Screening for Dyslipidemia in Youth with Type 1 Diabetes

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July 2012
Disclosures

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  Research Support: Eli Lilly, Novo Nordisk
Objectives

1. The practitioner will understand and be able to apply current ADA guidelines for screening and treatment of dyslipidemia in youth with diabetes.
Outline

• Background
• Lipids Screening
• Dyslipidemia treatment
• Summary
• Discussion
Dyslipidemia Background

- Atherosclerosis starts in childhood

- In adults, the risk for heart disease in patients with diabetes is equivalent to risk in patients with known coronary disease

- Early detection of abnormal cholesterol level and/or high blood pressure can decrease risk for heart disease later in life
Dyslipidemia Background

• Studies on lipid levels in childhood show an association with lipid levels in adults

• Data on treating diabetic youth with lipid lowering medication are limited

• No studies document lipid levels in childhood associated with CVD events in adulthood (studies do show association with cIMT)
Total Cholesterol, HDL, and non-HDL Cholesterol abnormalities in BDC T1DM patients (n=682) compared to 2001-02 NHANES (n=3,798)

18.6% were abnormal for either TC or HDL

Maahs et al, JPeds, 2005
LDL by age and diabetes type in SEARCH

<table>
<thead>
<tr>
<th>LDL (mg/dl)</th>
<th>&lt;10 yrs</th>
<th>≥ 10 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;70</td>
<td>T1D 10%</td>
<td>T1D 10%</td>
</tr>
<tr>
<td>71-100</td>
<td>T1D 44%</td>
<td>T1D 44%</td>
</tr>
<tr>
<td>101-129</td>
<td>T1D 35%</td>
<td>T1D 32%</td>
</tr>
<tr>
<td>130-159</td>
<td>T1D 10%</td>
<td>T1D 12%</td>
</tr>
<tr>
<td>160+</td>
<td>T1D 1%</td>
<td>T1D 3%</td>
</tr>
</tbody>
</table>

Kershnar, JPediatr 2006
Dyslipidemia

LDL-cholesterol
4.14 mmol/L = 160 mg/dl
3.37 mmol/L = 130 mg/dl
2.59 mmol/L = 100 mg/dl

### Recommendations of the ADA on Lipid Screening and Management in Children and Adolescents with Diabetes

**ADA, Diabetes Care 2003, Kershnar, JPediatr 2006**

<table>
<thead>
<tr>
<th></th>
<th>Type 1</th>
<th>Type 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial screening</strong></td>
<td>&gt; 2 years old at diagnosis if other CVD risk factors; otherwise at 12 years old (puberty)</td>
<td>At diagnosis regardless of age</td>
</tr>
<tr>
<td><strong>Re-screening if lipid profile is normal</strong></td>
<td>5 years</td>
<td>2 years</td>
</tr>
</tbody>
</table>
| **Initial management of dyslipidemia LDL-C concentration for pharmacologic treatment if initial management fails (10+ years)** | Glycemic control, diet, physical activity LDL-C > 160 mg/dL: begin medication LDL-C 130–159 mg/dL: “consider” medication based on other adult risk factors:  
  - smoking  
  - hypertension  
  - obesity (>= 95th percentile for age and sex)  
  - parental TC >= 240 mg/dL or family history of cardiovascular event in a parent before 55 years of age  
  - HDL-C <35 mg/dL | At diagnosis regardless of age                                         |
| **Optimal concentration** | LDL-C <100 mg/dL  
  HDL-C >35 mg/dL  
  Triglyceride <150 mg/dL | At diagnosis regardless of age                                         |
Defining ‘Dyslipidemia’

National Cholesterol Education Program (NCEP) guidelines

<table>
<thead>
<tr>
<th></th>
<th>Total Cholesterol (mg/dl)</th>
<th>LDL-c (mg/dl)</th>
<th>HDL-c (mg/dl)</th>
<th>Triglycerides (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATP II (1993)</td>
<td>&gt;200</td>
<td>&gt;130</td>
<td>&lt;35</td>
<td>&gt;200</td>
</tr>
<tr>
<td>ATP III (2001)</td>
<td>&gt;200</td>
<td>&gt;130</td>
<td>&lt;40*</td>
<td>&gt;150</td>
</tr>
</tbody>
</table>


ATP II, *JAMA*, 1993
# Defining ‘Dyslipidemia’

