Evaluation of the Use of Fasting Plasma Glucose as a New Diagnostic Criterion for Diabetes in Asian Indian Population

Several studies (1–4), including ours, have pointed out that the use of fasting plasma glucose (FPG) of ≥140 mg/dl (7.8 mmol/l) for the diagnosis of diabetes (5) resulted in a low sensitivity and that to improve its sensitivity, a lower value of 126 mg/dl (7.0 mmol/l) may therefore be suitable. Recently, the Expert Committee on the Diagnosis and Classification of Diabetes of the American Diabetes Association (ADA) recommended that for epidemiological studies, estimates of diabetes prevalence and incidence should be based on an FPG ≥126 mg/dl (6). The new cutoff was based on the observation that this degree of hyperglycemia usually reflected a serious metabolic abnormality associated with micro- and macrovascular complications. The term impaired fasting glucose (IFG) has been used for cases with FPG ≥110 and <126 mg/dl. To assess the change that could occur, we made a comparative analysis of the results obtained with the 2-h plasma glucose (PG) of ≥200 mg/dl and the present criterion, using the data from a large epidemiological survey in southern India (7).

The data available from the urban survey in the city of Madras, Tamil Nadu, India, conducted during 1994–1995, was used for the analysis. The details of the survey procedures are already published (7). Diabetes was diagnosed using the World Health Organization (WHO) criterion of 2-h PG value of ≥200 mg/dl and the clinical records of diagnosis and treatment of known cases. Impaired glucose tolerance (IGT) was diagnosed if the 2-h PG value was between 140 and 199 mg/dl. The study was performed in 2,183 adults (M:F, 1,081:1,102) aged ≥20 years, with a mean age of 40 ± 12 years. The age-adjusted prevalence of diabetes, adjusted to the 1991 census, was 11.6%. Among these subjects, 55% had known cases of diabetes. In the present analysis, FPG ≥126 mg/dl was used as the diagnostic criterion for newly diagnosed cases of diabetes. If the FPG was ≥110 and <126 mg/dl, it was considered to indicate IFG (6).

Considering a 2-h PG ≥200 mg/dl to be the reference criterion for the diagnosis of diabetes, FPG of ≥126 mg/dl provided a sensitivity of 83%, i.e., it detected 83% (114/137) of the diabetes cases. This value was higher than the 50% sensitivity obtained by using an FPG cutoff value of ≥140 mg/dl. Prevalence of newly diagnosed diabetes was 5.2% according to the WHO criterion and 4.3% by the new criterion. The difference was not statistically significant ($\chi^2 = 2.7$, $P = 0.1$). Among the subjects with newly detected diabetes, 17.3% with a 2-h PG of ≥200 mg/dl would be classified as nondiabetic. The prevalence was lower (2.6%) when an FPG cutoff value ≥140 mg/dl was used ($P < 0.001$ compared with the other two groups). Similarly, the difference between the two estimates of total diabetes prevalence was not statistically significant (11.6 and 10.7%) ($\chi^2 = 0.75$, $P = 0.39$), unlike the results occurring when an FPG cutoff value of ≥140 mg/dl was used, in which the estimated prevalence was much lower (9.0 vs. 11.6%) ($\chi^2 = 67.9$, $P < 0.001$). Using an FPG that was ≥110 and <126 mg/dl, IFG was present in only 48% of the cases classified as IGT by the WHO criterion (5).

An assessment of cardiovascular risk factors was also made. Measurements of blood pressure, age, sex, height, weight, and waist-to-hip ratio (WHR) were made for all subjects. Fasting serum cholesterol and triglycerides and 2-h plasma insulin measurements were made in 701 subjects. The cutoffs for normal values obtained using the means ± 2 SD in the normoglycemic, nonhypertensive population were as follows: BMI, 29.2 kg/m^2; WHR in men, ≥0.92; WHR in women, ≥0.88; cholesterol, ≥234 mg/dl; triglycerides, ≥204 mg/dl; 2-h plasma insulin, ≥55 μU/ml. The presence of increased levels of cholesterol or triglycerides was considered to represent dyslipidemia in this study. Hypertension was defined as systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥95 mmHg or was considered to be present if the person was being treated with antihypertensive drugs.

The cutoff values of FPG ≥126 and ≥140 mg/dl yielded similar prevalence rates for all the cardiovascular risk factors: hypertension, 36 and 39%, respectively; raised cholesterol or triglycerides, 57 and 62%; central obesity, 64% for both; obesity, 8.0 and 9.6%; elevated 2-h plasma insulin, 40 and 36%. In subjects having FPG ≥110 and <126 mg/dl (IFG), 77% had hyperinsulinemia. Although identification of IFG has only 48% sensitivity in detecting IGT (2-h PG, 140–199 mg/dl), it appears useful in the early diagnosis of cardiovascular risk factors.

Our results suggest that the prevalence of diabetes would be slightly underestimated by using the new criterion of FPG ≥126 mg/dl. However, because it is less time-consuming, easy to perform, and less expensive, it may be used as an alternative to the oral glucose tolerance test (OGTT) in large surveys.

It was noted that the lower cutoff value for FPG in the present criteria gave a percentage of cardiovascular risk factors similar to that given by FPG ≥140 mg/dl. Cardiovascular risk factors seem to occur even at a lower threshold of FPG. This finding corroborates the observation of Jackson et al. that in adults without known diabetes, the FPG was as closely associated as the 2-h PG with indexes of macrovascular disease (8). In another study, the association of peripheral vascular disease with FPG and with 2-h PG appeared similar in elderly Caucasians (9).

