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'Body Check up in Diabetes Patients'

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Abstract

Diabetes is a chronic illness that requires continuing medical care and patient self-management education to prevent acute complications and to reduce the risk of long-term complications. Diabetes care is complex and requires that many issues, beyond glycemic control, be addressed. A large body of evidence exists that supports a range of interventions to improve diabetes outcomes.

Keywords: Introduction, classification, diagnosis, and screening, initial evaluation, management, assessment of glycemic control, physical activity, prevention and management of diabetes complications, Special Considerations, Special Considerations, References.

Introduction

Diabetes is a chronic illness that requires continuing medical care and patient self-management education to prevent acute complications and to reduce the risk of long-term complications. Diabetes care is complex and requires that many issues, beyond glycemic control, be addressed. A large body of evidence exists that supports a range of interventions to improve diabetes outcomes.

These standards of care are intended to provide clinicians, patients, researchers, payors, and other interested persons with the components of diabetes care, treatment goals, and tools to evaluate the quality of care. While individual preferences, comorbidities, and other patient factors may require modification of

goals, targets that are desirable for most patients with diabetes are provided. These standards are not intended to preclude more extensive evaluation and management of the patient by other specialists as needed. For more detailed information, refer to Skyler (Ed.): *Medical Management of Type 1 Diabetes* (1) and Zimmerman (Ed.): *Medical Management of Type 2 Diabetes* (2).

The recommendations included are diagnostic and therapeutic actions that are known or believed to favorably affect health outcomes of patients with diabetes. A grading developed by the American Diabetes Association (ADA) and modeled after existing methods, was utilized to clarify and codify the

evidence that forms the basis for the recommendations. The level of evidence that supports each recommendation is listed after each recommendation using the letters A, B, C, or E.

Classification, diagnosis, and screening:

Classification- In 1997, the ADA issued new diagnostic and classification criteria. The classification of diabetes mellitus includes four clinical classes:

- Type 1 diabetes (results from β -cell destruction, usually leading to absolute insulin deficiency).
- Type 2 diabetes (results from a progressive insulin secretory defect on the background of insulin resistance).
- Other specific types of diabetes (due to other causes, e.g., genetic defects in β -cell function, genetic defects in insulin action, diseases of the exocrine pancreas, drug or chemical induced).
- Gestational diabetes mellitus (GDM) (diagnosed during pregnancy).

Diagnosis: Criteria for the diagnosis of diabetes in nonpregnant adults. Three ways to diagnose diabetes are available, and each must be confirmed on a subsequent day unless unequivocal symptoms of hyperglycemia are present. Although the 75-g oral glucose tolerance test (OGTT) is more sensitive and modestly more specific than fasting plasma glucose (FPG) to diagnose diabetes, it is poorly reproducible and rarely performed in practice. Because of ease of use, acceptability to patients, and lower cost, the FPG is the preferred screening and diagnostic test. It should be noted that the vast majority of people who meet diagnostic criteria for diabetes by OGTT, but not by FPG, will have an A1C value $<7.0\%$.

Hyperglycemia not sufficient to meet the diagnostic criteria for diabetes is categorized as either impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), depending on whether it is identified through FPG or an OGTT: IFG = FPG 110 mg/dl (6.1 mmol/l) to 125 mg/dl (6.9 mmol/l); IGT = 2-h plasma glucose 140 mg/dl (7.8 mmol/l) to 199 mg/dl (11.0 mmol/l).

Both categories, IFG and IGT, are risk factors for future diabetes and cardiovascular disease (CVD). Recently, IFG and IGT have been officially termed "pre-diabetes." Recent studies have shown that modest weight loss and regular physical activity can reduce the rate of progression of IGT to type 2 diabetes. Drug therapy (metformin, acarbose, and orlistat) and troglitazone (no longer clinically available) have been

shown to be effective in reducing progression to diabetes in single trials, though generally not as effective as intensive lifestyle interventions.

Screening: Generally, people with type 1 diabetes present with acute symptoms of diabetes and markedly elevated blood glucose levels. Type 2 diabetes is frequently not diagnosed until complications appear, and approximately one-third of all people with diabetes may be undiagnosed. Although the burden of diabetes is well known, the natural history is well characterized, and there is good evidence for benefit from treating cases diagnosed in the context of usual clinical care, there are no randomized trials demonstrating the benefits of early diagnosis through screening of asymptomatic individuals. Nevertheless, there is sufficient indirect evidence to justify opportunistic screening in a clinical setting of individuals at high risk. Criteria for testing for diabetes in asymptomatic, undiagnosed adults are listed in . The recommended screening test for nonpregnant adults is the FPG. The OGTT is more sensitive for the diagnosis of diabetes and pre-diabetes, but is impractical and expensive as a screening procedure.

The incidence of type 2 diabetes in children and adolescents has increased dramatically in the last decade. Consistent with screening recommendations for adults, only children and youth at increased risk for the presence or the development of type 2 diabetes should be tested.

Detection and diagnosis of GDM: Risk assessment for GDM should be undertaken at the first prenatal visit. Women with clinical characteristics consistent with a high risk for GDM (those with marked obesity, personal history of GDM, glycosuria, or a strong family history of diabetes) should undergo glucose testing as soon as possible. An FPG ≥ 126 mg/dl or a casual plasma glucose ≥ 200 mg/dl meets the threshold for the diagnosis of diabetes, if confirmed on a subsequent day. High-risk women not found to have GDM at the initial screening and average-risk women should be tested between 24 and 28 weeks of gestation. Testing should follow one of two approaches:

- One-step approach: perform a diagnostic OGTT
- Two-step approach: perform an initial screening by measuring the plasma or serum glucose concentration 1 h after a 50-g oral glucose load (glucose challenge test [GCT]) and perform a diagnostic OGTT on that subset of women exceeding the glucose threshold value on the GCT. When the

two-step approach is used, a glucose threshold value 140 mg/dl identifies ~80% of women with GDM, and the yield is further increased to 90% by using a cutoff of 130 mg/dl.

Diagnostic criteria for the 100-g OGTT is as follows: 95 mg/dl fasting, 180 mg/dl at 1 h, 155 mg/dl at 2 h, and 140 mg/dl at 3 h. Two or more of the plasma glucose values must be met or exceeded for a positive diagnosis. The test should be done in the morning after an overnight fast of 8–14 h. The diagnosis can be made using a 75-g glucose load, but that test is not as well validated for detection of at-risk infants or mothers as the 100-g OGTT.

Low risk status requires no glucose testing, but this category is limited to those women meeting all of the following characteristics:

- Age <25 years.
 - Weight normal before pregnancy.
 - Member of an ethnic group with a low prevalence of GDM.
 - No known diabetes in first-degree relatives.
 - No history of abnormal glucose tolerance.
 - No history of poor obstetric outcome.
- Recommendations: The FPG is the preferred test to screen for and diagnose diabetes in children and nonpregnant adults. (E)
- Screen for diabetes in high-risk, asymptomatic, undiagnosed adults and children within the health care setting. (E)
 - In those with prediabetes (IFG/IGT), lifestyle modification should be strongly recommended and progression of glycemic abnormalities followed by screening at least yearly. (A)
 - Screen for diabetes in pregnancy using risk factor analysis and screening tests as noted; the OGTT is the preferred screening test in pregnancy. (E)

Initial evaluation: A complete medical evaluation should be performed to classify the patient, detect the presence or absence of diabetes complications, assist in formulating a management plan, and provide a basis for continuing care. If the diagnosis of diabetes has already been made, the evaluation should review the previous treatment and the past and present degrees of glycemic control. Laboratory tests appropriate to the evaluation of each patient's general medical condition should be performed. A focus on the components of comprehensive care will assist the health care team to ensure optimal management of the patient with

diabetes. **MANAGEMENT:** People with diabetes should receive medical care from a physician-coordinated team. Such teams may include, but are not limited to, physicians, nurses, dietitians, pharmacists, and mental health professionals with expertise and a special interest in diabetes. It is essential in this collaborative and integrated team approach that individuals with diabetes assume an active role in their care.

