Clinical Practice Recommendations

Michael J. Fowler, MD

Editor's note: *This article is the final installment in a 12-part series reviewing the fundamentals of diabetes care for physicians in training. Previous articles in the series can be viewed at the* Clinical Diabetes *Web site (http://clinical.diabetesjournals.org).*

During the past 3 years, ***Clinical Diabetes*** has published "Diabetes Foundation," a 12-part series intended to explain and review facets of diabetes care for general physicians and physicians in training. The goal of the series has been to improve diabetes care for patients treated by such physicians because only a very small percentage of patients with diabetes have access to an endocrinologist.

Although previous articles have focused on individual topics related to diabetes care and have reviewed available scientific data, this final article will focus on summarizing recommendations from the American Diabetes Association (ADA) and integrating them as a set of clinical practice guidelines. Information supporting the recommendations has appeared in the previous installments of "Diabetes Foundation" and from the ADA.[1] Although there are always exceptions, it is likely that the majority of patients with diabetes or glucose abnormalities would benefit from implementation of many of these guidelines for both prevention of diabetes and prevention of the complications of diabetes and diabetes treatments.

Whom to Screen for Diabetes or Pre-Diabetes

Any patient who is experiencing symptoms of diabetes such as polyuria, polydipsia, or unexplained weight loss should be screened for diabetes, especially if they are obese or overweight (BMI > 25 kg/m^2). Asymptomatic adult patients should be tested at any age if they are overweight or obese and have an additional risk factor for diabetes. Children who are overweight (BMI greater than the 85th percentile or weight > 120% of ideal for height) should be screened for type 2 diabetes if they have a family history of type 2 diabetes, are of an ethnic background predisposed to diabetes, have signs of insulin resistance such as acanthosis nigricans on physical examination, have a maternal history of diabetes or gestational diabetes, or have other conditions typically associated with type 2 diabetes. Such testing in children should begin at the age of 10 years or at the onset of puberty. If tests are normal, such patients should be screened again in 3 years. Women who have had gestational diabetes should be screened for diabetes 6–12 weeks postpartum.

Diagnostic Criteria for Diabetes

Timely and accurate diagnosis of diabetes is crucial to appropriate and timely treatment. Diabetes is most commonly diagnosed by measurement of the fasting blood glucose level. Patients should have had no caloric intake for at least 8 hours before the measurement. Diabetes is defined as a plasma glucose level ≥ 126 mg/dl after such fasting. Diabetes may also be diagnosed by a random glucose measurement ≥ 200 mg/dl at any time of the day if symptoms of diabetes such as polyuria, polydipsia, or weight loss are present. Recently, an international expert committee recommended that A1C values ≥ 6.5% be used as a diagnostic criterion for diabetes; this recommendation may be implemented by the ADA in the near future.[2]

Prevention of Type 2 Diabetes

Patients with elevated blood glucose that is not sufficiently high to be diagnosed with diabetes are considered to have "pre-diabetes," which includes impaired fasting glucose or impaired glucose tolerance. Such patients should be counseled to strive for weight loss of 5–10% of body weight and 150 minutes per week of moderate activity such as walking. Metformin therapy may be considered for patients who are considered to be at very high risk to develop diabetes if no contraindications to therapy exist. Such patients should be screened on a yearly basis for the development of diabetes.[1]

Monitoring A1C

A1C should be monitored at least twice yearly in diabetic patients who have stable diabetes control and who are meeting treatment goals. In patients who are not meeting treatment goals or whose therapy is changing, quarterly monitoring

should be considered. It is important to keep in mind that A1C measurement is less accurate in patients with impaired renal function, hemoglobinopathy, and other conditions.[1]

Goals for Glycemic Control in Adults

Patients with type 1 or type 2 diabetes should strive for an A1C ≤ 7% to decrease their risk of developing the microvasuclar complications of diabetes. Additionally, long-term follow-up of patients with type 1 diabetes suggests that such a goal may reduce the risk of macrovascular disease. Treatment to an A1C level ≤ 7% may be especially beneficial early in the course of type 2 diabetes. Less aggressive glucose control may be indicated for patients who have factors complicating their glucose control, such as severe hypoglycemia, limited life expectancy, advanced complications of diabetes, or other comorbidities.[1]

Nutritional Therapy

People who have diabetes or pre-diabetes should be offered nutritional therapy to control or prevent diabetes, respectively. In patients who are overweight or obese, weight loss reduces insulin resistance and therefore may improve diabetes control. It may also prevent or delay the onset of type 2 diabetes in patients with pre-diabetes. Patients should also be taught to limit saturated fat to ≤ 7% of total daily calories. Consumption of *trans* fats should also be limited as much as possible. Patients should also be taught to account for the amount of carbohydrate they consume on a daily basis. There are several acceptable approaches, including counting grams of carbohydrate or learning carbohydrate exchanges. Use of the glycemic index in addition to accounting for total carbohydrate may improve glycemic control slightly more.[1]

