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Type 2 Diabetes Mellitus in the Pediatric Population

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Abstract

The incidence and prevalence of diabetes in youth in the United States is increasing. In particular, type 2 diabetes mellitus (T2DM) is becoming more common in individuals younger than 20 years. Nurse practitioners and other primary care providers that see children should be knowledgeable about the condition and confident in participating in multidisciplinary management. Screening should begin at age 10 or at puberty, whichever comes first. Providers should screen all children who are overweight or obese or of Native American, African American, Latino, Asian American, or Pacific Islander race or ethnicity. Children of these ethnicities have a greater risk for developing T2DM. Screening and diagnostic tests include fasting plasma glucose, the oral glucose tolerance test, and hemoglobin A1C. Once T2DM is diagnosed, management should focus on intensive lifestyle changes and weight loss with dietary changes and increased physical activity. Initial pharmacological treatment involves an oral antihyperglycemic agent and/or subcutaneous insulin therapy. Effective management of a child or adolescent with diabetes involves the creation of a multidisciplinary team consisting of an endocrinologist, social worker, diabetic educator, dietician, school personnel, psychologist, and the family. The family should participate in all aspects of care and commit to making lifestyle changes with the patient. As most youth diagnosed with T2DM are adolescents, they should be encouraged to practice independent care to enable successful transition to young adulthood. Providers should practice culturally sensitive care and individualize treatment and management plans for each patient.

Keywords: diabetes, pediatric, type 2 diabetes mellitus, youth

Type 2 Diabetes Mellitus in the Pediatric Population

Pediatric diabetes mellitus is on the rise. Both type 1 and type 2 are increasing in youth. The Centers for Disease Control (CDC, 2020) reports that an estimated 210,000 children and adolescents younger than 20 years old had diabetes by 2018. The SEARCH study is a national, ongoing study with multiple centers participating in research to discover new information regarding diabetes and youth. Information from the SEARCH study revealed increasing rates of diabetes among youth in the United States (US), especially among youth of minority racial and ethnic groups. From 2001 to 2009, the prevalence of type 1 diabetes mellitus (T1DM) increased by 21.1% while type 2 diabetes mellitus (T2DM) increased by 30.5% in most age, sex, and race or ethnicity groups (Dabelea, et al., 2014; Hamman et al., 2014). From 2002 to 2012, the annual increase in incidence was 1.8% for T1DM and 4.8% for T2DM (Mayer-Davis et al., 2017; Jensen & Dabelea, 2018). These results provide evidence of the increase of diabetes in youth and should not be overlooked. In particular, T2DM has become a more common condition in individuals younger than 20 over the last two decades, likely due to an increase in childhood obesity. Overweight and obesity are major risk factors for T2DM, and the prevalence and incidence of pediatric diabetes has increased in association with the rise of childhood obesity (Arslanian et al., 2018; Galuska et al., 2018; Dabelea et al., 2015; Narasimhan & Weinstock, 2014). Due to the increasing amount of overweight and obese children in the US, nurse practitioners (NPs) and other primary care providers (PCPs) who care for children should be aware and knowledgeable of diabetic conditions. The purpose of this article is to discuss the current screening guidelines, presentation, diagnosis, treatment, and multidisciplinary management of T2DM in youth.

Background

T2DM was previously thought to be a chronic disease seen only in adults; however, an increasing number of youths are developing insulin resistance and being diagnosed as type 2 diabetics. As in adults, T2DM is characterized by insulin resistance rather than an autoimmune process that leads to the destruction of beta cells. Type 1 diabetics will typically have autoantibodies present at the time of diagnosis and require insulin treatment to survive (Dabelea et al., 2015; Barrett, 2016; Xu & Verre, 2018; Zeitler et al., 2018). Type 2 diabetics will not typically have autoantibodies and will still have the ability to produce insulin despite insulin resistance and pancreatic beta cell failure. These cellular impairments are likely brought on by puberty and hormonal changes as well as genetic, environmental, or lifestyle factors, such as poor diet, lack of physical activity, and overweight or obesity; hence, the increasing rates of both childhood obesity and diabetes (Dabelea et al., 2015; Barrett, 2016; Arslanian et al., 2018; Zeitler et al., 2018).

Although there are distinct differences between type 1 and type 2 diabetes, it is important to note that it has become increasingly difficult to distinguish and diagnose children with the correct diabetes type. Some children will be asymptomatic or have symptoms attributed to both types, and it is possible for an overweight or obese child to have T1DM. Moreover, results from the Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY) study found up to 9.8% of children with a diagnosis of T2DM to have autoantibodies (Klingensmith et al., 2010).