These observations in Asian Indians support the rationale for the ADA's revised criteria for diagnosis of diabetes. The sensitivity for diagnosis of diabetes was significantly higher than that of the previous FPG cutoff value of ≥140 mg/dl. The classification of IFG also seems to be important for early detection of cardiovascular disease risk factors. However, it must be mentioned that when feasible, an OGTT definitely improves the sensitivity.

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Assessing the Antihyperglycemic Effect of Acarbose

Solid or liquid test meal?

The α-glucosidase inhibitor acarbose improves glycemic control by slowing carbohydrate absorption and reducing the rise of blood glucose levels after eating (1). Postprandial blood glucose has been measured in clinical trials to titrate the dose of acarbose (2), a procedure that may be useful in clinical practice. For this purpose, a standard test meal is required because the type and amount of carbohydrate influence glycemic responses (3). Meals containing glucose or lactose (milk) cannot be used because acarbose does not affect their absorption. Liquid formulas have been used for convenience (2), but they may not have the same effect as a normal diet.

To see whether the nature of the test meal influenced the antihyperglycemic effect of acarbose, six normal subjects (three men and three women: aged 34 ± 4 years; BMI 23.9 ± 1.4 kg/m^2) and six diabetic subjects (four men and two women: aged 62 ± 3 years; BMI 31.3 ± 2.0 kg/m^2; four treated by diet alone and two receiving glyburide) were studied on four separate mornings after overnight fasts. Each morning, subjects consumed either a liquid or a solid mixed meal with 50 mg acarbose or placebo, according to a randomized Latin square design. The liquid meal (336 ml Ensure, Abbott, Saint-Laurent, Quebec, Canada) contained 357 kcal, 54.5 g carbohydrate (50.0 g dextrins and sugars; 4.5 g dietary fiber), 9.6 g fat, and 13.4 g protein. The solid meal (Diabetes Screening Product [DSP], Ceapro, Edmonton, Alberta, Canada), containing 360 kcal, 53.8 g carbohydrate (41.1 g starch, 8.9 g sugars, and 3.8 g dietary fiber), 10.7 g fat, and 12.1 g protein, was taken with 1 cup of water. The DSP is a standardized test meal in the form of five wafers made from oats, honey, canola oil, and soy protein. Capillary blood glucose was measured before and at various intervals after the subjects started to eat, using a YSI analyzer (YSI, Yellow Springs, OH). Incremental areas under the curve (AUCs) were calculated geometrically (4). Blood glucose concentrations and AUCs after administration of acarbose and placebo were compared separately for each test meal and each subject group by the paired *t* test.

In normal subjects, acarbose had no significant effect on glycemic responses compared with placebo after the liquid meal, but blood glucose was significantly reduced at 15, 30, and 45 min after administration of the DSP (Fig. 1). The reduction of blood glucose AUCs by acarbose was not significant after the liquid meal (−35 ± 20%) but was significant after administration of the DSP (30 ± 11%; $P < 0.05$). In diabetic subjects, acarbose significantly reduced blood glucose after the liquid meal at 90 and 120 min and reduced AUC by 37 ± 5% ($P < 0.01$). After administration of the DSP, acarbose reduced blood glucose significantly at 30, 60, 90, and 120 min and reduced AUC by 38 ± 7% ($P < 0.01$). In diabetic subjects, the mean reduction in blood glucose induced by acarbose 60 min after administration of the DSP (2.7 ± 0.3 mmol/l) was

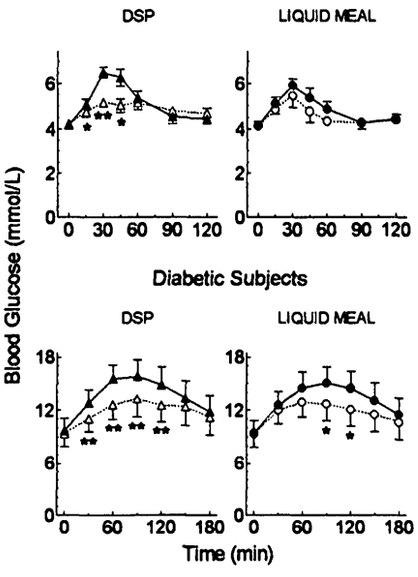

Figure 1—*Blood glucose responses in six normal and six diabetic subjects after a solid test meal (DSP) (▲) or liquid test meal with placebo (●) or 50 mg acarbose (△, ○). Values are means ± SE. *P < 0.05; **P < 0.01.*

1.7 times that after administration of the liquid meal (1.6 ± 0.6 mmol/l).

These results suggest that the antihyperglycemic effect of acarbose is more quickly and reliably demonstrated using a standardized starch-based test meal such as the DSP than after a liquid test meal. This difference is partly explained by the somewhat greater rise of blood glucose levels after the DSP than after the liquid meal. The delayed effect of acarbose after the liquid meal may also occur because the carbohydrate it contains, soluble dextrins and sucrose, empties more quickly from the stomach than does the starch in the solid meal, so that gastric emptying of the carbohydrate occurs before the acarbose tablet can dissolve and become active. One possible implication of these data is that the use of a liquid test meal to titrate acarbose dosage may result in the prescription of a higher dose than necessary to reduce blood glucose responses after normal solid meals. This higher dose, in turn, would tend to increase the chance of side effects and reduce patient compliance.

Measurement of blood glucose before and 60 min after, or even 30 min after, administration of the DSP alone, and after administration of DSP plus acarbose on another occasion, may be useful in clinical practice to guide acarbose dosage or to demonstrate to patients the magnitude of