The management plan should be formulated as an individualized therapeutic alliance among the patient and family, the physician, and other members of the health care team. Any plan should recognize diabetes self-management education as an integral component of care. In developing the plan, consideration should be given to the patient's age, school, or work schedule and conditions, physical activity, eating patterns, social situation and personality, cultural factors, and presence of complications of diabetes or other medical conditions. Treatment goals must be set together with the patient, family, and health care team. Patient self-management should be emphasized, and the plan should emphasize the involvement of the patient in problem solving as much as possible. A variety of strategies and techniques should be used to provide adequate education and development of problem-solving skills in the various aspects of diabetes management. Implementation of the management plan requires that each aspect be understood and agreed on by the patient and the care providers and that the goals and treatment plan are reasonable.

Glycemic control: Glycemic control is fundamental to the management of diabetes. Prospective randomized clinical trials such as the Diabetes Control and Complications Trial (DCCT) and the U.K. Prospective Diabetes Study (UKPDS) have shown that improved glycemic control is associated with sustained decreased rates of retinopathy, nephropathy, and neuropathy. In these trials, treatment regimens that reduced average A1C to ~7% (~1% above the upper limits of normal) were associated with fewer long-term microvascular complications; however, intensive control was found to increase the risk of severe hypoglycemia and weight gain. Epidemiological studies support the potential of intensive glycemic control in the reduction of CVD. Recommended glycemic goals for nonpregnant individuals. A major limitation to the available data is that they do not identify the optimum level of control for particular patients, as there are individual differences in the risks of hypoglycemia, weight gain, and other adverse effects. Furthermore, with multifactorial interventions,

it is unclear how different components (e.g., educational interventions, glycemic targets, lifestyle changes, and pharmacological agents) contribute to the reduction of complications. There are no clinical trial data available for the effects of glycemic control in patients with advanced complications, the elderly (65 years of age), or young children (<13 years of age). Less stringent treatment goals may be appropriate for patients with limited life expectancies, in the very young or older adults, and in individuals with comorbid conditions. Severe or frequent hypoglycemia is an indication for the modification of treatment regimens, including setting higher glycemic goals. More stringent goals can be considered in individual patients based on epidemiological analyses that suggest that there is no lower limit of A1C at which further lowering does not reduce risk of complications. However, the absolute risks and benefits of lower targets are unknown.

Elevated postchallenge (2-h OGTT) glucose values have been associated with increased cardiovascular risk independent of FPG in some epidemiological studies. Postprandial plasma glucose (PPG) levels >140 mg/dl are unusual in nondiabetic individuals, although large evening meals can be followed by plasma glucose values up to 180 mg/dl. There are now pharmacological agents that primarily modify PPG and thereby reduce A1C in parallel. Thus, in individuals who have premeal glucose values within target but who are not meeting A1C targets, consideration of monitoring PPG 1–2 h after the start of the meal and treatment aimed at reducing average PPG values <180 mg/dl may lower A1C. However, it should be noted that the effect of these approaches on the microvascular or macrovascular complications has not been studied.

For information on glycemic control for women with GDM, refer to the ADA position statement “Gestational Diabetes Mellitus”. For information on glycemic control during pregnancy in women with preexisting diabetes, refer to *Medical Management of Pregnancy Complicated by Diabetes* (3rd ed.).

Referral for diabetes management

For a variety of reasons, some people with diabetes and their health care providers do not achieve the desired goals of treatment. In such instances, additional actions suggested include enhanced diabetes self-management education, comanagement with a diabetes team, change in pharmacological therapy, initiation of or increase in self-monitoring of blood

glucose (SMBG), more frequent contact with the patient, and referral to an endocrinologist.

Intercurrent illness

The stress of illness frequently aggravates glycemic control and necessitates more frequent monitoring of blood glucose and urine or blood ketones. A vomiting illness accompanied by ketosis may indicate diabetic ketoacidosis (DKA), a life-threatening condition that requires immediate medical care to prevent complications and death; the possibility of DKA should always be considered. Marked hyperglycemia requires temporary adjustment of the treatment program, and, if accompanied by ketosis, frequent interaction with the diabetes care team. The patient treated with oral glucose-lowering agents or medical nutrition therapy (MNT) alone may temporarily require insulin. Adequate fluid and caloric intake must be assured. Infection or dehydration is more likely to necessitate hospitalization of the person with diabetes than the person without diabetes. The hospitalized patient should be treated by a physician with expertise in the management of diabetes, and recent studies suggest that achieving very stringent glycemic control may reduce mortality in the immediate post-myocardial infarction period. Aggressive glycemic management with insulin may reduce morbidity in patients with severe acute illness.

For information on management of patients in the hospital, refer to the ADA position statement titled “Hyperglycemic Crises in Patients with Diabetes Mellitus”.

Recommendations

- Lowering A1C has been associated with a reduction of microvascular and neuropathic complications of diabetes. (A)
- Develop or adjust the management plan to achieve normal or near-normal glycemia with an A1C goal of <7%. (B)
- Lowering A1C may lower the risk of myocardial infarction and cardiovascular death. (B)
- Aggressive glycemic management with insulin may reduce morbidity in patients with severe acute illness, perioperatively and following myocardial infarction. (B)
- Less stringent treatment goals may be appropriate for patients with a history of severe hypoglycemia, patients with limited life expectancies, very young children or older adults, and individuals with comorbid conditions. (E)

Assessment of glycemic control

Techniques are available for health providers and patients to assess the effectiveness of the management plan on glycemic control.

Self-monitoring of blood glucose

The ADA's consensus statements on SMBG provide a comprehensive review of the subject. Major clinical trials assessing the impact of glycemic control on diabetes complications have included SMBG as part of multifactorial interventions, suggesting that SMBG is a component of effective therapy. SMBG allows patients to evaluate their individual response to therapy and assess whether glycemic targets are being achieved. Results of SMBG can be useful in preventing hypoglycemia and adjusting medications, MNT, and physical activity.

The frequency and timing of SMBG should be dictated by the particular needs and goals of the patients. Daily SMBG is especially important for patients treated with insulin to monitor for and prevent asymptomatic hypoglycemia. For most patients with type 1 diabetes and pregnant women taking insulin, SMBG is recommended three or more times daily. The optimal frequency and timing of SMBG for patients with type 2 diabetes is not known, but should be sufficient to facilitate reaching glucose goals. When adding to or modifying therapy, type 1 and type 2 diabetic patients should test more often than usual. The role of SMBG in stable diet-treated patients with type 2 diabetes is not known.

Because the accuracy of SMBG is instrument- and user-dependent, it is important for health care providers to evaluate each patient's monitoring technique, both initially and at regular intervals thereafter. In addition, optimal use of SMBG requires proper interpretation of the data. Patients should be taught how to use the data to adjust food intake, exercise, or pharmacological therapy to achieve specific glycemic goals. Health professionals should evaluate at regular intervals the patient's ability to use SMBG data to guide treatment.

