Relationship Between Fasting and Day-Long Plasma Glucose Concentrations in Diet-Treated Patients With Type 2 Diabetes

F. Abbasi and Gerald M. Reaven

To define the relationship between fasting and postprandial hyperglycemia, plasma glucose concentrations were determined before and after breakfast and lunch in 42 diet-treated patients with type 2 diabetes. Breakfast was consumed at 8:00 AM and lunch at 12:00 PM, with blood drawn hourly from 8:00 AM to 4:00 PM for measurement of plasma glucose concentration. The results demonstrated highly significant correlation coefficients (*r*) between fasting plasma glucose concentration and any individual hourly value (*r* values varying between 0.86 and 0.91). Furthermore, fasting plasma glucose concentrations and the total integrated glucose response areas, post-breakfast (8:00 AM to 12:00 PM), post-lunch (12:00 PM to 4:00 PM), and day-long (8:00 AM to 4:00 PM) were also highly correlated, with *r* values of 0.95, 0.91, and 0.94, respectively. These results demonstrate that fasting and postprandial glucose concentrations are almost perfectly correlated in diet-treated patients with type 2 diabetes, and that determination of fasting plasma glucose concentrations in these individuals provides an excellent estimate of degree of glycemic control.

THE RESULTS OF THE United Kingdom Prospective Diabetes Study (UKPDS) have provided powerful evidence that improved glycemic control can decrease the microangiopathic complications of type 2 diabetes.[1] The findings of the UKPDS, as well as the availability of new antihyperglycemic drugs, have resulted in renewed efforts to achieve good glycemic control in patients with type 2 diabetes. In this context, questions have been raised as to the utility of fasting plasma glucose concentration as an adequate indicator of glycemic control,[2-5] with the possibility being raised that measurements of postprandial plasma glucose concentration may provide greater clinical insight. In this context, it should be emphasized that the relationship between fasting and postprandial hyperglycemia will be a complex one, varying as a function of the relative amounts and kinds of macronutrients ingested at each meal, the insulin secretory response of the individual patient, as well as the form of pharmacologic treatment. In an effort to begin exploring this issue, we have measured plasma glucose concentration at hourly intervals for 8 hours, before and after breakfast and lunch, in 42 diet-treated patients with type 2 diabetes. Using these data, we then defined the relationship between fasting plasma glucose concentration and the subsequent hourly plasma glucose concentrations. The results of this analysis indicate that the correlation between fasting and day-long plasma glucose concentration is remarkably high in diet-treated patients with type 2 diabetes.

METHODS

The study was approved by the Stanford Human Subjects Committee, and each volunteer gave written informed consent before entering the General Clinical Research Center (GCRC). Forty-two patients volunteered for this study: 28 men and 14 women. Their demographic and metabolic characteristics are listed in Table 1. The values for both fasting plasma glucose concentrations and concentrations of glycosylated hemoglobin (HbA_{1c}) were measured after at least 4 weeks of stable plasma glucose levels on a weight maintenance diet, off all pharmacological treatment. The participants were free of diabetic vascular complications, and had a normal blood count and chemical screening battery.

After demonstrating glycemic stability, patients were admitted to the GCRC of Stanford Medical Center. After an overnight fast, plasma glucose[6] concentrations were measured at hourly intervals from 8:00 AM to 4:00 PM. On the day these measurements were made, subjects consumed identical isocaloric test meals containing (as percentage of total calories) 15% protein, 40% fat, and 45% carbohydrate. Subjects were given breakfast at 8:00 AM (20% of daily calories) and lunch at noon (40% of daily calories). After breakfast and lunch, the subjects consumed only water or noncaloric decaffeinated beverages until the study ended at 4:00 PM.

Table 1. Demographic and Metabolic Characteristics of the Study Subjects

Characteristic	Mean ± SE	Range
Age (yr)	58 ± 2	33-71
Gender (M/F)	28/14	—
Body mass index (kg/m^2)	28.9 ± 0.7	20-36.3
Duration of diabetes (yr)	6 ± 1	0.2-25
Fasting plasma glucose (mmol/L)	12.2 ± 0.4	7.6-17.0
Hemoglobin A_{1c} (%)	10.3 ± 0.4	7.4-16.5

The data are expressed as mean ± SEM. Statistical analysis consisted of the calculation of Pearson's correlation coefficients between the fasting plasma glucose concentration and (1) integrated plasma glucose response from 8 AM to noon (post-breakfast glycemic response); (2) integrated plasma glucose response from noon to 4 PM (post-lunch glycemic response); (3) total 8-hour integrated plasma glucose response; and (4) individual hourly values from 9:00 AM to 4:00 PM. The post-breakfast, post-lunch, and day-long integrated responses were calculated by the trapezoidal approach.

