

Utility of Casual Postprandial Glucose Levels in Type 2 Diabetes Management

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OBJECTIVE — Because readily available glycemic indicators are needed to guide clinical decision-making for intensification of diabetes therapy, our goals were to define the relationship between casual postprandial plasma glucose (cPPG) levels and HbA_{1c} in patients with type 2 diabetes and to determine the predictive characteristics of a convenient glucose cutoff.

RESEARCH DESIGN AND METHODS — We examined the relationship between cPPG levels (1–4 h post meal) and HbA_{1c} levels in 1,827 unique patients who had both determinations during a single office visit.

RESULTS — The population studied was predominantly African American and middle-aged, with average cPPG of 201 mg/dl and HbA_{1c} of 8.4%. The prevalence of HbA_{1c} $\geq 7.0\%$ was 67% and HbA_{1c} $> 6.5\%$ was 77%. Overall, cPPG and HbA_{1c} were linearly correlated ($r = 0.63$, $P < 0.001$). The correlation between cPPG and HbA_{1c} was strongest in patients treated with diet alone ($n = 348$, $r = 0.75$, $P < 0.001$) and weaker but still highly significant for patients treated with oral agents ($n = 610$, $r = 0.64$, $P < 0.001$) or insulin ($n = 869$, $r = 0.56$, $P < 0.001$). A cutoff cPPG > 150 mg/dl predicted an HbA_{1c} level $\geq 7.0\%$ in the whole group, with a sensitivity of 78%, a specificity of 62%, and an 80% positive predictive value. The same cPPG cutoff of 150 mg/dl predicted an HbA_{1c} level $> 6.5\%$, with a sensitivity of 74%, a specificity of 66%, and an 88% positive predictive value.

CONCLUSIONS — When rapid-turnaround HbA_{1c} determinations are not available, a single cPPG level > 150 mg/dl may be used during a clinic visit to identify most inadequately controlled patients and allow timely intensification of therapy.

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Intensive management of diabetes has been shown to decrease the risk of microvascular complications in patients with either type 1 or type 2 diabetes (1,2), and lower glucose levels are associated with reduced mortality from coronary heart disease in patients with type 2 diabetes (3–5). To provide a goal for management, guidelines published by the American Diabetes Association (ADA) suggest that optimal glycemic control is reached when HbA_{1c} is $< 7.0\%$ (6), whereas the American College of Endo-

crinology (ACE) and the International Diabetes Federation set that goal at $\leq 6.5\%$ (7,8). Accordingly, intensive diabetes management requires recognition of patients with inadequate glycemic control for whom therapy can be initiated or intensified until glycemic goals are reached.

Whereas HbA_{1c} remains the main glycemic indicator used to determine the success of diabetes treatment (2,9,10), a recent result often is not available during patient visits to guide adjustment of therapy. Rapid-turnaround HbA_{1c} methodol-

ogy is commercially available, but such determinations are not widely used in outpatient practice settings. In addition, patients frequently do not perform home blood glucose monitoring (11,12). To determine whether readily available casual glucose measurements obtained 1–4 h postprandially during office visits might constitute an acceptable alternative to guide timely adjustment of therapy, we studied the relationship of such glucose values to simultaneously measured HbA_{1c} levels. We also investigated the utility of casual glucose measurements in predicting a HbA_{1c} $\geq 7.0\%$ or $> 6.5\%$, indicating a need for intensification of therapy.

RESEARCH DESIGN AND METHODS

This study was conducted at the Grady Diabetes Clinic in Atlanta, Georgia, an outpatient facility that provides comprehensive diabetes care to inner-city residents. Most patients are African Americans and have type 2 diabetes (classified on the basis of typical clinical characteristics) (13). Patient characteristics available in the Grady Diabetes Patient Tracking System (DPTS) include date of birth, sex, race, date of diagnosis of diabetes, and type of therapy at presentation and at each subsequent visit. Patients were selected if they had type 2 diabetes, had an initial visit to the clinic between 1991 and 1998, had been followed in the Diabetes Clinic for at least 6 months (to exclude patients with new-onset diabetes in whom recent improvements in glucose control may not yet be reflected in their HbA_{1c} levels), and had a casual postprandial plasma glucose ([cPPG] 1–4 h postprandially; patients were asked when they last ate) and HbA_{1c} measured on the same day. For patients with multiple visits during the 1991–1998 period, only the last visit was selected. Based on the available data, we identified 1,827 unique patients having these characteristics.

