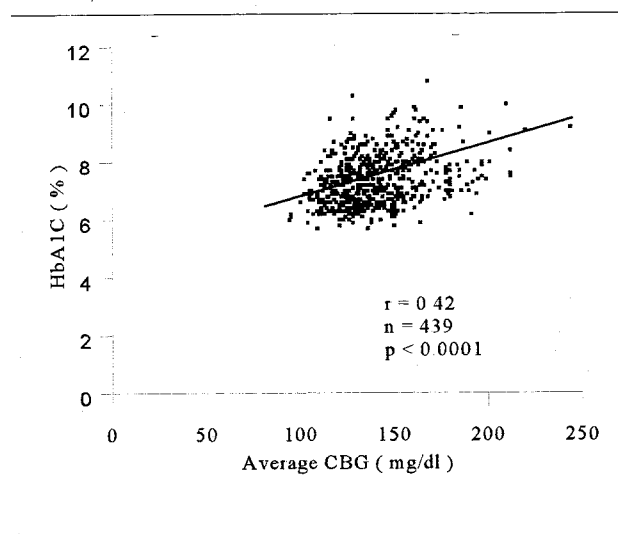
Results of the cooperative Diabetes Control and Complications Trial (DCCT) have emphasized the importance of normal glycemia in individuals with insulin-dependent diabetes mellitus (IDDM).¹ One approach to achieving this goal is to use intensive insulin therapy, which requires the measurement of several capillary blood glucose (CBG) determinations per day as a guide to frequent adjustments in subcutaneous insulin dosage.² Theoretically, average CBG values should predict hemoglobin A_{1C} (HbA_{1C}), and previous short-term studies³⁻⁷ support the strength of this relationship. However, the studies were performed under rigidly controlled conditions and showed correlation coefficients ranging from .47 to .98.

To address the question of the clinical usefulness of average CBG over the long term, we evaluated the relationship between monthly average CBG and HbA_{1C} in 14 intensively treated type I diabetic subjects over a 1- to 5-year period. Our data suggest that the long-term relationship between average CBG and HbA_{1C} is weaker than previously reported, and that large interindividual variation in the strength of this relationship exists among intensively managed diabetic patients.

... MATERIALS AND METHODS ...

Data from 14 intensively managed type I diabetic subjects who participated in the DCCT were reviewed retrospectively. Enrollment criteria for the DCCT included IDDM subjects aged 13 to 39 years with diabetes of 1 to 5 years duration who were C-peptide deficient and who lacked hypertension, hypercholesterolemia, severe diabetic complications, or other serious medical conditions, as previously described.¹ Data from all subjects randomized to the intensive treatment arm of the DCCT from the University of New Mexico center are included in this report. These data originally were obtained for use in patient management, rather than for research pur-

Figure 1. Univariate Regression Analysis Between Monthly Hemoglobin A_{1c} (HbA_{1c}) and Average Monthly Capillary Blood Glucose (CBG) (n = 439; r = .42; P < 0.0001)



poses. Subjects had a mean age of 32 ± 5 years (range, 24 to 40 years) and were studied at the University of New Mexico center over a 1- to 5-year period (mean interval, 4.3 ± 1.0 years).

All patients were instructed on proper blood-letting methods and glucose meter usage. All agreed to monitor their CBG levels before meals and at bedtime. Thirteen patients administered three or four insulin injections per day; the other used a continuous subcutaneous insulin pump. The mean HbA_{1c} level during the study period was $7.40 \pm 1.04\%$ (normal, $<6.05\%$).¹

Table 1. Results of Regression Analyses for Individual Patients

Patient ID	Correlation Coefficient	Sample Size
1	.47	32
2	.54	42
3	.05	52
4	.35	27
5	.74	25
6	.31	21
7	.70	23
8	.42	37
9	.44	16
10	.63	35
11	.67	20
12	.53	31
13	.13	46
14	.52	32

Subjects used the Glucometer M (Miles Inc, Elkhart, IN) or the One Touch II blood glucose monitoring system (Lifescan Inc, Milpitas, CA) for the duration of this study to obtain home blood glucose measurements. Both monitors have memory for the internal storage of blood glucose data. The meters calculated the averages automatically by dividing the sum of all entered CBG values by the total number of tests performed.

Patients were seen by study personnel monthly (mean interval, 35 ± 2 days SEM), at which time average CBG values were recorded directly from the patients' machines and samples were taken for determination of HbA_{1c}. CBG and HbA_{1c} data were collected during the same clinic visit. HbA_{1c} levels were determined by using high-performance liquid chromatography, as previously described.⁸ A total of 439 data points were obtained.

Average monthly CBG and HbA_{1c} values were compared by univariate regression analysis for the entire group and for each subject. Tabulated results are expressed as means \pm SD, unless otherwise specified.

... RESULTS ...