Recommendations

- SMBG is an integral component of diabetes therapy. (B)
- Include SMBG in the management plan. (E)

- Instruct the patient in SMBG and routinely evaluate the patient's technique and ability to use data to adjust therapy. (E)

A1C

By performing an A1C test, health providers can measure a patient's average glycemia over the preceding 2–3 months and, thus, assess treatment efficacy. A1C testing should be performed routinely in all patients with diabetes, first to document the degree of glycemic control at initial assessment and then as part of continuing care. Since the A1C test reflects mean glycemia over the preceding 2–3 months, measurement approximately every 3 months is required to determine whether a patient's metabolic control has been reached and maintained within the target range. Thus, regular performance of the A1C test permits detection of departures from the target in a timely fashion. For any individual patient, the frequency of A1C testing should be dependent on the clinical situation, the treatment regimen used, and the judgment of the clinician.

Glycemic control is best judged by the combination of the results of the patient's SMBG testing (as performed) and the current A1C result. The A1C should be used not only to assess the patient's control over the preceding 2–3 months but also as a check on the accuracy of the meter (or the patient's self-reported results) and the adequacy of the SMBG testing schedule. contains the correlation between A1C levels and mean plasma glucose levels based on data from the DCCT.

Recommendations

- Perform the A1C test at least two times a year in patients who are meeting treatment goals (and who have stable glycemic control) and quarterly in patients whose therapy has changed or who are not meeting glycemic goals. (E)

MNT

MNT is an integral component of diabetes management and diabetes self-management education. A review of the evidence and detailed information can be found in the ADA technical review and position statement titled "Evidence-Based Nutrition Principles and Recommendations for the Treatment and Prevention of Diabetes and Related Complications". People with diabetes should receive individualized MNT as needed to achieve treatment goals, preferably

provided by a registered dietitian familiar with the components of diabetes MNT. Goals of MNT that apply to all persons with diabetes are as follows:

- Attain and maintain recommended metabolic outcomes, including glucose and A1C levels; LDL cholesterol, HDL cholesterol, and triglyceride levels; blood pressure; and body weight.
- Prevent and treat the chronic complications and comorbidities of diabetes. Modify nutrient intake and lifestyle as appropriate for the prevention and treatment of obesity, dyslipidemia, CVD, hypertension, and nephropathy.
- Improve health through healthy food choices and physical activity.
- Address individual nutritional needs, taking into consideration personal and cultural preferences and lifestyle while respecting the individual's wishes and willingness to change.

Goals of MNT that apply to specific situations include the following:

- For youth with type 1 diabetes, provide adequate energy to ensure normal growth and development; integrate insulin regimens into usual eating and physical activity habits.
- For youth with type 2 diabetes, facilitate changes in eating and physical activity habits that reduce insulin resistance and improve metabolic status.
- For pregnant and lactating women, provide adequate energy and nutrients needed for optimal outcomes.
- For older adults, provide for the nutritional and psychosocial needs of an aging individual.
- For individuals treated with insulin or insulin secretagogues, provide self-management education for treatment (and prevention) of hypoglycemia, acute illnesses, and exercise-related blood glucose problems.
- For individuals at risk for diabetes, decrease risk by encouraging physical activity and promoting foods choices that facilitate moderate weight loss or at least prevent weight gain.

Achieving nutrition-related goals requires a coordinated team effort that includes the person with diabetes. Because of the complexity of nutrition issues, it is recommended that a registered dietitian, knowledgeable and skilled in implementing nutrition therapy into diabetes management and education, is the team member who provides MNT. However, it is essential that all team members are knowledgeable about nutrition therapy and are supportive of the

person with diabetes who needs to make lifestyle changes.

MNT involves a nutrition assessment to evaluate the patient's food intake; metabolic status, lifestyle and readiness to make changes, goal setting, dietary instruction, and evaluation. To facilitate adherence, the plan should be individualized and take into account cultural, lifestyle, and financial considerations. Monitoring of glucose and A1C, lipids, blood pressure, and renal status is essential to evaluate nutrition-related outcomes. If goals are not met (**Tables 6 and 8**), changes must be made in the overall diabetes care and management plan.

Recommendations

- People with diabetes should receive individualized MNT as needed to achieve treatment goals, preferably provided by a registered dietitian familiar with the components of diabetes MNT. (B)

Physical activity

ADA technical reviews on exercise in patients with diabetes have summarized the value of exercise in the diabetes management plan. Regular exercise has been shown to improve blood glucose control, reduce cardiovascular risk factors, contribute to weight loss, and improve well-being. Furthermore, regular exercise may prevent type 2 diabetes in high-risk individuals. Before beginning a physical activity program, the patient with diabetes should have a detailed medical evaluation with appropriate diagnostic studies. This examination should screen for the presence of macro- and microvascular complications that may be worsened by the physical activity program (see next section regarding coronary heart disease [CHD] screening). Identification of areas of concern will allow the design of an individualized physical activity plan that can minimize risk to the patient.

All levels of physical activity, including leisure activities, recreational sports, and competitive professional performance, can be performed by people with diabetes who do not have complications and have good glycemic control. The ability to adjust the therapeutic regimen (insulin therapy and MNT) to allow safe participation is an important management strategy.

Recommendations

- A regular physical activity program, adapted to the presence of complications, is recommended for all patients with diabetes who are capable of participating. (B)

Prevention and management of diabetes complications

I. CVD: management of risk factors and screening for coronary artery disease

CVD is the major cause of mortality for persons with diabetes. It is also a major contributor to morbidity and direct and indirect costs of diabetes. Type 2 diabetes is an independent risk factor for macrovascular disease, and its common coexisting conditions (e.g., hypertension and dyslipidemia) are also risk factors.

Studies have shown the efficacy of reducing cardiovascular risk factors in preventing or slowing CVD. Evidence is summarized in the following sections and reviewed in detail in the ADA technical reviews on hypertension, dyslipidemia, aspirin therapy, and smoking cessation and in the consensus statement on CHD in people with diabetes. Emphasis should be placed on reducing cardiovascular risk factors, when possible, and clinicians should be alert for signs and symptoms of atherosclerosis.

A. Blood pressure control

Hypertension (blood pressure $\geq 140/90$ mmHg) is a common comorbidity of diabetes, affecting 20–60% of people with diabetes, depending on age, obesity, and ethnicity. Hypertension is also a major risk factor for CVD and microvascular complications such as retinopathy and nephropathy. In type 1 diabetes, hypertension is often the result of underlying nephropathy. In type 2 diabetes, hypertension is likely to be present as part of the metabolic syndrome (i.e., obesity, hyperglycemia, dyslipidemia) that is accompanied by high rates of CVD.

Randomized clinical trials have demonstrated the incontrovertible benefit of lowering blood pressure to <140 mmHg systolic and <80 mmHg diastolic in persons with diabetes. Epidemiologic analyses show that blood pressures $>120/80$ mmHg are associated with increased cardiovascular event rates and mortality in persons with diabetes. Therefore, a target blood pressure goal of $<130/80$ mmHg is reasonable if it can be safely achieved.

Although there are no well-controlled studies of diet and exercise in the treatment of hypertension in persons with diabetes, reducing sodium intake and body weight (when indicated), avoiding excessive alcohol consumption, and increasing activity levels have been shown to be effective in reducing blood pressure in nondiabetic individuals. These nonpharmacological strategies may also positively affect glycemia and lipid control.

Lowering of blood pressure with regimens based on antihypertensive drugs, including ACE inhibitors, angiotensin receptor blockers (ARBs), β -blockers, diuretics, and calcium channel blockers, has been shown to be effective in lowering cardiovascular events. Several studies suggest that ACE inhibitors may be superior to dihydropyridine calcium channel blockers (DCCBs) in reducing cardiovascular events. ACE inhibitors have been shown to improve cardiovascular outcomes in high cardiovascular risk patients with or without hypertension. In patients with congestive heart failure, ACE inhibitors are associated with better outcomes when compared to ARBs. ARBs also improve cardiovascular outcomes in the subset of patients with hypertension, diabetes, and end-organ injury. The compelling effect of ACE inhibitors or ARBs in patients with albuminuria or renal insufficiency provide additional rationale for use of these agents (see section II below).