RESULTS

The mean (± SEM) plasma glucose response in the 42 diet-treated patients is shown in Fig 1. The experimental pop-

From the Department of Medicine, Stanford University, School of Medicine Stanford, CA.

Submitted April 23, 2001; accepted October 4, 2001.

Supported by grants from the National Institutes of Health (RR-00070 and DK-30732).

Address reprint requests to Gerald M. Reaven, MD, Falk Cardiovascular Research Center, Stanford University School of Medicine, 300 Pasteur Dr, Stanford, CA 94305-5406.

0026-0495/02/5104-0010$35.00/0

doi:10.1053/meta.2002.31325

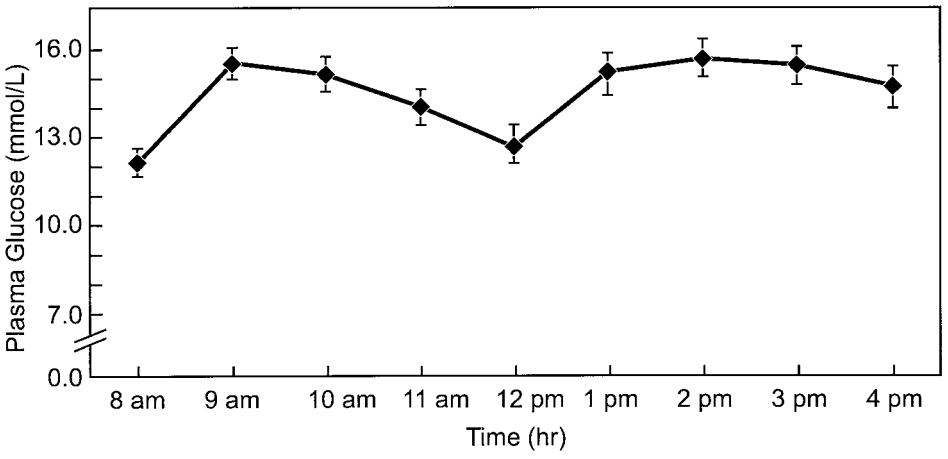

Fig 1. Mean (± SEM) plasma glucose concentrations before and after breakfast and lunch from 8:00 AM to 4:00 PM in 42 patients with diet-treated type 2 diabetes. Breakfast was eaten at 8:00 AM and lunch at 12:00 PM.

ulation was quite hyperglycemic, and the glycemic excursions after the 2 meals were reasonably comparable.

The total integrated glucose responses for the 4 hours following breakfast and lunch, as well as the total integrated response for the entire 8-hour period, are listed in Table 2. The excursions following the 2 meals were similar, as were the ranges of the responses. Finally, the approximate 3-fold variation between the lowest and the greatest post-meal response indicates that the degree of glycemic control varied to a reasonable extent in our study population.

Figure 2 presents the relationship between fasting plasma glucose concentration and the 1-hour post-breakfast and lunch responses and the total 8-hour integrated glucose response. To evaluate the impact of differences in fasting plasma glucose concentration on these relationships, the 42 patients were divided into tertiles on the basis of their degree of fasting hyperglycemia, and identified in the figure by different symbols. It is evident from Fig 2 that the correlation coefficients between fasting plasma glucose and the 3 estimates of postprandial hyperglycemia were highly significant ($r = 0.86$ to 0.95, $P < .0001$). Furthermore, there does not seem to be any apparent deviation from the overall relationships as a function of differences in fasting plasma glucose concentration. Likewise, fasting plasma glucose concentration was also significantly correlated with the total integrated glucose responses for the 4 hours following breakfast ($r = 0.95$, $P < .0001$) and lunch ($r = 0.91$, $P < .0001$).