The data were collected in part as baseline evaluation for the Improving Primary Care for African Americans with Diabetes (IPCAAD) study, a randomized, controlled trial to determine whether interventions aimed at provider behavior can improve diabetes control in a patient

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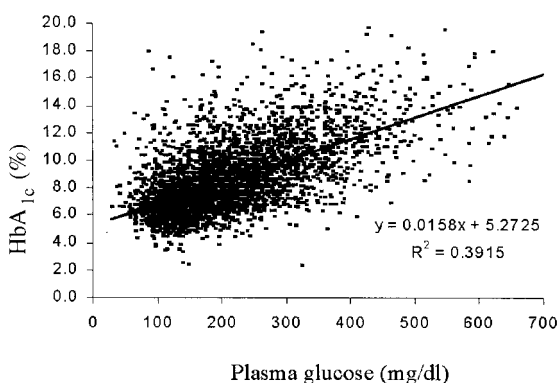
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Abbreviations: cPPG, casual postprandial plasma glucose; ROC, receiver operating characteristic.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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Figure 1—cPPG versus HbA_{1c}.

population at high risk for complications due to diabetes (14). The primary goal was to identify a cPPG cutoff that would identify close to 80% of patients with elevated HbA_{1c} ($\geq 7.0\%$ or $>6.5\%$, indicating inadequate control by American Diabetes Association and American College of Endocrinology criteria, respectively).

Analysis

Both plasma glucose and HbA_{1c} levels were measured at the Grady Memorial Hospital Laboratory. Plasma glucose levels were measured using a Hitachi 717 instrument (Roche, Indianapolis, IN). HbA_{1c} was determined with National Glycohemoglobin Standardization Program-certified instruments: a Diamat high-performance liquid chromatography system from Biorad (Hercules, CA) before 1997, and a Hitachi 717 immunoturbidimetric system from Roche (Indianapolis, IN) after 1997. Both assays had a normal range of 3.5–6.0% and were believed to provide comparable results ($r = 0.98$). Although a small number of patients in the present study had subnormal HbA_{1c} levels, such values usually cannot be explained on the basis of hemoglobinopathies and may reflect shortened survival of red cells. We used linear regression analysis to study the relationship between cPPG and HbA_{1c}. Receiver operating characteristic (ROC) analysis was used to study the sensitivity, specificity, and positive predictive value of specific cPPG cutoffs in predicting HbA_{1c}. ROC curves were generated using True Epistat statistical software (Richardson, TX), which also provides a calculated area under the ROC curve. The larger the area under the curve, the more accurate the test; an associated P value <0.05 was considered statistically significant.

RESULTS— The mean age (\pm SD) of the 1,827 patients was 57 ± 13 years, and mean duration of diabetes was 8.1 ± 8.0 years; 91% were African American, and 66% were women. The average HbA_{1c} was $8.4 \pm 2.6\%$, and mean cPPG was 201 ± 94 mg/dl. Treatment consisted of diet alone (average HbA_{1c} 7.2%, $n = 348$), oral agents (HbA_{1c} 8.3%, $n = 610$), and insulin alone or in combination with oral agents (HbA_{1c} 9.1%, $n = 869$). The HbA_{1c} level was $\geq 7.0\%$ in 67% of patient visits and $>6.5\%$ in 77% of visits.

Figure 1 shows that cPPG was significantly correlated with HbA_{1c} ($r = 0.63$, $P < 0.001$). Because patients treated with insulin were expected to have higher variability in their plasma glucose, we also studied the relationship between cPPG and HbA_{1c} according to type of therapy. The correlation between cPPG and HbA_{1c} was strongest in patients treated with diet alone ($r = 0.75$, $P < 0.001$). Even though the correlation between cPPG and HbA_{1c} was weaker in patients treated with oral agents ($r = 0.64$, $P < 0.001$) or insulin ($r = 0.56$, $P < 0.001$), it remained highly significant. Figure 2 shows the average (SE) HbA_{1c} for patients with cPPG in the

ranges 76–125, 126–175, 176–225, 226–275, 276–325, and 326–375 mg/dl; an average cPPG of 105 mg/dl corresponded to HbA_{1c} of 7.6%, cPPG of 153 mg/dl corresponded to HbA_{1c} of 8.0%, and cPPG of 201 mg/dl corresponded to HbA_{1c} of 8.8%.