The β -blocker arm of the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) was terminated after interim analysis showed that β -blockers were substantially less effective in reducing congestive heart failure than diuretic therapy. However, it should be noted that diuretics were not allowed in this arm of the trial.

Before beginning treatment, patients with elevated blood pressures should have their blood pressure reexamined within 1 month to confirm the presence of hypertension unless the systolic blood pressure is ≥ 160 mmHg or the diastolic blood pressure is ≥ 100 mmHg, in which case treatment should be immediately initiated. Patients with hypertension should be seen as often as needed until adequate blood pressure control is obtained and then seen as necessary. In these patients, other cardiovascular risk factors, including hyperlipidemia, smoking, urinary albumin excretion (assessed before initiation of treatment), and glycemic control, should be carefully assessed and treated. Many patients will require three or more drugs to reach target goals.

Recommendations

Screening and diagnosis

- Blood pressure should be measured at every routine diabetes visit. Patients found to have systolic blood pressure ≥ 130 or diastolic blood pressure ≥ 80 mmHg should have blood pressure confirmed on a separate day. (E)
- Orthostatic measurement of blood pressure should be performed to assess for the presence of autonomic neuropathy. (E)

Goals

- Patients with diabetes should be treated to a systolic blood pressure <130 mmHg. (B)
- Patients with diabetes should be treated to a diastolic blood pressure <80 mmHg. (B)

Treatment

- Patients with a systolic blood pressure of 130–139 mmHg or a diastolic blood pressure of 80–89 mmHg should be given lifestyle and behavioral therapy alone for a maximum of 3 months and then, if targets are not achieved, in addition, should be treated pharmacologically. (E)
- Patients with hypertension (systolic blood pressure ≥ 140 or diastolic blood pressure ≥ 90 mmHg) should receive drug therapy in addition to lifestyle and behavioral therapy. (A)
- Initial drug therapy may be with any drug class currently indicated for the treatment of hypertension. However, some drug classes (ACE inhibitors, β -blockers, and diuretics) have been repeatedly shown to be particularly beneficial in reducing CVD events during the treatment of uncomplicated hypertension and are therefore preferred agents for initial therapy. If ACE inhibitors are not tolerated, ARBs may be used. Additional drugs may be chosen from these classes or another drug class. (A)
- If ACE inhibitors or ARBs are used, monitor renal function and serum potassium levels. (E)
- In patients with type 1 diabetes, with or without hypertension, with any degree of albuminuria, ACE inhibitors have been shown to delay the progression of nephropathy. (A)
- In patients with type 2 diabetes, hypertension and microalbuminuria, ACE inhibitors and ARBs have been shown to delay the progression to macroalbuminuria. (A)
- In those with type 2 diabetes, hypertension, macroalbuminuria

(>300 mg/day), nephropathy, or renal insufficiency, an ARB should be strongly considered. (A)

- If one class is not tolerated, the other should be substituted. (A)
- In patients >55 years of age, with hypertension or without hypertension but with another cardiovascular risk factor (history of CVD, dyslipidemia, microalbuminuria, smoking), an ACE inhibitor (if not contraindicated) should be considered to reduce the risk of cardiovascular events. (A)
- In patients with microalbuminuria or overt nephropathy, in whom ACE inhibitors or ARBs are not well tolerated, a non-DCCB or β -blocker should be considered. (C)
- In patients with a recent myocardial infarction, β -blockers, in addition, should be considered to reduce mortality. (A)
- In elderly hypertensive patients, blood pressure should be lowered gradually to avoid complications. (E)
- Patients not achieving target blood pressure on three drugs, including a diuretic, and/or patients with significant renal disease (see below) should be referred to a specialist experienced in the care of patients with hypertension. (E)

B. Lipid management

Patients with type 2 diabetes have an increased prevalence of lipid abnormalities that contributes to higher rates of CVD. Lipid management aimed at lowering LDL cholesterol, raising HDL cholesterol, and lowering triglycerides has been shown to reduce macrovascular disease and mortality in patients with type 2 diabetes, particularly those who have had prior cardiovascular events.

In three secondary prevention studies using HMG (hydroxymethylglutaryl) CoA reductase inhibitors (statins), patients with diabetes achieved significant reductions in coronary and cerebrovascular events). A primary prevention study using statins showed a similar trend of reduced events in the small number of patients with diabetes. In two studies using the fibric acid derivative gemfibrozil, reductions in cardiovascular end points were also achieved. In the Helsinki Heart Study, a primary prevention trial, a trend toward significant reductions in CHD events was observed in the small group of subjects with diabetes. In the Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial (VA-HIT), a secondary trial, a significant reduction in events occurred with improved HDL and triglycerides and no change in LDL cholesterol.

MNT, increased physical activity, and weight loss should allow some patients to reach these lipid levels. Nutrition intervention should be tailored according to each patient's age, type of diabetes, pharmacological treatment, lipid levels, and other medical conditions and should focus on the reduction of saturated fat, cholesterol, and transunsaturated fat intake. Glycemic control can also beneficially modify plasma lipid levels. In particular, triglycerides may be significantly reduced with optimal glucose lowering.

Pharmacological treatment is indicated if there is an inadequate response to lifestyle modifications and improved glucose control. The first priority of pharmacological therapy is to lower LDL cholesterol to a target goal of <100 mg/dl (2.60 mmol/l). For LDL lowering, statins are the drugs of choice. Statins raise HDL modestly, but a greater increase is usually achieved with fibrates.

In patients with LDL between 100 mg/dl (2.60 mmol/l) and 129 mg/dl (3.30 mmol/l), a variety of treatment strategies are available, including more aggressive nutrition intervention and pharmacological treatment with a statin. In addition, if the HDL is <40 mg/dl and the LDL is between 100 and 129 mg/dl, a fibric acid derivative might be used.

Niacin is the most effective drug for raising HDL but can significantly increase blood glucose, particularly at a high dose. More recent studies demonstrate that at modest doses (750–2,000 mg/day), significant benefit with regards to LDL, HDL, and triglyceride levels are accompanied by modest changes in glucose that are generally amenable to adjustment of diabetes therapy. Combination therapy, with a statin and a fibrate or statin and niacin, may be efficacious for patients needing treatment for all three lipid fractions, but this combination is associated with an increased risk for abnormal transaminase levels, myositis, or rhabdomyolysis.

Following the recommendations of the National Cholesterol Education Program's Report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents, LDL cholesterol should be lowered to 110 mg/dl (2.80 mmol/l) in children with cardiovascular risk factors in addition to diabetes.