## ADA guidelines

<table>
<thead>
<tr>
<th>Risk</th>
<th>LDL-c (mg/dl)</th>
<th>HDL-c* (mg/dl)</th>
<th>Triglycerides (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>&gt;=130</td>
<td>&lt;40</td>
<td>&gt;=400</td>
</tr>
<tr>
<td>Borderline</td>
<td>100-129</td>
<td>40-59</td>
<td>150-399</td>
</tr>
<tr>
<td>Low</td>
<td>&lt;100</td>
<td>&gt;=60</td>
<td>&lt;150</td>
</tr>
</tbody>
</table>

* For women, HDL values should be increased by 10 mg/dl

ADA, *Diabetes Care*, 2003; 26: s83-s86
Dyslipidemia Evaluation

Lipids screening for T1DM youth

• If positive family history or unknown history
  – Lipids screening (fasting) after 2 yrs of age and glucose control obtained after diagnosis

• If negative family history
  – Lipids screening after 12 yrs of age and glucose control obtained after diagnosis

• Repeat every 5 years if normal (LDL< 100)

ADA, *Diabetes Care* 2003
Silverstein, Klingensmith et al, *Diabetes Care*, January 2005
Dyslipidemia Management

- Lowering LDL has proven benefit in adults
- Primary goal of therapy is to lower LDL to target:

<table>
<thead>
<tr>
<th>LDL (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Borderline</td>
</tr>
<tr>
<td>Abnormal</td>
</tr>
</tbody>
</table>

- Less than 100               |
- 100-129                     |
- 130 or higher
Dyslipidemia Management

If fasting lipids abnormal:

• Optimize blood sugar control

• Decrease fat in diet
  – Limit saturated fat to <7% of calories
  – Minimize intake of trans fat
  – Limit dietary cholesterol to <200 mg/day

• Increase exercise; weight loss as necessary

• Smoking cessation

ADA, Diabetes Care 2003
Silverstein, Klingensmith et al, Diabetes Care, January 2005
Dyslipidemia Management

Pharmacologic therapy

- Age > 10 years old
- LDL > 160 mg/dl
  - 130-159 mg/dl: consider based on profile or once lifestyle modification attempted

- Statins (first line?)
- Resins **approved** for use in Pediatrics
- Fibric acid derivatives if TG > 1000 mg/dl*
- ezetimibe (Zetia)
# Lipid-Lowering Agents

## Maximum Effect on Serum Lipid Levels

<table>
<thead>
<tr>
<th>Pharmacologic Class</th>
<th>LDL-C</th>
<th>Triglycerides</th>
<th>HDL-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bile acid-binding resins</td>
<td>Decreases 10-30%</td>
<td>Increases 3-10%</td>
<td>Unchanged</td>
</tr>
<tr>
<td>Fibric acid derivatives</td>
<td>Decreases 5-10%*</td>
<td><strong>Decreases 30-60%</strong></td>
<td>Increases 5-10%</td>
</tr>
<tr>
<td>Niacin</td>
<td>Decreases 10-25%</td>
<td>Decreases 5-30%</td>
<td><strong>Increases 15-25%</strong></td>
</tr>
<tr>
<td>HMG-CoA reductase inhibitors (statins)</td>
<td><strong>Decreases 20-40%</strong></td>
<td>Decreases 10-30%</td>
<td>Increases 5-15%</td>
</tr>
</tbody>
</table>

* Fenofibrate may increase LDL-C levels.
Dyslipidemia Management

- Pharmacologic therapy
  - Goal is LDL < 100 mg/dl

** Counsel youth ‘at risk’ for pregnancy regarding lipid lowering agents and stop drug immediately if pregnancy suspected

- ISPAD guidelines for lipids screening & management similar to ADA

Current ADA guidelines recommend:

- Screening of lipids beginning after 2 or 12 years of age depending on family history
- Repeat at least every 5 years (every 2 yrs in T2DM) (more often if screening is abnormal)
- Treatment options include:
  - Lifestyle modification (glycemic control, diet, exercise)
  - After 10 years old, consideration of oral medications depending on type and degree of lipid abnormality
Research

• Evidence in youth with diabetes is needed to support ADA guidelines

• More research is needed in this area to start to prevent CVD early in youth with diabetes
Thank You

Web Links

• www.barbaradaviscenter.org

• www.diabetes.org
  American Diabetes Association