To be useful for health care providers in decision-making for intensification of therapy, a test should be both sensitive, to detect most patients with poor glycemic control, and specific, to exclude patients with good glycemic control. Our primary goal was to identify a cPPG cutoff that would have a sensitivity and a positive predictive value of $\sim 80\%$. Using ROC analysis, we found that cPPG was a significant predictor of an HbA_{1c} $\geq 7.0\%$ and $>6.5\%$, with an area under the ROC curve of 0.78 for both ($P < 0.001$ for both). A cPPG cutoff value of 150 mg/dl constituted a convenient indicator that predicted an HbA_{1c} level $\geq 7.0\%$ in the whole group with a sensitivity of 78% and a specificity of 62%. The same cutoff predicted an HbA_{1c} level $>6.5\%$ with a sensitivity of 74% and a specificity of 66%.

Although the sensitivity and specificity of a cutoff provide useful information to identify good or poor glycemic control in a population of patients, positive predictive value is the main determinant of the utility of a cutoff with respect to individuals within the population. In this study population, in which the prevalence of an HbA_{1c} level $\geq 7.0\%$ was 67% and the prevalence of HbA_{1c} $>6.5\%$ was 77%, a cPPG cutoff of 150 mg/dl had a positive predictive value of 80% in identifying an HbA_{1c} level $\geq 7.0\%$ and a positive predictive value of 88% in identifying an HbA_{1c} level $>6.5\%$. For each HbA_{1c} target, the positive predictive value was highest in insulin-treated pa-

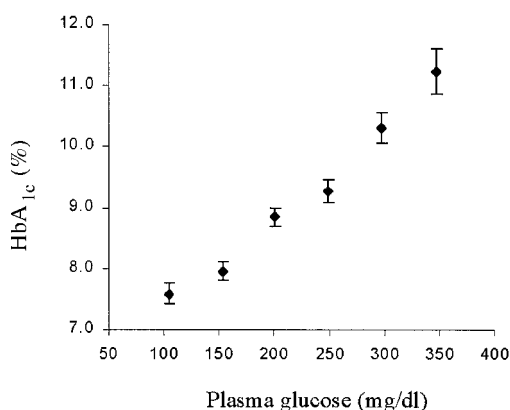


Figure 2—Average HbA_{1c} (SE) corresponding to average cPPG of the following cPPG groups: 76–125, 126–175, 176–225, 226–275, 276–325, and 326–375 mg/dl.

Table 1—Sensitivity, specificity, and PPV of cPPG ≥ 150 mg/dl in identifying $\text{HbA}_{1c} \geq 7.0$ and $>6.5\%$

Therapy	$\geq 7.0\%$				$>6.5\%$			
	Prevalence	Sensitivity	Specificity	PPV	Prevalence	Sensitivity	Specificity	PPV
All patients	67	78	62	80	77	74	66	88
Diet alone	46	63	76	68	57	57	77	77
Oral agents	67	81	56	79	78	76	57	86
Insulin	75	79	55	84	84	77	62	91

tients and lowest in patients managed with diet alone (Table 1).

CONCLUSIONS— Our study shows that a cPPG level can be used to guide intensification of diabetes therapy in the absence of home glucose monitoring records or a current HbA_{1c} level. In our clinic, cPPG of 150 mg/dl identified 78% of those with $\text{HbA}_{1c} \geq 7.0$ and 74% of patients with $\text{HbA}_{1c} >6.5\%$. The selection of the cutoff of 150 mg/dl was based largely on the associated positive predictive values; the overlapping of the points in Fig. 1 obscures the fact that, in a population of patients with diabetes, a cPPG of 150 mg/dl obtained during a typical clinic visit often reflects a surprisingly high HbA_{1c} level (Fig. 2). The specificity of this cutoff was 62–66%, i.e., one-third of patients with adequate HbA_{1c} levels would be falsely identified as inadequately controlled, but the predictive value of the 150 mg/dl cutoff was 80–88%, i.e., 80–90% of patients with plasma glucose level >150 mg/dl also had an elevated HbA_{1c} . The cPPG was better correlated with HbA_{1c} in patients treated with diet alone or with oral agents as compared with patients treated with insulin (alone or in combination with oral agents). Although the present study was aimed at identifying a cutoff that could be used to guide practical patient management to achieve glycemic control, the findings are consistent with our previous examination of the utility of fasting and random plasma glucose levels in predicting poor glycemic control (15) as well as with previous observations of greater variability in plasma glucose values in insulin-treated patients (16).

Even though fasting plasma glucose has been used along with HbA_{1c} as a marker of glycemic control (17,18), many studies suggest that its utility is limited or that it is inferior to a nonfasting glucose. Avignon et al. (19) showed that, in pa-

tients with type 2 diabetes treated with diet alone or with oral agents, nonfasting plasma glucose was better than fasting plasma glucose in predicting glycemic control as reflected by HbA_{1c} . Even in insulin-treated patients with type 2 diabetes, the combination of prelunch and predinner blood glucose measurement seemed to reflect overall glycemic control better than the fasting glucose, as long as patients were on a stable insulin regimen (20). Information from the Diabetes Control and Complications Trial also showed that, in patients with type 1 diabetes, fasting plasma glucose tended to underestimate the HbA_{1c} level, whereas postmeal plasma glucose was a better indicator of HbA_{1c} and glycemic control, especially when measured after lunch (21).