Recommendations

General recommendations

- Lowering LDL cholesterol is associated with a reduction in cardiovascular events. (A)

- Lowering triglycerides and increasing HDL cholesterol are associated with a reduction in cardiovascular events. (B)

Goals

- Lower LDL cholesterol to <100 mg/dl (2.6 mmol/l) as the primary goal of therapy for adults. (B)
- Lower triglycerides to <150 mg/dl (1.7 mmol/l) and raise HDL cholesterol to >40 mg/dl (1.15 mmol/l). In women, an HDL goal 10 mg/dl higher may be appropriate. (C)

Screening

- In adult patients, test for lipid disorders at least annually and more often if needed to achieve goals. In adults with low-risk lipid values (LDL <100 mg/dl, HDL >60 mg/dl, triglycerides <150), repeat lipid assessments every 2 years. (E)
- In children >2 years of age, perform a lipid profile after diagnosis of diabetes and when glucose control has been established. If values are considered low risk and there is no family history, assessments should be repeated every 5 years. (E)

Treatment

- MNT focusing on the reduction of saturated fat and cholesterol intake, weight loss, and increased physical activity has been shown to improve the lipid profile in patients with diabetes. (A)
- Patients who do not achieve lipid goals with lifestyle modifications require pharmacological therapy. (A)
- Statins should be used as first-line pharmacologic therapy for LDL lowering. (A)
- Therapy with fibrates in patients with low HDL has been shown to reduce CVD rates and progression of carotid intimal medial progression. (A)
- When prescribing fibrates or niacin, in combination therapy with a statin, care is needed to minimize the risk of adverse effects. (E)

C. Anti-platelet in diabetes

The use of aspirin in diabetes is reviewed in detail in the ADA technical reviews on aspirin therapy. Aspirin blocks thromboxane synthesis by acetylating platelet cyclo-oxygenase and has been used as a primary and secondary therapy to prevent cardiovascular events in diabetic and nondiabetic individuals. One large meta-analysis and several clinical trials demonstrate the efficacy of using aspirin as a preventive measure for

cardiovascular events including stroke and myocardial infarction. Many trials have shown an ~30% decrease in myocardial infarction and a 20% decrease in stroke in a wide range of patients, including young and middle-aged patients, patients with and without a history of CVD, males and females, and patients with hypertension.

Dosages used in most clinical trials ranged from 75 to 325 mg/day. There is no evidence to support any specific dose, but using the lowest possible dosage and enteric-coated preparations may help reduce side effects. There is no evidence for a specific age at which to start aspirin, but at ages below 30 years, when the risk of CVD is low, there is no evidence of benefit of aspirin for primary prevention.

Clopidogrel has been demonstrated to reduce CVD rates in diabetic individuals. Adjunctive therapy in very high-risk patients or as alternative therapy in aspirin-intolerant patients should be considered.

Recommendation

- Use aspirin therapy (75–325 mg/day) in all adult patients with diabetes and macrovascular disease. (A)
- Consider beginning aspirin therapy (75–325 mg/day) for primary prevention in patients 40 years of age with diabetes and one or more other cardiovascular risk factors. (A)
- Do not use aspirin in patients <21 years of age because of the increased risk of Reye's syndrome. (A)
- Consider aspirin therapy for patients between 30 and 40 years of age with other cardiovascular risk factors. (B)

D. Smoking cessation

Issues of smoking in diabetes are reviewed in detail in the ADA technical reviews on smoking cessation. A large body of evidence from epidemiological, case-control, and cohort studies provides convincing documentation of the causal link between cigarette smoking and health risks. Cigarette smoking accounts for one of every five deaths in the U.S. and is the most important modifiable cause of premature death. Much of the prior work documenting the impact of smoking on health did not discuss separately results on subsets of individuals with diabetes, suggesting the identified risks are at least equivalent to those found in the general population. Other studies of individuals with diabetes consistently found a heightened risk of morbidity and premature death associated with the

development of macrovascular complications among smokers. Smoking is also related to the premature development of microvascular complications of diabetes and may have a role in the development of type 2 diabetes.

A number of large randomized clinical trials have demonstrated the efficacy and cost-effectiveness of counseling in changing smoking behavior. Such studies, combined with the others specific to individuals with diabetes, suggest that smoking cessation counseling is effective in reducing tobacco use,

The routine and thorough assessment of tobacco use is important as a means of preventing smoking or encouraging cessation. Special considerations should include assessment of level of nicotine dependence, which is associated with difficulty in quitting and relapse.

Recommendations

- Advise all patients not to smoke. (A)
- Include smoking cessation counseling and other forms of treatment as a routine component of diabetes care. (B)

E. CHD screening and treatment

CHD screening and treatment are reviewed in detail in the ADA consensus statement on CHD in people with diabetes. To identify the presence of CHD in diabetic patients without clear or suggestive symptoms of coronary artery disease (CAD), a risk factor–based approach to the initial diagnostic evaluation and subsequent follow-up is recommended. At least annually, cardiovascular risk factors should be assessed. These risk factors include dyslipidemia, hypertension, smoking, a positive family history of premature coronary disease, and the presence of micro- or macroalbuminuria. Candidates for screening exercise stress (electrocardiogram [ECG]) testing include those with 1) typical or atypical cardiac symptoms; 2) an abnormal resting ECG; 3) a history of peripheral or carotid occlusive disease; 4) sedentary lifestyle, age >35 years, and plans to begin a vigorous exercise program; or 5) those with two or more risk factors noted above. There is, however, no current evidence that exercise testing in asymptomatic patients with risk factors improves prognosis. Patients with abnormal exercise ECG and patients unable to perform an exercise ECG require additional or alternative testing. Currently, stress nuclear perfusion and stress

echocardiography are valuable next-level diagnostic procedures. A consultation with a cardiologist is recommended regarding further work-up.

Recommendations

- Perform exercise stress testing in asymptomatic diabetic patients based on the criteria outlined above. Consider a risk factor–based strategy for the diagnosis of CAD that might include stress ECG and/or stress echocardiography and/or perfusion imaging. (E)
- Refer patients with signs and symptoms of CVD or with positive noninvasive test for CAD to a cardiologist for further evaluation. (E)
- In patients with treated congestive heart failure, metformin use is contraindicated. The thiazolidinediones are associated with fluid retention, and their use can be complicated by the development of congestive heart failure. Caution in prescribing thiazolidinediones in the setting of known congestive heart failure or other heart diseases as well as in patients with preexisting edema or concurrent insulin therapy is required. (E)

II. Nephropathy screening and treatment

Diabetic nephropathy occurs in 20–40% of patients with diabetes and is the single leading cause of end-stage renal disease (ESRD). Persistent albuminuria in the range of 30–299 mg/24 h (microalbuminuria) has been shown to be the earliest stage of diabetic nephropathy in type 1 diabetes and a marker for development of nephropathy in type 2 diabetes. Microalbuminuria is also a well-established marker of increased CVD risk .

Patients with microalbuminuria who progress to macroalbuminuria (300 mg/24 h) are likely to progress to ESRD over a period of years . Over the past several years, a number of interventions have been demonstrated to reduce the risk and slow the progression of renal disease.

Intensive diabetes management with the goal of achieving near normoglycemia has been shown in large prospective randomized studies to delay the onset of microalbuminuria and the progression of microalbuminuria to macroalbuminuria in patients with type 1 and type 2 diabetes . The UKPDS provided strong evidence that control of blood pressure can reduce the development of nephropathy . In addition, large prospective randomized studies in patients with type 1 diabetes have demonstrated that

achievement of lower levels of systolic blood pressure (<140 mmHg) achieved with treatment using ACE inhibitors provides a selective benefit over other antihypertensive drug classes in delaying the progression from microalbuminuria to macroalbuminuria and can slow the decline in glomerular filtration rate (GFR) in patients with macroalbuminuria.

In addition, ACE inhibitors have been shown to reduce severe CVD (i.e., myocardial infarction, stroke, death), thus further supporting the use of these agents in patients with microalbuminuria . ARBs have also been shown to reduce the rate of progression from micro- to macroalbuminuria as well as end-stage renal disease in patients with type 2 diabetes. Some evidence suggests that ARBs have a smaller magnitude of rise in potassium compared with ACE inhibitors in people with nephropathy.

A meta-analysis of several small studies has shown that protein restriction may be of benefit in some patients whose nephropathy seems to be progressing despite optimal glucose and blood pressure control.