More often than not, children with T2DM will be overweight or obese and may already have other comorbidities related to an increased body mass index (BMI), such as hypertension or dyslipidemia. Furthermore, these youth are at higher risk for developing complications or other comorbidities due to diabetes as T2DM in youth leads to a more rapid progression of

comorbidities and risk for complications as compared to adults and other youth with T1DM (Dabelea et al., 2015; Barrett, 2016; Xu & Verre, 2018; Zeitler et al., 2018).

Presentation, Screening, and Diagnosis

Children with diabetes can be symptomatic or asymptomatic. Symptomatic children may present with the classic symptoms of polyuria, polydipsia, and unintentional weight loss, accompanied with or without nausea, vomiting, and dehydration. Metabolic disturbances, diabetic ketoacidosis, or hyperosmolar states may also be present at the time of diagnosis. The American Academy of Pediatrics (AAP) recommends symptomatic children to be tested for ketosis with either serum or urine ketones and evaluating for ketoacidosis by obtaining a venous pH level (Copeland et al., 2013). Asymptomatic children may be diagnosed from incidental findings of screening tests done due to the presence of diabetic risk factors (Klingensmith et al., 2016; Xu & Verre, 2018). Additional signs or conditions related to insulin resistance include acanthosis nigricans, hypertension, hyperlipidemia, polycystic ovary syndrome, or small-for-gestational-age birth weight (Arslanian et al., 2018).

NPs and other providers should screen all children with risk factors for diabetes as well as children presenting with signs and symptoms of diabetes. When screening, it is important to note that the onset of T2DM prior to puberty is rare, and nearly all youth in North America diagnosed with the condition are overweight or obese (Arslanian et al., 2018). The American Diabetes Association ([ADA], 2020a) recommends screening to begin at age 10 or at the onset of puberty, depending on whichever comes first, and if the child is overweight or obese with one or more of the following factors: a maternal history of diabetes or gestational diabetes mellitus during the child's gestation, a family history of T2DM in a first or second degree relative, and Native American, African American, Latino, Asian American, or Pacific Islander race or

ethnicity. It should be noted that children of these ethnicities have a higher risk for developing T2DM (Mayer-Davis et al., 2014; Jensen & Dabelea, 2018).

The ADA (2020b) and International Society of Pediatric and Adolescent Diabetes ([ISPAD], 2018) recommend three different tests for diabetes screening: fasting plasma glucose (FPG), oral glucose tolerance test (OGTT), and hemoglobin A1C (HbA1c). These tests may be used for both screening and diagnosis. Diagnosis will require two abnormal tests results from the same samples or two separate samples. If two different tests are performed (i.e. HbA1c and FPG), and both indicate diabetes, this can also confirm the diagnosis (ADA, 2020b).

FPG is a convenient one-time blood draw. It does require fasting for at least 8 hours prior to testing.

The OGTT requires fasting, as well as additional time to perform the test. Providers should follow the World Health Organization (WHO) guidelines and use a glucose load of 1.75mg/kg (or a maximum of 75 grams) anhydrous glucose dissolved in water. After 2 hours of ingesting the solution, plasma glucose should be checked.

HbA1c is also a convenient one-time blood draw and does not require fasting or additional time to perform the test. Additionally, this test may be more sensitive and specific for detecting diabetes when compared to the OGTT (Ehehalt et al., 2017). All HbA1c tests should be performed in a laboratory using a method that is National Glycohemoglobin Standardization Program (NGSP) certified and standardized to the Diabetes Control and Complications Trial (DCCT) assay for reliable and accurate results. Despite the benefits and standardization of the test, there are multiple factors that can affect a child's HgbA1c level including ethnicity, age, medications, hemoglobinopathies, and disorders that affect red blood cell turnover (Vajravelu &

Lee, 2018). Providers suspecting diabetes should keep this in mind when interpreting HbA1c results.

The ADA (2020b) criteria for the diagnosis of prediabetes and diabetes are the same for children, adolescents, and adults. The criteria for diagnosing prediabetes includes the following: HbA1c 5.7% to 6.5%, FPG greater than or equal to 100 mg/dL but less than 126 mg/dL, and 2-hour plasma glucose greater than or equal to 140 mg/dL but less than 200 mg/dL during an OGTT. The criteria for diagnosing diabetes is HbA1c greater than or equal to 6.5%, FPG greater than or equal to 126 mg/dL, 2-hour plasma glucose greater than or equal to 200 mg/dL during an OGTT, or in a patient with classic symptoms of hyperglycemia a random plasma glucose greater than 200 mg/dL. Providers considering a diagnosis of T2DM for their patients should also obtain a pancreatic autoantibodies panel to further confirm the diagnosis and exclude T1DM. For providers screening at-risk children, tests should be repeated every 3 years at a minimum and more frequently if the child has an increasing BMI (ADA, 2020b).