Hypoglycemia

Hypoglycemia can be a life-threatening complication of diabetes therapy. Treatment of hypoglycemia should consist of 15–20 g of carbohydrate administered orally if the patient is conscious and capable of ingesting it. The glucose level should be rechecked 15 minutes after treatment is administered, and carbohydrate treatment should be repeated if hypoglycemia persists. Once recovered, the patient may need to consume a meal or snack to prevent recurrence of hypoglycemia. Glucagon should be prescribed to all patients who are at significant risk of developing severe hypoglycemia (requiring assistance from another person), and family members and caregivers of such patients should be trained in its administration. Patients who experience severe hypoglycemia or who develop limited ability to sense hypoglycemia should be instructed to raise their glycemic targets to avoid further severe hypoglycemia. Such a strategy may also restore some level of hypoglycemia awareness if the patient is able to avoid all hypoglycemia for several weeks.[1]

Monitoring for Diabetes Complications

Monitoring for the development of diabetes complications, although tedious, is probably just as important as monitoring the adequacy of glycemic control. Diabetic nephropathy is a common cause of morbidity in patients with type 1 or type 2 diabetes. Therefore, patients should be monitored for its development and progression. The first line of defense in preventing diabetic nephropathy or limiting its progression is optimization of blood glucose control.

Patients should be tested annually for the development of elevated albumin excretion. Testing should commence at the diagnosis of type 2 diabetes or, in the case of type 1 diabetes, 5 years after initial diagnosis. Testing may consist of a urine microalbumin-to-creatinine ratio (spot measurement) or a 24-hour urine collection. Serum creatinine should be measured in all adults with diabetes regardless of whether they have developed elevated protein excretion.

In the presence of elevated albumin excretion, patients should be treated with ACE inhibitors or angiotensin receptor blockers (ARBs). If one class is not tolerated, the other should be used.

Patients require monitoring for side effects such as hyperkalemia, elevated creatinine, and angioedema while using these medications. Although they are usually well tolerated, pregnancy is a contraindication to their use. Patients using such medications should have their creatinine and albumin excretion monitored regularly. Patients should also limit protein in the diet to 0.8–1.0 g/kg of body weight per day. Progression of disease despite these measures or evidence of other pathological processes should prompt referral to a renal specialist.

Because of the high rate of comorbidity, patients with type 1 diabetes should be monitored for the development of autoimmune thyroid disease every 1–2 years or if they develop symptoms of thyroid dysfunction. Patients with growth failure, persistent gastrointestinal symptoms, or unexplained weight loss should be screened for celiac disease by checking anti-tissue transglutaminase or anti-endomysial antibody levels.[1]

Lipid and Blood Pressure Control

Hypertension and hyperlipidemia are common comorbidities of type 2 diabetes, which constitutes the majority of diabetes in the United States. They are also frequently present in patients with type 1 diabetes. When combined with diabetes, they can dramatically

increase the risk of macrovascular disease such as coronary artery disease. Therefore, blood pressure and lipids should be monitored regularly.

Blood pressure should be checked at routine diabetes visits. Patients should have their blood pressure checked while at rest, with their arm relaxed and the cuff at heart level. Goal blood pressure for patients with diabetes is < 130/80 mmHg. Elevated readings should be confirmed on a subsequent day.

Patients with systolic blood pressure of 130–139 mmHg or diastolic blood pressure of 80–89 mmHg may be treated with lifestyle therapy consisting of increased cardiovascular exercise and limited sodium intake. If blood pressure is not controlled with lifestyle intervention within 3 months, medication may be added to control blood pressure.

Patients with systolic blood pressure > 140 mmHg or diastolic blood pressure > 90 mmHg should receive both lifestyle and pharmacological intervention. If patients need pharmacological treatment for hypertension, the treatment regimen should include either an ACE inhibitor or an ARB because of their renoprotective properties. If a patient does not tolerate one of these classes, the other class should be used if possible. Addition of a diuretic may be necessary because most patients require therapy with more than one agent to adequately control hypertension.

In children and adolescents, if blood pressure is consistently elevated between the 90th and 95th percentile for age, sex, and height, the child should engage in lifestyle modification for a period of up to 1 year. ACE inhibitors are the drug of choice if pharmacological treatment is necessary, and the goal blood pressure is < 130/80 mmHg or < the 90th percentile for age, sex, and height. Physicians should also remember to screen for other causes of hypertension in children, such as cardiovascular malformations.

It is important to remember that ACE inhibitors and ARBs are contraindicated in pregnancy.