While screening for microalbuminuria can be performed by three methods—1) measurement of the albumin-to-creatinine ratio in a random, spot collection; 2) 24-h collection with creatinine, allowing the simultaneous measurement of creatinine clearance; and 3) timed (e.g., 4-h or overnight) collection—*the analysis of a spot sample for the albumin-to-creatinine ratio is strongly encouraged*. The other two alternatives (24-h collection and a timed specimen) are rarely necessary. At least two of three tests measured within a 6-month period should show elevated levels before a patient is designated as having microalbuminuria. Abnormalities of albumin excretion. Physicians may use the Levey modification of the Cockcroft and Gault equation to calculate estimated GFR (eGFR) from serum creatinine and to stage the patient’s renal disease. The eGFR can easily be calculated by going to www.kidney.org/professionals/dogi/gfr_calculator.cfm.

The role of annual microalbuminuria assessment is less clear after diagnosis of microalbuminuria and institution of ACE inhibitor or ARB therapy and blood pressure control. Many experts, however, recommend continued surveillance to assess both response to therapy and progression of disease.

Consider referral to a physician experienced in the care of diabetic renal disease either when the GFR has fallen to $<80 \text{ ml} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$ or if difficulties occur in the management of hypertension or hyperkalemia. It is suggested that consultation with a nephrologist be obtained when the eGFR is $<30 \text{ ml} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$. Early referral of such patients has been found to reduce cost and improve quality of care and keep people off dialysis longer.

For a complete discussion on the treatment of nephropathy, see the ADA's position statement "Diabetic Nephropathy".

Recommendations

General recommendations

- To reduce the risk and/or slow the progression of nephropathy, optimize glucose control. (A)
- To reduce the risk and/or slow the progression of nephropathy, optimize blood pressure control. (A)

Screening

Perform an annual test for the presence of microalbuminuria in type 1 diabetic patients with diabetes duration of ≥ 5 years and in all type 2 diabetic patients, starting at diagnosis. (E)

Treatment

- In the treatment of both micro- and macroalbuminuria, either ACE inhibitors or ARBs should be used. (A)
- In patients with type 1 diabetes, with or without hypertension, with any degree of albuminuria, ACE inhibitors have been shown to delay the progression of nephropathy. (A) • In patients with type 2 diabetes, hypertension and microalbuminuria, ACE inhibitors and ARBs have been shown to delay the progression to macroalbuminuria. (A) • In patients with type 2 diabetes, hypertension, macroalbuminuria, and renal insufficiency (serum creatinine $>1.5 \text{ mg/dl}$), ARBs have been shown to delay the progression of nephropathy. (A) • If one class is not tolerated, the other should be substituted. (E)
- With presence of nephropathy, initiate protein restriction to $0.8 \text{ g} \cdot \text{kg}^{-1} \text{ body wt} \cdot \text{day}^{-1}$ ($\sim 10\%$ of daily calories), the current adult recommended dietary allowance for protein. Further restriction may be useful in slowing the decline of GFR in selected patients. (B)

- Use of DCCBs are less effective in slowing nephropathy progression compared with ARB therapy in those with diabetes with nephropathy and macroalbuminuria. (B)
- Consider the use of non-DCCBs or β -blockers in patients unable to tolerate ACE inhibitors and/or ARBs. (E)
- If ACE inhibitors or ARBs are used, monitor serum potassium levels for the development of hyperkalemia. (B)
- Consider referral to a physician experienced in the care of diabetic renal disease when the eGFR has fallen to $<60 \text{ ml} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$ or if difficulties occur in the management of hypertension or hyperkalemia. (B)

III. Diabetic retinopathy screening and treatment

Diabetic retinopathy is a highly specific vascular complication of both type 1 and type 2 diabetes. The prevalence of retinopathy is strongly related to the duration of diabetes. Diabetic retinopathy is estimated to be the most frequent cause of new cases of blindness among adults aged 20–74 years.

Intensive diabetes management with the goal of achieving near normoglycemia has been shown in large prospective randomized studies to prevent and/or delay the onset of diabetic retinopathy. In addition to glycemic control, several other factors seem to increase the risk of retinopathy. The presence of nephropathy is associated with retinopathy. High blood pressure is an established risk factor for the development of macular edema and is associated with the presence of proliferative diabetic retinopathy (PDR). Lowering blood pressure, as shown in the UKPDS, has been shown to decrease the progression of retinopathy. Several case series and a controlled prospective study suggest that pregnancy in type 1 diabetic patients may aggravate retinopathy. During pregnancy and 1 year postpartum, retinopathy may be transiently aggravated; laser photocoagulation surgery can minimize this risk.

One of the main motivations for screening for diabetic retinopathy is the established efficacy of laser photocoagulation surgery in preventing visual loss. Two large National Institutes of Health-sponsored trials, the Diabetic Retinopathy Study (DRS) and the Early Treatment Diabetic Retinopathy Study (ETDRS), provide the strongest support for the therapeutic benefit of photocoagulation surgery.

The DRS tested whether scatter (panretinal) photocoagulation surgery could reduce the risk of vision loss from PDR. Severe visual loss (i.e., best acuity of 5/200 or worse) was seen in 15.9% of untreated vs. 6.4% of treated eyes. The benefit was greatest among patients whose baseline evaluation revealed high-risk characteristics (HRCs) (chiefly disc neovascularization or vitreous hemorrhage with any retinal neovascularization). Of control eyes with HRCs, 26% progressed to severe visual loss vs. 11% of treated eyes. Given the risk of a modest loss of visual acuity and of contraction of visual field from panretinal laser surgery, such therapy has been primarily recommended for eyes approaching or reaching HRCs.

The ETDRS established the benefit of focal laser photocoagulation surgery in eyes with macular edema, particularly those with clinically significant macular edema. In patients with clinically significant macular edema after 2 years, 20% of untreated eyes had a doubling of the visual angle (e.g., 20/50 to 20/100) compared with 8% of treated eyes. Other results from the ETDRS indicate that, provided careful follow-up can be maintained, scatter photocoagulation surgery is not recommended for eyes with mild or moderate nonproliferative diabetic retinopathy (NPDR). When retinopathy is more severe, scatter photocoagulation surgery should be considered, and usually should not be delayed, if the eye has reached the high-risk proliferative stage. In older-onset patients with severe NPDR or less than high-risk PDR, the risk of severe visual loss and vitrectomy is reduced ~50% by laser photocoagulation surgery at these earlier stages.

Laser photocoagulation surgery in both the DRS and the ETDRS was beneficial in reducing the risk of further visual loss, but generally not beneficial in reversing already diminished acuity. This preventive effect and the fact that patients with PDR or macular edema may be asymptomatic provide strong support for a screening program to detect diabetic retinopathy. For a detailed review of the evidence and further discussion, see the ADA's technical review and position statement on this subject.

Recommendations

General recommendations

- Optimal glycemic control can substantially reduce the risk and progression of diabetic retinopathy. (A)
- Optimal blood pressure control can reduce the risk and progression of diabetic retinopathy. (A)

- Aspirin therapy does not prevent retinopathy or increase the risks of hemorrhage. (A)

Screening

- Patients with type 1 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist within 3–5 years after the onset of diabetes. (B)
- Patients with type 2 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist shortly after the diagnosis of diabetes. (B)
- Subsequent examinations for type 1 and type 2 diabetic patients should be repeated annually by an ophthalmologist or optometrist who is knowledgeable and experienced in diagnosing the presence of diabetic retinopathy and is aware of its management. Examinations will be required more frequently if retinopathy is progressing. (B)
- When planning pregnancy, women with preexisting diabetes should have a comprehensive eye examination and should be counseled on the risk of development and/or progression of diabetic retinopathy. Women with diabetes who become pregnant should have a comprehensive eye examination in the first trimester and close follow-up throughout pregnancy and for 1 year postpartum. This guideline does not apply to women who develop GDM because such individuals are not at increased risk for diabetic retinopathy. (B)

Treatment

- Laser therapy can reduce the risk of vision loss in patients with HRCs. (A)
- Promptly refer patients with any level of macular edema, severe NPDR, or any PDR to an ophthalmologist who is knowledgeable and experienced in the management and treatment of diabetic retinopathy. (A)

IV. Foot care

Amputation and foot ulceration are one of the most common consequences of diabetic neuropathy and a major cause of morbidity and disability in people with diabetes. Early recognition and management of independent risk factors can prevent or delay adverse outcomes.