Treatment

The initial treatment of T2DM should involve therapeutic lifestyle changes. In addition to dietary changes, adding physical exercise, and education, the AAP recommends that all children and adolescents start metformin at the time of diagnosis (Copeland et al., 2013). The ADA (2020a) also recommends that those with a HbA1c less than 8.5% and no acidosis or ketosis be started on metformin. Metformin is considered the first-line pharmacological treatment for youth with T2DM and was previously the only US Food and Drug Administration (FDA) approved oral diabetic agent for the pediatric population. Providers should start with 500 to 1000 mg daily for 7 to 15 days and titrate the dose up once a week over a period of 3 to 4 weeks, depending on the patient's tolerance. The maximum dose is 1000 mg twice a day (Zeitler et al., 2018). Patients

that have a HbA1c greater than 8.5%, with no acidosis, and with or without ketosis should be started on both metformin and insulin. Insulin should start at 0.25 to 0.5 units/kg and can be titrated up to a maximum of 1.5 units/kg. If optimal glucose levels are not met with both metformin and insulin therapy, additional medication may be considered. Liraglutide, a glucagon-like peptide-1 receptor agonist, was recently approved for use in children 10 years of age and older (FDA, 2019). The ADA (2020a) updated their recommendations to consider the use of liraglutide if glycemic targets are not met with metformin and basal insulin, and there is no family history of medullary thyroid carcinoma or multiple endocrine neoplasia type 2.

Insulin can later be weaned if glycemic targets are continually met, and the child may only need to take metformin. Patients and their families should be performing self-monitored blood glucose (SMBG) at home in order to track glycemic levels and measure progress to goals. Insulin should be weaned over a period of 2 to 6 weeks, and the dose should be decreased by 10 to 30% every few days (Zeitler et al., 2018). The goal of treatment should be a HbA1c less than 7.0%, and glycemic targets and the process of SMBG should be individualized (Panagiotopoulos et al., 2018; Arslanian et al., 2018; ADA, 2020a).

Management

Once a diagnosis of T2DM has been made and initial treatment has been completed, it is crucial that providers carefully manage the care of these patients. As in adults, T2DM is a chronic condition, and excellent management requires participation from multiple disciplines. Creating a multidisciplinary team including a primary provider, endocrinologist, social worker, diabetic educator, dietician, school personnel, psychologist, and family members may be beneficial and enable more effective long-term management (ADA, 2020a). Each discipline has a specific role in managing a child with diabetes.

It is essential that providers recommend intensive lifestyle changes with a focus on weight loss, including increasing physical activity, and dietary measures. The ADA (2020a) recommends a family lifestyle change involving the parents or caregivers in nutrition counseling, incorporating physical activity, and understanding medical management (such as using insulin or metformin) in order to successfully manage and guide the child. As youth with T2DM are typically nearing or are of adolescence, they should be educated and encouraged to participate in independent care; this includes SMBG, understanding appropriate dietary habits, participating in daily physical activity, and knowing signs and symptoms of hypoglycemia or hyperglycemia. Diabetic educators can be especially helpful in educating the patient and family in ways that are easy for them to understand and retain the information and providing them with resources (Galuska et al., 2018).

Dietary Changes

As most youth with T2DM are overweight or obese, weight loss should be the primary focus of management. Dieticians who are knowledgeable about T2DM in youth should be involved in nutrition counseling for these families. Recommendations include replacing sugary beverages, such as soda or juice, with water and calorie-free beverages, increasing fruit and vegetable intake, reducing consumption of processed or prepackaged foods, and exchanging high caloric and high fat foods for more nutrient-dense, low-caloric options. Dietary interventions should be family centered and everyone in the household should be making the same changes together in order to encourage the patient to create and sustain healthy eating habits. Parents or caregivers should also be educated on healthy diet choices and how to read nutrition labels. Dieticians or diabetic educators should educate families in a culturally sensitive matter taking

into account food preferences and providing appropriate options and/or substitutions (Xu & Verre, 2018; Zeitler et al., 2018).

Physical Activity

Adding or increasing the amount of physical activity is another necessary lifestyle change for young diabetics. Thirty to sixty minutes of moderate to vigorous activity daily is recommended and can be split into multiple activities during the day (Arslanian et al., 2018; Zeitler et al., 2018). Families should be involved in this lifestyle change as well, with at least one family member available to participate in the activity with the child and provide encouragement. Activities such as taking the stairs instead of the elevator, parking far from a store entrance to increase walking, walking to school or the store if nearby, or doing household chores or yard work are ways to incorporate more daily physical activity. Screen time should also be kept to a two-hour minimum to decrease sedentary lifestyle (Zeitler et al., 2018).

