CME CREDIT

New guidelines streamline diabetes diagnosis

S. SETHU K. REDDY, MD
Department of Endocrinology, Cleveland Clinic.

THE NEW GUIDELINES for diagnosing diabetes mellitus, which were released by the American Diabetes Association in July 1997,[1] should simplify the diagnostic process and help physicians identify more persons with previously undetected diabetes.

The new guidelines discourage the use of glucose tolerance testing, which because of its complexity was often underused in clinical practice, and instead call for using the easily administered fasting plasma glucose level. Another change in the screening guidelines is that the threshold of the fasting plasma glucose level is lower—for persons without symptoms of diabetes, the upper limit of normal is now set at 126 mg/dL rather than 140 mg/dL (TABLE 1).

For persons without symptoms, the upper limit of normal is now 126 mg/dL

WHY THE LOWER THRESHOLD?

The older guidelines, issued by the National Diabetes Data Group in 1979,[2] used a fasting plasma glucose level of 140 mg/dL or higher, a 2-hour glucose tolerance test result of 200 mg/dL or higher, or both as the criteria for diagnosing diabetes. However, the two test results are not equivalent: only about one fourth of persons with a 2-hour glucose tolerance test result of 200 mg/dL or higher have a fasting plasma glucose level as high as 140 mg/dL. Another disadvantage of the old criteria is that glucose tolerance testing is expensive, time-consuming, inconvenient for patients, and often inappropriately used as a diagnostic test. Fasting plasma glucose levels are also more reliable and consistent than glucose tolerance test results.

In several studies,[1,3,4] the risk of retinopathy rose sharply when persons had 2-hour glucose tolerance results of approximately 200 mg/dL or higher. In the same studies, the equivalent cutpoint for fasting plasma glucose was between 120 and 126 mg/dL. All these reasons led the American Diabetes Association and the Centers for Disease Control and Prevention to lower the screening threshold.

WHY USE FASTING GLUCOSE LEVELS RATHER THAN HEMOGLOBIN A_{1c}?

Since hemoglobin A_{1c} (HbA_{1c}) levels reflect long-term glucose levels, why not use the HbA_{1c} level to diagnose diabetes rather than fasting plasma glucose levels, which reflect just a single point in time? The HbA_{1c} level is useful in the follow-up of persons with diabetes. However, there is one major problem in using it as a diagnostic tool: there are many different methods of measuring it, meaning that values obtained in different laboratories may be different. Efforts are underway to standardize this test.

In addition, in many laboratories, the normal HbA_{1c} range is derived from a statistical sample of apparently healthy individuals—including many who, in all probability, have undetected diabetes, resulting in a "normal" value that may be too high. HbA_{1c} is also more expensive to measure than the fasting plasma glucose level. Finally, falsely low HbA_{1c} values may arise in those with abnormal hemoglobins or in those with reduced red blood cell life spans.

WILL THE NEW DIAGNOSTIC CRITERIA LEAD TO AN "EPIDEMIC" OF DIABETES?

According to data from the third National Health and Nutrition Survey, using the old criteria, an estimated 14.26% of US persons 40 to 74 years old have diabetes. Using a fasting blood plasma level of 126 mg/dL as the cri-

TABLE 1

Criteria for the diagnosis of diabetes mellitus

Any of the following*:

Symptoms of diabetes (polyuria, polydipsia, unexplained weight loss) plus a casual plasma glucose concentration ≥ 200 mg/dL

or

A fasting plasma glucose concentration ≥ 126 mg/dL (measured after at least 8 hours of no caloric intake)

or

An abnormal oral glucose tolerance test result† (a plasma glucose concentration ≥ 200 mg/dL 2 hours after a glucose load of 75 grams of anhydrous glucose dissolved in water)

*In the absence of unequivocal hyperglycemia with acute metabolic decompensation, these criteria should be confirmed by repeat testing on another day

†Not recommended for routine clinical use

SOURCE: ADAPTED FROM THE REPORT OF THE EXPERT COMMITTEE ON THE DIAGNOSIS AND CLASSIFICATION OF DIABETES MELLITUS. DIABETES CARE 1997; 20:1183–1197

TABLE 2

Who should be screened for diabetes?