Results of the correlation and linear regression analyses are represented in Figure 1. The relationship between average CBG and HbA_{1c} resulting from the univariate regression analysis on all 439 data points is described by the following linear regression equation:

$$\text{HbA}_{1c} = 4.826 + (0.018)(\text{average CBG}[\text{mg dl}^{-1}]),$$

with $r = .42$ ($P < 0.001$) and a root mean squared error of 0.88. Individual r values ranged from .05 to .74 (Table 1).

... DISCUSSION ...

Previous short-term reports have shown a variable correlation between average CBG and HbA_{1c}.³⁻⁷ These studies are summarized in Table 2. The high correlation coefficients reported in the DCCT⁵ and in the studies by Nathan et al⁶ and Svendsen et al⁷ may be the result of the inclusion of postprandial glucose values in the CBG average. Moreover, the DCCT and the study by Svendsen et al reported the average of plasma glucose levels that were collected in capillary tubes as part of a seven-point glucose profile over the course of a single day. In the studies by Gebhart et al³ and Cefalu et al,⁴ postprandial glucose values were not included in the CBG average, and lower correlation coefficients were observed. Since subjects in the

Table 2. Summary of Previous Studies, Showing Study Design and the Reported Correlation Coefficients Between HbA_{1C} and Average CBG

Study/Year	Duration of Study	Interval for Mean CBG	No. of Samples/		No. of Patients	HbA _{1C} vs CBG
			Average	No. of Averages		
Current Study, 1995	1-5 yr	1 mo	~105	439	14	.42
Gebhart et al, 1991	6 wk	1 wk	*†	17	17	.549
		6 wk				.667
Cefalu et al, 1988	3 wk	3 days	*‡	62	62	.47
DCCT, 1987	12 mo	1 day	7	*	278	.80
Nathan et al, 1984	2 mo	2 mo	*	21	21	.96
Svendson et al, 1982	5 wk	1 day	75	30	30	.98

HbA_{1C} = hemoglobin A_{1C}; CBG = capillary blood glucose; DCCT = Diabetes Control and Complications Trial

*Specific numeric data not reported

†2.9 to 3.3 CBG values per day, averaged over 1 or 6 weeks

‡Preprandial and bedtime samples

DCCT assess and adjusted their diabetes treatment regimen primarily on the basis of preprandial CBG determinations, the average CBG results obtained from these subjects may not reflect their true average plasma glucose concentration (and hence, their HbA_{1C}) as well as for patients who routinely collect both pre- and postprandial CBG data.

Our study differs from previous studies in that it was performed in an outpatient setting, with patients receiving intensive insulin therapy, and its duration ranged from 1 to 5 years, the longest period yet reported. Our results indicate that the long-term average CBG—HbA_{1C} relationship is weaker in a real-life outpatient setting over a prolonged period than in a short-term, rigidly controlled situation. Nevertheless, a significant positive correlation between the average CBG and HbA_{1C} exists over the long term. Therefore, we believe that this measure does provide useful information.

Factors that may have contributed to the lower correlation coefficient observed in this study include our examination of the relationship between HbA_{1C} and the simple mean of CBG and the use of data originally collected for purposes of patient management. The simple CBG average is the information readily available to the patient as it is calculated automatically by the glucose meter. Tahara and Shima⁹ recently reported that HbA_{1C} more closely reflects the weighted mean of the antecedent plasma glucose values, with recent values contributing more heavily to the HbA_{1C} measurement. Moreover, because the information collected was obtained originally for patient-management purposes, rather than for research, our subjects were unaware that they were participating in a study on CBG. It is therefore unlikely that they used special precautions when performing CBG

testing. Hence, data obtained in our study more realistically reflect the technique used by the general diabetic population.

Physicians should be aware of patient-to-patient variability inherent in the average CBG—HbA_{1C} relationship. The strength of the relationship between these two variables differed within our group of clinically similar patients. Among the 14 patients, we found correlation coefficients that varied from .05 to .74 (Table 1). Because of this variability, clinicians may find it useful to record an individual patient's CBG and HbA_{1C} values over a long period, and to determine the strength of the relationship for the individual patient before using the CBG average in clinical decision making for that patient. Ultimately, home blood glucose monitors may be equipped with a program to allow for automatic calculation of a patient's predicted HbA_{1C} given the data stored in the machine and the predetermined relationship between average CBG and HbA_{1C} for each individual.

Areas for further investigation include the identification of the optimum number of CBG determinations per day that are necessary for establishing a more reliable prediction of HbA_{1C} as well as an evaluation of the importance of including a CBG determination during sleep (such as at 3:00 AM) to improve the reliability of the average CBG parameter. In summary, the monthly CBG average may provide useful information at no additional cost to both patients and healthcare providers. Nevertheless, clinicians must be aware of the limitations of this method.

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