Psychosocial Factors

Racial or ethnic minority groups account for the majority of youth with T2DM (Hamman et al., 2014; Mayer-Davis et al., 2017). Providers should recognize potential social issues and understand that finances, housing or living conditions, food instability, limited access to services, or cultural barriers may cause difficulties in management for the patient and family (ADA, 2020a; Arslanian et al., 2018). Providers should be sensitive to these stressors and personalize care while providing appropriate resources. Social workers are an important part of the multidisciplinary team and can provide additional assistance and resources to the family.

Providers should also assess the patient's psychosocial status. The diagnosis of T2DM leads to some overwhelming lifestyle changes for a family, and especially for the patient. Adolescents with T2DM reported more feelings of depression and a lower quality of life when

compared to those with T1DM (Hood et al., 2014). Assessing the patient's coping skills and mental health is another necessary component for proper management; psychologists may also be part of the multidisciplinary team for further evaluation and additional help.

In addition to socioeconomic or environmental stressors, most of the youth with T2DM are adolescents and may have additional stressors. Adolescents in particular are subject to increased social or psychological stressors that may increase participation in risky behaviors such as tobacco or alcohol use or unprotected sex. Individuals should be counseled on smoking and alcohol use, and females should be educated on contraceptive use to avoid pregnancy (Zeitler et al., 2018).

Complications

While metformin is the appropriate pharmacological treatment for T2DM, the TODAY study found that glycemic control was maintained for only about half of the patients on metformin monotherapy. This suggests that T2DM in youth is much more aggressive and can lead to the development of complications early on, if not properly managed (Narasimhan & Weinstock, 2014). Potential complications include nephropathy, neuropathy, retinopathy, non-alcoholic fatty liver disease (NAFLD), obstructive sleep apnea (OSA), polycystic ovary syndrome (POS), cardiovascular disease, and dyslipidemia. Some of these conditions may be present at diagnosis. The ADA (2020a) recommends obtaining blood pressure measurements, a fasting lipid panel, liver enzyme panel, and urine albumin to creatinine ratio (ACR) at the time of diagnosis. A dilated eye exam and foot exam should also be performed at the time of diagnosis or soon after (ADA, 2020a).

Blood pressure (BP) should be measured at each visit and should not be greater than the 90th percentile for age, sex, and height. Lifestyle interventions to lose weight should be

encouraged for adolescents aged 13 years and older with a BP greater than 120/80 mmHg. If there is no change with intervention after 6 months, antihypertensive therapy should be started with angiotensin converting enzyme inhibitors or angiotensin receptor blockers (ADA, 2020a).

Desired levels of lipids for children and adolescents are as follows: low density lipid (LDL) cholesterol less than 100 mg/dL, high density lipid cholesterol greater than 35 mg/dL, and triglycerides less than 150 mg/dL. Measures for controlling lipid levels should focus on blood glucose control and dietary measures. If LDL remains above the target goal after 6 months of lifestyle interventions, statin therapy should be started. If lipids are at goal, they should be checked annually (ADA, 2020a).

Albuminuria may be present for many adolescents at the time of diagnosis. In the TODAY study (2013), 6.3% of youth had microalbuminuria at baseline, but this number rose to 16.6% after follow-up at the end of the study. An elevated urine ACR should be obtained at diagnosis and confirmed with two out of three samples. Estimated glomerular filtration rate (GFR) should also be obtained at time of diagnosis. Providers should monitor kidney function and recheck urine ACR and estimated GFR in pediatric patients annually (ADA, 2020a).

A dilated eye exam should be performed at the time of diagnosis or as soon as possible to evaluate for retinopathy. Comprehensive foot examinations with monofilaments should also be performed to assess for neuropathy. Screening for retinopathy and neuropathy should be completed annually, and prevention for both retinopathy and neuropathy involve optimizing blood glucose levels (ADA, 2020a).

Lastly, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) should be obtained at the time of diagnosis to evaluate for NAFLD and non-alcoholic steatohepatitis. Weight loss can improve these conditions; however, persistently elevated liver enzymes may

warrant a referral to a gastroenterologist. An ALT and AST should also be obtained annually (ADA, 2020a).

Future Implications

Pediatric diabetes continues to be a growing issue. As T2DM continues to increase in youth, providers should be knowledgeable about evidence-based screening, diagnosis, and management. Distinguishing between diabetes phenotypes can be difficult, but providers should be thorough in their assessments in order to start appropriate treatment. The foundation of treatment and management should be based on lifestyle changes to promote weight loss and healthy habits. Proactively involving the family in intensive lifestyle changes can improve chances for achieving optimal glucose levels and proper management early on to help prevent long term complications. Adolescents should be encouraged to be independent in their diabetes management in order to be successful during the transition to young adulthood. Care should always be individualized, culturally sensitive, and involve multidisciplinary team members. While the amount of information and research on pediatric diabetes continues to increase, future studies should continue to explore ways to prevent or reduce the risks and complications of developing T2DM, including any lifestyle and pharmacological interventions that may best treat and manage this special population.

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