Table 3 lists the correlation coefficients between the fasting plasma glucose concentration and the individual hourly values from 9:00 AM to 4:00 PM in the entire study population. It is obvious that the very close relationship between the fasting plasma glucose concentration and the integrated post-meal glucose response, shown in Fig 2, was also seen when the fasting plasma glucose concentration was correlated with the hourly postprandial values in response to breakfast and lunch ($r = 0.86$ to 0.91, $P < .001$).

Table 2. Postprandial Glycemic Responses of the 42 Diet-Treated Patients With Type 2 Diabetes

Glycemic Response	Mean ± SE	Range
Post-breakfast (mmol/L · 4 h)	57.5 ± 2.1	36.7-81.4
Post-lunch (mmol/L · 4 h)	60.0 ± 2.6	34.2-90.4
Day-long (mmol/L · 8 h)	117.5 ± 4.6	72.5-168.0

DISCUSSION

Perhaps the most useful way to put our results in perspective is to begin by making a distinction between the importance of postprandial hyperglycemia in defining the risk of vascular complications in patients with diabetes, as differentiated from the relationship between fasting and postprandial hyperglycemia. There should be little question following the publication of the results of the UKPDS[1] of the association between hyperglycemia and microangiopathy in patients with type 2 diabetes. Patients spend a large proportion of the 24-hour period in the postprandial state, and the magnitude of hyperglycemia is certainly accentuated during these periods. Thus, it stands to reason that the greater the degree of postprandial hyperglycemia, the more at risk an individual to the long-term microvascular complications of type 2 diabetes. There should be no confusion as to the importance of postprandial hyperglycemia in this context.

On the other hand, acceptance of the fact that degree of postprandial hyperglycemia plays a central role in determining the risk of microangiopathy in patients with type 2 diabetes, does not mean that its measurement provides the most useful information as to the degree glycemic control in these patients. Indeed, it is obvious from the results in Table 3 that fasting and postprandial plasma glucose concentrations were highly correlated throughout the day in the 42 hyperglycemic patients we studied. Given these results, it seems clear that measurement of fasting plasma glucose concentration in diet-treated patients with type 2 diabetes provides as much information as to degree of glycemic control as would any measurement of postprandial glucose level throughout the day.

It should be emphasized that our results were obtained under carefully controlled conditions in a research ward, with identical test meals serving as the glycemic stimulus. Thus, our results do not negate the potential utility of health-care professionals using variations in postprandial glycemia as an educational tool. For example, by changing life-style variables, eg,