The risk of ulcers or amputations is increased in people who have had diabetes >10 years, are male, have poor glucose control, or have cardiovascular,

retinal, or renal complications. The following foot-related risk conditions are associated with an increased risk of amputation:

- Peripheral neuropathy with loss of protective sensation.
- Altered biomechanics (in the presence of neuropathy).
- Evidence of increased pressure (erythema, hemorrhage under a callus).
- Bony deformity.
- Peripheral vascular disease (decreased or absent pedal pulses).
- A history of ulcers or amputation.
- Severe nail pathology.

Targeted patient education and appropriate footwear can reduce the risk of ulceration. For a detailed review of the evidence and further discussion, see the ADA's technical review and position statement titled "Preventive Foot Care in Persons With Diabetes".

Problems involving the feet, especially ulcers and wound care, may require care by a podiatrist, orthopedic surgeon, or rehabilitation specialist experienced in the management of persons with diabetes. For a complete discussion on wound care, see the ADA's consensus statement on diabetic foot wound care.

Recommendations

- A multidisciplinary approach is recommended for persons with foot ulcers and high-risk feet, especially those with a history of prior ulcer or amputation. (A)
- The foot examination can be accomplished in a primary care setting and should include the use of a Semmes-Weinstein monofilament, tuning fork, palpation, and a visual examination. (B)
- Educate all patients, especially those with risk factors or prior lower-extremity complications, about the risk and prevention of foot problems and reinforce self-care behavior. (B)
- Refer high-risk patients to foot care specialists for ongoing preventive care and life-long surveillance. (C)
- Refer patients with significant claudication for further vascular assessment and consider exercise and surgical options. (C)
- Perform a comprehensive foot examination annually on patients with diabetes to identify risk factors predictive of ulcers and amputations. Perform a

visual inspection of patients' feet at each routine visit. (E)

Preventive care

I. Preconception care

Major congenital malformations remain the leading cause of mortality and serious morbidity in infants of mothers with type 1 and type 2 diabetes. Observational studies indicate that the risk of malformations increases continuously with increasing maternal glycemia during the first 6–8 weeks of gestation, as indexed by first trimester A1C concentrations. There is no threshold for A1C values above which the risk begins or below which it disappears. However, malformation rates above the 1–2% background rate seen in nondiabetic pregnancies appear to be limited to pregnancies in which first trimester A1C concentrations are >1% above the normal range.

Five nonrandomized studies have compared rates of major malformations in the infants between women who participated in preconception diabetes care programs and women who initiated intensive diabetes management after they were already pregnant. The preconception care programs were multidisciplinary and designed to train patients in diabetes self-management with diet, intensified insulin therapy, and SMBG. Goals were set to achieve normal blood glucose concentrations, and >80% of subjects achieved normal A1C concentrations before they became pregnant. In all five studies, the incidence of major congenital malformations in women who participated in preconception care (range 1.0–1.7% of infants) was much lower than the incidence in women who did not participate (range 1.4–10.9% of infants). One limitation of these studies is that participation in preconception care was self-selected by patients rather than randomized. Thus, it is impossible to be certain that the lower malformation rates resulted fully from improved diabetes care. Nonetheless, the overwhelming evidence supports the concept that malformations can be reduced or prevented by careful management of diabetes before pregnancy.

Planned pregnancies greatly facilitate preconceptional diabetes care. Unfortunately, nearly two-thirds of pregnancies in women with diabetes are unplanned, leading to a persistent excess of malformations in infants of diabetic mothers. To minimize the occurrence of these devastating malformations, standard care for all women with diabetes who have child-bearing potential should include 1) education

about the risk of malformations associated with unplanned pregnancies and poor metabolic control and 2) use of effective contraception at all times, unless the patient is in good metabolic control and actively trying to conceive.

Women contemplating pregnancy need to be seen frequently by a multidisciplinary team experienced in the management of diabetes before and during pregnancy. Teams may vary but should include a diabetologist, an internist or a family physician, an obstetrician, a diabetes educator, a dietitian, a social worker, and other specialists as necessary. The goals of preconception care are to 1) integrate the patient into the management of her diabetes, 2) achieve the lowest A1C test results possible without excessive hypoglycemia, 3) assure effective contraception until stable and acceptable glycemia is achieved, and 4) identify, evaluate, and treat long-term diabetic complications such as retinopathy, nephropathy, neuropathy, hypertension, and CAD.

For further discussion, see the ADA's technical review and position statement on this subject.

Recommendations

- A1C levels should be normal or as close to normal as possible in an individual patient before conception is attempted. (B)
- ACE inhibitors should be discontinued before pregnancy. (C)
- All women with diabetes and child-bearing potential should be educated about the need for good glucose control before pregnancy. They should participate in family planning. (E)
- Women with diabetes who are contemplating pregnancy should be evaluated and, if indicated, treated for diabetic retinopathy, nephropathy, neuropathy, and CVD. (E)
- Among the drugs commonly used in the treatment of patients with diabetes, statins are pregnancy category X and should be discontinued prior to conception if possible. ACE inhibitors and ARBs are category C in the first trimester (maternal benefit may outweigh fetal risk in certain situations), but category D in later pregnancy, and should generally be discontinued prior to pregnancy. Among the oral antidiabetic agents, metformin and acarbose are classified as category B and all others as category C; potential risks and benefits of oral antidiabetic agents in the preconception period must be carefully weighed, recognizing that sufficient data are not available to establish the safety of these agents in

pregnancy. They should generally be discontinued in pregnancy. (E)

II. Immunization

Influenza and pneumonia are common, preventable infectious diseases associated with high mortality and morbidity in the elderly and in people with chronic diseases. There are limited studies reporting the morbidity and mortality of influenza and pneumococcal pneumonia specifically in people with diabetes. Observational studies of patients with a variety of chronic illnesses, including diabetes, show that these conditions are associated with an increase in hospitalizations for influenza and its complications. Based on a case-control series, influenza vaccine has been shown to reduce diabetes-related hospital admission by as much as 79% during flu epidemics. People with diabetes may be at increased risk of the bacteremic form of pneumococcal infection and have been reported to have a high risk of nosocomial bacteremia, which has a mortality rate as high as 50%. Safe and effective vaccines are available that can greatly reduce the risk of serious complications from these diseases. There is sufficient evidence to support that people with diabetes have appropriate serologic and clinical responses to these vaccinations. The Centers for Disease Control's Advisory Committee on Immunization Practices recommends influenza and pneumococcal vaccines for all persons over 65 years of age as well as for all persons of any age with diabetes.

For a complete discussion on the prevention of influenza and pneumococcal disease in people with diabetes, consult the technical review and position statement on this subject.