Consider testing all persons age 45 and older (if normal, repeat every 3 years)

Consider testing at a younger age, or more frequently, for any of the following:

- Obese persons (≥ 120% desirable body weight or body mass index ≥ 27 kg/m^2)
- First-degree relatives of persons with diabetes
- Members of high-risk ethnic groups (eg, African American, Hispanic, Native American)
- Mothers of babies weighing > 9 lb at birth
- Women with a history of gestational diabetes
- Hypertensive patients (≥ 140/90 mm Hg)
- Dyslipidemic patients (HDL cholesterol ≤ 35 mg/dL or triglyceride ≥ 250 mg/dL or both)
- Patients with previous findings of impaired glucose tolerance (140–199 mg/dL on 2-hour test) or impaired fasting glucose (110–125 mg/dL)

SOURCE: ADAPTED FROM THE REPORT OF THE EXPERT COMMITTEE ON THE DIAGNOSIS AND CLASSIFICATION OF DIABETES MELLITUS. DIABETES CARE 1997; 20:1183–1197

terion, the prevalence would be 12.27%.

At present, only approximately half of persons with diabetes are identified. If physicians start using the fasting plasma glucose level with the lower threshold, they will probably identify more persons with diabetes, who are at risk of developing complications of diabetes.

WHOM TO SCREEN?

Undetected type 2 diabetes is common, accounting for as many as 50% of people with the disease. Earlier detection and treatment may lead to fewer complications. However, to increase the cost-effectiveness of testing undiagnosed, otherwise healthy persons, testing should be reserved for high-risk populations (TABLE 2).

TYPE 1 AND TYPE 2, NOT IDDM AND NIDDM

The new guidelines also do away with the terms "insulin-dependent diabetes mellitus" (IDDM) and "non-insulin-dependent diabetes mellitus" (NIDDM), on the grounds that these terms were an attempt to classify the disease on the basis of treatment. Also, some patients did not fit into either category. The new classification system is based on the disease process; the categories are as follows:

Type 1 diabetes, which is due to beta cell destruction, usually leading to absolute insulin deficiency.

Type 2 diabetes, which can range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with insulin resistance.

Other types of diabetes, due to specific genetic defects, diseases of the exocrine pancreas, endocrinopathies, drugs or chemicals, infections, uncommon immune-mediated diseases, or other genetic syndromes.

Fasting glucose levels are more reproducible than glucose tolerance test results

Gestational diabetes, for which the new guidelines recommend screening only in women at higher risk (ie, older than 25 years, overweight, with a family history, or Hispanic, Native American, Asian, or African American).

HOW TO USE THE NEW ANTIDIABETIC AGENTS

For more than 20 years, the sulfonylureas were the only oral antidiabetic agents available. All sulfonylureas work the same way: primarily by increasing insulin secretion by the pancreas. In the past few years, however, several new agents that have different mechanisms of action have become available.[5]

Acarbose inhibits enzymes that break down starches in the small intestine, thereby delaying carbohydrate absorption.

Metformin primarily decreases hepatic glucose production, and also increases insulin sensitivity in muscle cells.

Troglitazone increases insulin sensitivity. There have been isolated reports in the US and in Europe of severe hepatotoxicity in patients taking troglitazone. As this article went to press, these reports have prompted the US Food and Drug Administration to recommend baseline and periodic checking of liver enzymes in patients prescribed troglitazone.

The new guidelines do away with the terms IDDM and NIDDM

Toward rational use of oral antidiabetic drugs

How should these antidiabetic drugs be used? Diabetes experts are still trying to answer this question, but one approach is to determine where the individual patient is on the timeline of the natural progression of type 2 diabetes, and choose the drug appropriate for the stage of the disease.

In the early phase of type 2 diabetes, as insulin sensitivity decreases and blood glucose levels gradually rise, insulin secretion also rises in an attempt by the body to compensate. However, there comes a time when the beta cells of the pancreas become exhausted and begin to wear out. In this phase, insulin levels begin to fall, while blood sugar levels rise more sharply than before.

A clue to the patient's degree of disease progression is if he or she is still gaining weight at the time of diagnosis. Weight gain, in the absence of antidiabetic therapy, indicates that the patient still has adequate insulin secretion.

There are two implications from this insight. First, because blood sugar levels tend to rise with time, one must vigilantly, monitor the fasting plasma glucose and HbA_{1c} levels at regular intervals (two to four times per year), and increase the dosage of antidiabetic agents as needed. And second, different drugs may be more appropriate at different times: acarbose, metformin, and troglitazone earlier on when there is still some insulin secretion, sulfonylureas and insulin later on when the beta cells are exhausted.

Situational use of oral agents

Individual characteristics of the patient also favor or militate against certain agents.

Postprandial hyperglycemia. Acarbose is indicated.

Liver disease. Acarbose and low-dose sulfonylurea therapy are favored; metformin and troglitazone should be avoided.

Obese patients. Metformin and troglitazone are favored.

Kidney disease. Troglitazone is favored; metformin should be avoided.

Elderly patients. Acarbose, troglitazone, sulfonylureas are favored.

Fasting blood glucose higher than 200 mg/dL. Sulfonylureas and metformin are favored.

REFERENCES

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