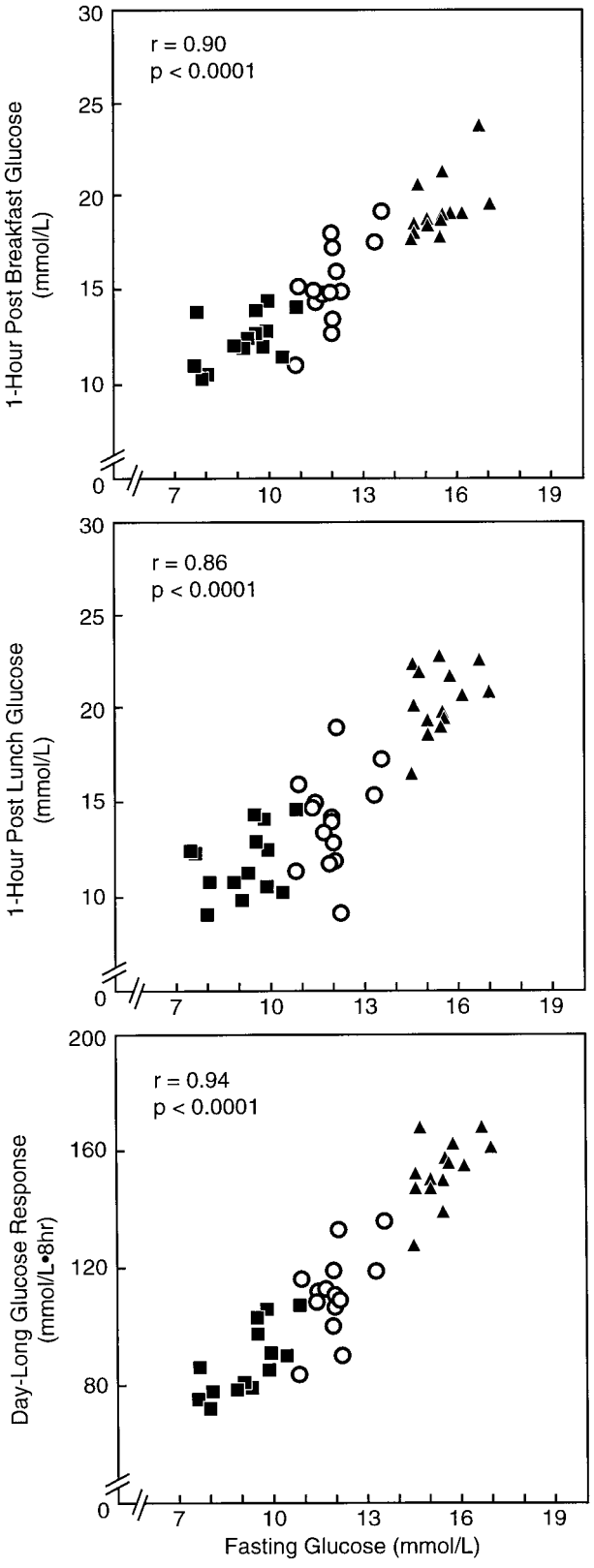

Fig 2. Relationship between fasting plasma glucose concentrations and the post-meal glucose responses. The 42 patients are divided into tertiles on the basis of their fasting plasma glucose concentrations: lowest tertile (■), middle tertile (○), and highest tertile (▲).

Table 3. Correlation Coefficients (*r*) Between Fasting Plasma Glucose Concentration and Subsequent Hourly Values

Postprandial Glucose	Correlation Coefficient*
9:00 AM	0.90
10:00 AM	0.91
11:00 AM	0.91
Noon	0.91
1:00 PM	0.86
2:00 PM	0.88
3:00 PM	0.90
4:00 PM	0.91

*P value $<$ .0001 for all time points.

meal size, macronutrient content, level of physical activity, etc, variations in postprandial glucose excursions following such interventions may help patients understand the impact of these variables on their efforts to achieve good glycemic control. On the other hand, the importance of such educational efforts should not obscure the fact that postprandial glucose excursions, when measured in response to two standard meals, are highly correlated with the fasting plasma glucose concentration.

Finally, presence of an almost perfect correlation between fasting and postprandial glucose concentrations in diet-treated patients with type 2 diabetes does not mean this relationship would be as close once pharmacologic treatment is initiated. In this latter instance, knowledge of fasting plasma glucose concentration might not provide as much insight as to degree of glycemic control as would a measure at a given postprandial time. To the best of our knowledge, the information needed to make that decision is not available. Furthermore, given the apparent dependence of postprandial hyperglycemia on the characteristics of different pharmacologic agents, amount of food consumed at any given meal, the nature of the macronutrients ingested, and the time after the measurement is made, it could be argued that fasting plasma glucose concentration might still provide the most reproducible guide to overall evaluation of glycemic control. Until these questions can be answered, it seems premature to conclude that determination of postprandial hyperglycemia be substituted for fasting plasma glucose concentration as a guide to treatment of type 2 diabetes.

REFERENCES

1. UK Prospective Diabetes Study Group: Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes. Lancet 352:837-853, 1998

2. Trovati M, Burzacca S, Mularoni E, et al; A comparison of the predictive power for overall blood glucose control of a "good" fasting level in type 2 diabetic patients on diet alone or with oral agents. Diabet Med 9:134-137, 1992

3. Avignon A, Radauceanu A, Monnier L: Nonfasting plasma glucose is a better marker of diabetic control than fasting plasma glucose in type 2 diabetes. Diabetes Care 20:1822-1826, 1997

4. Home P: Is the regulation of prandial glucose important in type 2 diabetes? Diabetes Metab 1999;25:20-21, 1999

5. Bastyr JE, Stuart CA, Brodows RG, et al: Therapy focused on lowering postprandial glucose, not fasting glucose, may be superior for lowering HbA_{1c}. Diabetes Care 23:1236-1241, 2000

6. Kadish AH, Litle RL, Sternberg JC: A new and rapid method for determination of glucose by measurement of rate of oxygen consumption. Clin Chem 14:116-131, 1968