Recommendations

- Annually provide an influenza vaccine to all diabetic patients 6 months of age or older. (C)
- Provide at least one lifetime pneumococcal vaccine for adults with diabetes. A one-time revaccination is recommended for individuals >64 years of age previously immunized when they were <65 years of age if the vaccine was administered >5 years ago. Other indications for repeat vaccination include nephrotic syndrome, chronic renal disease, and other immunocompromised states, such as postorgan transplantation. (C)

Special Considerations

I. Care of older adults with diabetes

Diabetes is an important health condition for the aging population; at least 15% of patients over the age of 65 years have diabetes. The number of older persons with diabetes can be expected to grow rapidly over the coming decades. Unfortunately, there are no long-term studies demonstrating the benefits of tight glycemic control in persons over 65 years of age. In approaching the elderly patient, a thoughtful individualized approach, consistent with the heterogeneity of the aging process, should be used. However, patients who can be expected to live long enough to reap the benefits of long-term glycemic control (10–20 years) and who are active, cognitively intact, and willing to undertake the responsibility of self-management should be encouraged to do so.

For patients with advanced diabetes complications, life-limiting comorbid illness, or cognitive or functional impairment, it is reasonable to set less intensive target goals. These patients are less likely to benefit from reducing the risk of microvascular complications and more likely to suffer serious adverse effects from hypoglycemia. Chronic hyperglycemia can cause a catabolic state leading to malnutrition, functional impairment, and symptoms with decreased quality of life. Also, patients with poorly controlled diabetes may be subject to acute complications of diabetes, including hyperglycemic hyperosmolar coma. Older patients can be treated with the same drug regimens as younger patients, but special care is required in prescribing and monitoring drug therapy. Metformin is often contraindicated because of renal insufficiency or heart failure. Sulfonylureas and other insulin secretagogues can cause hypoglycemia. Insulin can also cause hypoglycemia as well as requiring good visual and motor skills and cognitive ability of the patient or a caregiver. Thiazolidinediones should not be used in patients with congestive heart failure (New York Heart Association [NYHA] Class III and IV). α -Glucosidase inhibitors are safe but may not be well tolerated and may not be effective as monotherapy. Drugs should be started at the lowest dose and titrated up gradually until targets are reached or side effects develop.

Cardiovascular risk reduction continues to be important as in younger patients; there is strong evidence from clinical trials of the value of treating hypertension in the elderly. There is less evidence for

lipid-lowering and aspirin therapy, although diabetes patients have such an elevated risk for CVD that aggressive management of lipids and aspirin use when not contraindicated are probably reasonable interventions.

II. Children and adolescents

Approximately three-quarters of all newly diagnosed cases of type 1 diabetes occur in individuals younger than 18 years of age. Care of this group requires integration of diabetes management with the complicated physical and emotional growth needs of children, adolescents, and their families.

Diabetes care for children of this age-group should be provided by a team that can deal with these special medical, educational, nutritional, and behavioral issues.

At the time of initial diagnosis, it is extremely important to establish the goals of care and to begin diabetes self-management education. A firm educational base should be provided so that the individual and family can become increasingly independent in the self-management of diabetes. Glycemic goals may need to be modified to take into account the fact that most children younger than 6 or 7 years of age have a form of “hypoglycemic unawareness,” in that they lack the cognitive capacity to recognize and respond to hypoglycemic symptoms and may be at greater risk for the sequelae of hypoglycemia.

Intercurrent illnesses are more frequent in young children. Sick-day management rules, including assessment for ketosis with every illness, must be established and taught to prevent severe hyperglycemia and DKA that requires hospitalization and may lead to severe morbidity and even death (21). MNT should be provided at diagnosis, and at least annually thereafter, by an individual experienced with the nutritional needs of the growing child and the behavioral issues that have an impact on adolescent diets. Caution must be exercised to avoid overaggressive dietary manipulation in the very young. Assessment of lifestyle needs should be accompanied by possible modifications of the diabetes regimen. For example, an adolescent who requires more flexibility might be switched to a basal/bolus insulin program with preprandial rapidly acting insulin administration or continuous subcutaneous insulin injection (CSII).

A major issue deserving emphasis in this age-group is that of “adherence.” No matter how sound the medical regimen, it can only be as good as the ability of the family and/or individual to implement it. Family involvement in diabetes remains an important component of optimal diabetes management throughout childhood and into adolescence. Health care providers who care for children and adolescents, therefore, must be capable of evaluating the behavioral, emotional, and psychosocial factors that interfere with implementation and then must work with the individual and family to resolve problems that occur and/or to modify goals as appropriate.

The incidence of type 2 diabetes in children and adolescents has been shown to be increasing. Although there are insufficient data to make definite recommendations, a recent ADA consensus statement provides guidance to the prevention, screening, and treatment of type 2 diabetes in young people. The ideal goal of treatment is normalization of blood glucose and A1C values. Accurate diagnosis and classification of diabetes is crucial in determining appropriate treatment for these patients. Many patients can be managed initially with MNT and exercise, but most will eventually require drug therapy. Successful control of comorbidities, such as hypertension and hyperlipidemia, is also important. For further discussion, see the ADA consensus statement “Type 2 Diabetes in Children and Adolescents” (11).

Information should be supplied to the school or day care setting so that school personnel are aware of the diagnosis of diabetes in the student and of the signs, symptoms, and treatment of hypoglycemia. It is desirable that blood glucose testing be performed at the school or day care setting before lunch and when signs or symptoms of abnormal blood glucose levels are present. Many children may require support for insulin administration by either injection or CSII before lunch at school or in day care.

For further discussion, see the ADA’s position statement “The Care of Children With Diabetes in the School and Day Care Setting” (106).

Strategies for successful guideline implementation

In recent years, numerous health care organizations, ranging from large health care systems such as the U.S. Veteran’s Administration to small private practices, have implemented strategies to improve diabetes care. Successful programs have published results showing improvement in important outcomes

such as A1C measurements as well as process measures such as provision of eye exams. Features of successful programs reported in the literature include:

- Adoption of practice guidelines, with participation of the providers in the process. Guidelines should be readily accessible at the point of service, such as on patient charts, in examining rooms, or on office computer systems.
- Systems changes, such as provision of automated reminders to providers and patients, profiling or reporting of data to providers, and identification of patients at risk because of abnormal target values or a lack of reported values.
- Practice changes, such as scheduling of dedicated diabetes visits and group visits.
- Delivery of diabetes self-management education.
- Availability of case management services, usually by a nurse.
- Availability and involvement of expert consultants, such as endocrinologists and diabetes educators.
- Because these interventions are generally provided as components of a multifactorial intervention, it is difficult to assess the contribution of each component; however, it is clear that optimal diabetes management requires an organized, systematic approach and involvement of a health care team.
- Simple tools such as flow charts may be useful in smaller practices.

Footnotes

- The recommendations in this paper are based on the evidence reviewed in the following publication: Standards of care for diabetes (Technical Review). *Diabetes Care* 17:1514–1522, 1994. Originally approved 1988. Most recent review/revision, October 2002.

Abbreviations: ARB, angiotensin receptor blocker; CAD, coronary artery disease; CHD, coronary heart disease; CSII, continuous subcutaneous insulin injection; CVD, cardiovascular disease; DCCB, dihydropyridine calcium channel blocker; DKA, diabetic ketoacidosis; DRS, Diabetic Retinopathy Study; ECG, electrocardiogram; eGFR, estimated GFR; ESRD, end-stage renal disease; ETDRS, Early Treatment Diabetic Retinopathy Study; FPG, fasting plasma glucose; GCT, glucose challenge test; GDM, gestational diabetes mellitus; GFR, glomerular

filtration rate; HRC, high-risk characteristic; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; MNT, medical nutrition therapy; NPDR, nonproliferative diabetic retinopathy; OGTT, oral glucose tolerance test; PDR, proliferative diabetic retinopathy; PPG, postprandial plasma glucose; SMBG, self-monitoring of blood glucose; UKPDS, U.K. Prospective Diabetes Study.

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