

Dyslipidemia and type 1 diabetes mellitus

History:

A 15-year-old girl is seen in the endocrinology clinic for a routine follow-up visit for type 1 diabetes. She was diagnosed with diabetes at 12 years old and has had chronic poor glycemic control. She has had two previous admissions for diabetic ketoacidosis. A fasting cholesterol panel was last checked 2 years ago and showed a borderline elevation of low-density lipoproteins (LDL). Her fasting cholesterol panel was rechecked at today's visit.

Her mother has hypothyroidism. There is no known history of hyperlipidemia or early cardiovascular disease in the family.

Physical examination:

- Height 158 cm (25th percentile)
- Weight 53 kg (50th percentile)
- Body mass index (BMI) 21.2 (64th percentile)
- Blood pressure 134/79
- No enlargement of the thyroid gland

Laboratory studies:

Lipid profile: Total cholesterol: 230 mg/dL

- Triglycerides: 177 mg/dL
- HDL cholesterol: 62 mg/dL
- LDL cholesterol: 139 mg/dL

Hemoglobin A1c: 11.5%

Questions:

1. Which statement describes the most appropriate screening strategy for dyslipidemia in children with type 1 diabetes?
- All children should have a lipid screen upon diagnosis of type 1 diabetes, regardless of age.
 - If family history is not of concern, the first lipid screen should be obtained at puberty (≥ 10 years of age).
 - If family history is not of concern, routine lipid screening is not recommended in children with type 1 diabetes.
 - The first lipid screen should be obtained 5 years after the diagnosis of type 1 diabetes.

Answer: b. If family history is not of concern, the first lipid screen should be obtained at puberty (≥ 10 years of age).

Discussion: Coronary artery disease is the leading cause of death in those with type 1 diabetes. Individuals diagnosed with type 1 diabetes have increased frequency and earlier onset of cardiovascular disease. Studies have shown as much as a tenfold increased risk of atherosclerosis in patients with type 1 diabetes compared with the general population.

The American Diabetes Association recommends that children with type 1 diabetes have an initial lipid screen at the start of puberty (≥ 10 years of age). If there is a family history of hypercholesterolemia or cardiovascular disease before the age of 55 years old, or if the family history is not known, it is recommended that a lipid screen be considered soon after diagnosis in children older than 2 years old. For children diagnosed with type 1 diabetes who have already started or completed puberty, a lipid screen is recommended shortly after diagnosis and after glucose control has been established.

2. What is the most appropriate initial treatment for this patient's dyslipidemia?

- a. Recommend weight loss.
- b. Initiate statin therapy.
- c. Improve glycemic control and implement therapeutic lifestyle modifications.
- d. Initiate therapy with a bile acid sequestrant.

Answer: c. Improve glycemic control and implement lifestyle modifications.

Discussion: This patient's hemoglobin A1c of 11.5 percent demonstrates poor glycemic control. Improving glycemic control, along with implementing therapeutic lifestyle changes focused on diet and physical activity, is the first step in managing dyslipidemia in children with type 1 diabetes. This patient's BMI is not in the overweight or obese range. Therefore, weight loss is not indicated. Bile acid sequestrants have been shown to reduce total cholesterol and LDL levels in adolescents, but they are not recommended as first-line LDL-lowering therapy.

The American Diabetes Association recommends starting statin therapy in children ≥ 10 years old if the LDL level is >160 mg/dL after 6 months of lifestyle modification. Statin therapy is recommended for an LDL level between 130–159 mg/dL after a 6-month trial of lifestyle changes if one or more adult risk factors are present. Adult risk factors include smoking, hypertension, BMI >95 th percentile for age and sex, parental total cholesterol >240 mg/dL or family history of adverse cardiovascular events in a parent <55 years of age or HDL <35 mg/dL. The target LDL level on medical therapy is ≤ 100 mg/dL.

3. Which of the following statements best explains why patients with type 1 diabetes are at increased risk for cardiovascular disease?

- a. Cardiovascular disease is thought to be related to hyperglycemia, but the mechanism underlying the relationship is not well understood.
- b. Children with type 1 diabetes are often obese and, therefore, at higher risk of cardiovascular disease.
- c. Subcutaneous insulin therapy causes increased risk of cardiovascular disease.
- d. Increased risk of cardiovascular disease is due to the underlying autoimmune process in patients with type 1 diabetes.

Answer: a. Cardiovascular disease in patients with type 1 diabetes is thought to be related to hyperglycemia, but the mechanism underlying the relationship is not well understood.

Discussion: The cause of increased atherosclerosis in type 1 diabetes is not well understood. In type 2 diabetes, other risk factors for the early development of atherosclerosis often exist, such as obesity, hypertension and dyslipidemia. This is not the case in type 1 diabetes, however, where the rate of obesity is not significantly different than in the general population. Neither insulin therapy nor the underlying autoimmunity of type 1 diabetes are known to be associated with the increased risk of cardiovascular disease.

In type 1 diabetes, hyperglycemia leads to modification of proteins by advanced glycation end products. This process leads to microangiopathy, which results in the well-known complications of retinopathy, nephropathy and neuropathy. Macroangiopathy also occurs and is characterized by cardiovascular, cerebrovascular and peripheral vascular disease. Hyperglycemia causes an atherogenic pattern of dyslipidemia, vascular inflammation and oxidative stress and vascular endothelial dysfunction.

Key points:

1. Individuals with type 1 diabetes are at a significantly increased risk of developing cardiovascular disease. Coronary artery disease is the leading cause of mortality in type 1 diabetes.
2. If family history is not a concern, children with type 1 diabetes should have an initial lipid screen at the start of puberty (≥ 10 years of age). In those diagnosed during or after puberty, the initial lipid screen can be obtained at diagnosis once glycemic control has been established.
3. A 6-month trial of optimizing glycemic control and therapeutic lifestyle modification is the initial treatment for dyslipidemia in children with type 1 diabetes. If LDL levels are not in the target range, statin therapy can be considered in children ≥ 10 years of age.

References/suggested reading:

1. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Summary Report. *Pediatrics*. 2011 Dec; 128 Suppl 5:S213–56.
2. Standards of Medical Care in Diabetes – 2012. American Diabetes Association. *Diabetes Care*. 2012 Jan; Vol 35, Supplement 1.
3. Kavey RW, et al. Cardiovascular Risk Reduction in High-Risk Pediatric Patients. A Scientific Statement From the American Heart Association Expert Panel on Population and Prevention Science; the Councils on Cardiovascular Disease in the Young, Epidemiology and Prevention, Nutrition, Physical Activity and Metabolism, High Blood Pressure Research, Cardiovascular Nursing, and the Kidney in Heart Disease; and the Interdisciplinary Working Group on Quality of Care and Outcomes Research. *Circulation*. 2006; 114:2710–2738.
4. Glaser NS, et al. Detecting and treating hyperlipidemia in children with type 1 diabetes mellitus: are standard guidelines applicable to this special population? *Pediatric Diabetes* 2011; 12:442–459.