

DIABETES: UPDATE ON MANAGEMENT AND TREATMENT

Lawrence S. Phillips, MD

Division of Endocrinology and Metabolism, Emory University School of Medicine

(*Ethn Dis.* 2003;13[suppl3]:S3-32-S3-33)

An increasing number of Americans has diabetes—a chronic disease characterized by persistent hyperglycemia (high blood glucose levels). Left untreated, diabetes can cause serious complications affecting the circulatory and nervous systems, kidneys, eyes, and feet.

Dr. Lawrence Phillips is the principal investigator for the research study, “Improving Primary Care of African Americans with NIDDM” and the “Training Program in Endocrinology, Metabolism, and Diabetes.” He is conducting 3 clinical trials in diabetes management. His recommendations on management are:

- Be comprehensive—avoid over-emphasis on glucose alone.
- Include a focus on postprandial hyperglycemia for both diagnosis and treatment.
- Avoid “clinical inertia”—intensify therapy when indicated.
- Use stepped intensification of therapy.
- Treat to target for blood pressure, lipids, and glucose.

“The key ingredients of diabetes treatment are blood pressure, lipids, aspirin, glucose, urine albumin/creatinine ratio, a yearly eye exam, and a foot exam each visit,” Dr. Phillips said.

Dr. Phillips reviewed the glucose tolerance categories and warned that full recognition of diabetes must include measurement of post-challenge glucose levels. “We must do more glucose tolerance testing,” he said. “Fifty-five percent of diabetics are diagnosed only after a glucose tolerance test.” This compares with 8% diagnosed after fasting only and 37% diagnosed after fasting and post-challenge glucose level measurement. These findings are based on 1,272 subjects in NHANES III—the National Health and Nutrition Examination Survey conducted by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC).

“The goal must be normal glucose,” Dr. Phillips said. There are definite correlations between rates of myocardial infarction and retinopathy with rises in percentages of blood sugar.

“Patients with diabetes have the highest glucose levels after meals,” Dr. Phillips said. “That is why you can’t just test before meals.” The DECODE study from Europe showed that postprandial hyperglycemia increases mortality in subjects who are not known as diabetic.

“Postprandial glucose is often high even when the HbA_{1c} is

less than 7%,” Dr. Phillips said. Research by Bonora et al focused on 371 outpatients who had average HbA_{1c} of 6.6% and average 2-hour postprandial glucose of 182 mg/dL. Sixty-five percent of the patients had HbA_{1c} less than 7% and 68% of those had 2-hour postprandial glucose of more than 160. “You cannot use HbA_{1c} as assurance that postprandial glucose is in a safe range,” Dr. Phillips said.

TAKE-HOME MESSAGE #1

- Use glucose tolerance tests to detect early diabetes—recognize post-challenge hyperglycemia;
- Postprandial hyperglycemia is common and increases the risk of cardiovascular disease;
- Use combination therapies in management—treat both fasting and postprandial hyperglycemia.

Diabetes management is a partnership between the patient and the provider, Dr. Phillips pointed out. “Inadequate diabetes control is not just the patient’s problem,” he said. “Healthcare providers must do something. If a patient is obese but does not exercise or lose weight, the healthcare provider should intensify therapy for high glucose levels.” In research studies at Grady Hospital in Atlanta, getting providers to intensify more often (when glucose levels were high) led to lower HbA_{1c} levels after 12 months of care.

TAKE-HOME MESSAGE #2

- Patients’ “health survival skills” should include keeping appointments, taking medicine, dieting, exercising, monitoring glucose, and stopping smoking.
- Healthcare providers should be responsible largely for control of blood pressure, lipids and glucose, and use of aspirin. “If these values are abnormal, do something,” Dr. Phillips said. “Do not give in to ‘clinical inertia.’”

Dr. Phillips discussed 2 types of therapy for type 2 diabetes. The therapies are different for patients with high glucose levels before breakfast and those with high glucose levels after meals.

Therapies for fasting glucose: sulfonylureas; biguanides; thiazolidinediones; long-lasting insulin given at bedtime; and combination therapy.

“Sulfonylureas stimulate insulin secretion in most patients and are inexpensive,” Dr. Phillips said. “However, they may increase the risk of hypoglycemia and weight gain, due largely to the retention of calories formerly lost as glucose in the urine.”

“The biguanide **metformin** causes little weight gain and little hypoglycemia and is inexpensive,” Dr. Phillips said. On the downside, it may cause gastrointestinal upsets, such as diarrhea, nausea, vomiting, bloating, flatulence, and anorexia, he pointed out. These symptoms can be minimized by slow titration and dosing with meals. Since the drug is excreted by the kidneys, there is also an increased risk of lactic acidosis if the patient becomes dehydrated, and the drug is contraindicated in patients with elevated creatinine levels.

“Thiazolidinediones are well-tolerated and there is no hypoglycemia, but they are expensive,” Dr. Phillips said. “The patient’s glucose levels fall more slowly with these drugs than with other drugs.” The negatives include a possible rise in LDL cholesterol, the risk of weight gain and edema, and the risk of congestive heart failure, he said.

“Bedtime insulin is convenient to use and results in a large drop in HbA_{1c} in most patients,” Dr. Phillips said. “On the other hand, it must be given by injection and is associated with weight gain. The main risk is nocturnal hypoglycemia,” he noted. The risk of nocturnal hypoglycemia can be decreased by using glargine instead of NPH.

Therapies for after-meal glucose: glucose inhibitors—acarbose and miglitol to decrease the breakdown of carbohydrates to form simple sugars in the gut; the meglitinide repaglinide; the D-phenylalanine derivative nateglinide to stimulate early insulin release to mimic normal physiology; and short-acting insulin given before meals—injected or inhaled insulin.

“Acarbose and miglitol reduce postprandial hyperglycemia,” Dr. Phillips said. “Taken by themselves rather than in combination, these 2 drugs will not cause hypoglycemia and will not promote weight gain.” They are relatively inexpensive but they have gastrointestinal side effects, including flatulence, diarrhea, and nausea, Dr. Phillips said. He recommended starting with low doses (25 mg before meals) and titrating slowly.

Stepped care for diabetes—2002

Treat cardiovascular risk factors; aspirin; screen for complications; education in glucose monitoring; diet; exercise

Add oral agents

± metformin ± PP targeted oral agent ± TZD

Add bedtime Lente or glargine insulin

Switch to mealtime Lispro + bedtime insulin ± metformin + TZD

“Repaglinide acts fairly rapidly and can be taken at mealtime. It reduces both postprandial and fasting glucose and can be used in patients with kidney failure,” Dr. Phillips said. “However, it is relatively expensive and hypoglycemia after meals is common.”

“Nateglinide stimulates early insulin release,” Dr. Phillips said. “It mimics normal mealtime physiology and can be used one to 30 minutes before meals. It produces relatively little hypoglycemia.” On the negative side, it is “not effective in patients with SU failure and may be less effective in patients with longstanding disease and less residual B-cell function,” he explained.

“Short-acting insulin given before meals reduces postprandial hypoglycemia and HbA_{1c},” Dr. Phillips said. “It is effective in a wide variety of patients, even though there has been relatively little experience with it in treating type 2 diabetes.” It must be given by injection or inhaled and can cause severe hypoglycemia, he noted.

TAKE-HOME MESSAGE #3

- Diabetes can be controlled.
- Complex polypharmacy often is needed. This includes therapies aimed at fasting glucose and those aimed at postprandial glucose.
- Achievement of near-normal glucose levels throughout the day—as needed to help prevent diabetes complications and reduce cardiovascular risk—will require mealtime diabetes therapy.