The availability during clinic visits of a glycemic indicator that reflects HbA_{1c} would be a useful tool to guide intensification of diabetes therapy in inadequately controlled patients. Providers frequently believe they cannot evaluate a patient's glycemic status unless they have a current HbA_{1c} level or records of the patient's home blood glucose monitoring. A previous HbA_{1c} level would probably be of little help, because we have shown previously that when both a current plasma glucose and a 2-month-old HbA_{1c} measurement are available, health care providers tend to put more emphasis on the plasma glucose level in their clinical decision-making (22). Therefore, the use of a specific cutoff for a casual plasma glucose that identifies most inadequately controlled patients could prompt providers to advance pharmacologic therapy when needed and help minimize the problem of “clinical inertia”—failure to intensify therapy when indicated (23). Consistent with this hypothesis, we have found a higher likelihood of action by physicians (less clinical inertia), an increase in intensification of therapy, and corresponding improvement in HbA_{1c} levels when a

cPPG of 180 mg/dl was used to prompt intensification of therapy (24).

Our study has some limitations. Because the specificity of a 150-mg/dl glucose cutoff is 62–66%, approximately one-third of patients with adequate HbA_{1c} levels would be falsely identified as poorly controlled and might have their therapy advanced, therefore putting them at risk of hypoglycemia. However, we have previously shown that hypoglycemia tends to be uncommon and mild in patients with type 2 diabetes, even in a setting in which intensive diabetes therapy is guided by treatment algorithms based on glucose levels obtained during office visits (25). Use of the 150-mg/dl guideline in the Grady Medical Clinic has not been believed to result in major problems with hypoglycemia, and we have found, in a retrospective analysis, that among patients who had an $\text{HbA}_{1c} <6.5\%$ and who had their pharmacologic therapy advanced, only 12% reported hypoglycemia on follow-up 3 months later (unpublished data). Nonetheless, clinical judgement should be exercised in decision-making. Therefore, physicians often see patients who present with high glucose levels but have had no recent HbA_{1c} levels and must choose between immediate action on the basis of guidelines that are useful but imperfect or delayed action via ordering repeat HbA_{1c} tests and follow-up appointments, which may or may not be kept. Because HbA_{1c} levels in Americans with diabetes have risen from an average of 7.8% in 1988–1994 to 8.1% in 1999–2000 (26), we favor ordering the test but also intensifying therapy if glucose levels are >150 mg/dl. Although it seems likely that capillary glucose (faster and less expensive) could be used instead of plasma glucose based on comparability in other settings (27,28), we did not test this hypothesis directly, and it is possible that cutoffs would need to be standardized to individual test systems (27,29). It is also possible that the relationship between cPPG and HbA_{1c} would be tighter if adjusted for time of day and hours since the last meal (30), along with differences in age, BMI, etc., but the resulting complexity (a nomogram of cutoffs) would likely make the guideline too cumbersome to use in practice. A similar “keep it simple” approach is generally preferred for screening for gestational diabetes (31,32).

Finally, it should be emphasized that

the predictive values will be influenced by the prevalence of inadequate glycemic control in the patient population. As shown in our results, a better predictive value for identification of suboptimal glycemic control is obtained in subgroups in which poor glycemic control is more prevalent. Therefore, the cutoff plasma glucose of 150 mg/dl had better predictive value in patients treated with insulin or oral agents compared with patients managed with diet alone, because the patients treated with pharmacologic agents tended to have higher HbA_{1c} levels. Such observations suggest that the 150-mg/dl cPPG cutoff may be particularly useful to guide management in settings in which HbA_{1c} levels tend to be high, such as in some primary care sites (33–35).

In conclusion, we have identified a cutoff for casual plasma glucose that may be used as an indicator of glycemic control in patients with type 2 diabetes when home blood glucose monitoring records or current HbA_{1c} levels are not available. More frequent use of this marker to prompt intensification of therapy should help overcome “clinical inertia,” reduce HbA_{1c} levels, and improve diabetes outcomes. Although clinical judgment should still be exercised in the decision to advance therapy, expanded use of the 150-mg/dl glucose cutoff may be particularly important in the effort to improve diabetes management in the primary care setting.

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