Fasting lipid profiles should be checked annually in most adults with diabetes. In patients whose baseline lipids represent low risk (HDL > 50 mg/dl, LDL < 100 mg/dl, and triglycerides < 150 mg/dl), lipid tests may be repeated every other year. All patients with diabetes should attempt lifestyle modifications, including getting regular cardiovascular exercise, controlling weight, and minimizing consumption of cholesterol and saturated and *trans* fats. In patients without known cardiovascular disease, goal LDL is < 100 mg/dl; patients with known cardiovascular disease may be treated to an LDL level < 70 mg/dl.

Statin therapy is considered the first-line treatment to lower LDL cholesterol to goal if lifestyle intervention alone is not successful. The ADA recommends statin therapy regardless of baseline LDL levels in patients with diabetes who also have history of coronary artery disease or who are > 40 years of age with one or more other risk factors for cardiovascular disease. If patients treated with statins do not reach their goal lipid levels on maximum tolerated doses, the goal of a 30–40% reduction from baseline is an alternative. Other goals include a triglyceride level < 150 mg/dl and HDL cholesterol > 40 mg/dl in men and > 50 mg/dl in women. However, control of LDL cholesterol remains the primary goal of treatment.

As with other patients treated with statins, patients with diabetes should be monitored for potential side effects such as myalgias, elevated hepatic enzymes, or, rarely, rhabdomyolysis. Combination therapy with other lipid medications may be considered, but such therapy has not been thoroughly evaluated with regard to efficacy.

For children and adolescents, a fasting lipid profile should be checked in those > 2 years of age at the time of diagnosis with diabetes if there is a family history of cardiovascular disease developing before the age of 50 years or hypercholesterolemia (total cholesterol > 240 mg/dl). If such a history is not present, then testing should occur at the onset of puberty. After the age of 10 years, statin therapy is recommended for those with LDL > 160 mg/dl despite lifestyle intervention or > 130 mg/dl in those with one or more cardiovascular risk factors other than diabetes.[1]

Foot Care

All patients with diabetes should undergo an annual foot examination to identify issues predisposing to ulceration or amputation. Examination should include vascular assessment (usually pulse measurement) as well as neurological assessment such as 10-g monofilament testing, vibration sensitivity, or ankle reflexes. Patients should also be educated to check their feet daily for areas of injury, callusing, or other abnormalities. Patients with loss of protective sensation in the feet may benefit from ongoing care from foot-care specialists. Patients who experience claudication should be evaluated for peripheral vascular disease.[1]

Diabetes Hospital Care

Patients with diabetes should have their diabetes clearly labeled in their medical record. They should also have regular glucose monitoring included on hospital orders. Goals for inpatient glycemic control depend on patients' condition. Critically ill surgical patients should have glucose levels maintained as close to 110 mg/dl

as possible, usually through a continuous intravenous insulin infusion. Critically ill nonsurgical patients should have glucose levels maintained at < 140 mg/dl. In noncritically ill patients, a fasting glucose goal of < 126 mg/dl and random glucose levels < 180–200 mg/dl is reasonable. Insulin is the preferred treatment for glucose control in the inpatient setting. In some facilities, these goals may be considered overly aggressive because of the risk of hypoglycemia.

Prandial insulin should be administered as closely as possible to mealtimes, and correction insulin in addition to prandial insulin is recommended. A treatment plan for treatment of hypoglycemia should be identified for all patients receiving diabetes therapy. A1C testing is indicated for patients who have not had such testing performed in the past 3 months or in whom such test results are not available. Glucose monitoring is also indicated for patients receiving treatments or therapies that are associated with a high incidence of diabetes such as total parental nutrition and glucocorticoid treatment.

Conclusion

Diabetes therapy can be very complicated for patients as well as physicians. Treatment can be laborious, and its many details must be well organized and understood by all people involved in carrying out the diabetes regimen. As with other areas of medicine, the important details of diabetes care can be easily overlooked in the setting of limited time for office or hospital visits, treatment of comorbidities, and other distractions involved in medical care. The above guidelines are intended to summarize clinical treatment recommendations based on evidence and experience on the part of the ADA. Background and reasoning for most of these recommendations is located in the previous articles in this series, which can be accessed at the *Clinical Diabetes* Web site (http://clinical.diabetesjournals.org). Adherence to these guidelines should empower physicians and other health care practitioners to provide their patients with the best possible care and to increase their likelihood of successful treatment outcomes.[1]

REFERENCES

[1]American Diabetes Association: Standards of medical care in diabetes—2009. *Diabetes Care* 32 (Suppl. 1):S13–S61, 2009

[2]International Expert Committee: International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes. *Diabetes Care* 32:1327–1334, 2009

Michael J. Fowler, MD, is an assistant professor of medicine in the Division of Diabetes, Endocrinology, and Metabolism, Vanderbilt Eskind Diabetes Clinic, at Vanderbilt University Medical Center in Nashville, Tenn. He is an associate editor of Clinical Diabetes.