Diabetes Mellitus in Children and Adolescents

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Diabetes Mellitus in Children and Adolescents

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Diabetes Mellitus
Historical Perspective

• Hippocrates – coined the term diabetes, from the Greek word for “siphon”
  – “a melting down of the flesh and limbs into urine”

• 1897 – L. Emmett Holt, Diseases of Infancy and Childhood
  – Diabetes is very infrequent in childhood… causes are heredity, gout, insanity… injuries to the head precede some cases
Diabetes Mellitus

Definition

- Chronic hyperglycemia due to an absolute or relative deficiency of insulin
- Criteria for the diagnosis of diabetes
  - Plasma glucose > 200 mg/dL at any time of day on two occasions (or one occasion in the presence of symptoms of diabetes)
  - Fasting (>8 hours) plasma glucose > 126 mg/dL
  - Plasma glucose > 200 mg/dL 2-hour post-75 gram glucose load (oral glucose tolerance test)

Different forms

- Type 1 DM (insulin-dependent or juvenile)
- Type 2 DM (non-insulin-dependent or adult-onset)
- MODY (maturity-onset diabetes of youth) – inherited in an autosomal-dominant pattern, impaired insulin secretion with minimal or no defects in insulin action
- Cystic fibrosis-related diabetes
- Pancreatic agenesis or damage, mitochondrial disorders, pharmacologically induced forms of diabetes

Diabetes Mellitus in Youth

Type 1
- autoimmune
- insulin deficient
- peak onset = 10-14 yrs.
- most common in caucasians
- usually FHx +

Type 2
- not autoimmune
- insulin resistant
- previously uncommon ~ 2% of newly dx’d cases
- rapidly increasing incidence (8-10 fold)
- peak onset = 13 yrs.
- usually FHx +
Type 2 Diabetes Mellitus

Demographics

- Majority of cases are members of high-risk ethnic groups (Native Americans, African Americans, Hispanics, Pacific Islanders)
- Strong family history of T2DM
- Physical exam – obesity, acanthosis nigricans – indicates insulin resistance
- Associated conditions –
  - hypertriglyceridemia
  - hyperinsulinemia
  - hyperlipidemia

Type 2 Diabetes Mellitus

Progression of glucose and insulin

Type 2 Diabetes Mellitus

Medications

- Some patients can be managed with diet and exercise alone
- Insulin sensitizing agent – metformin enhances liver insulin sensitivity and reduces hepatic gluconogenesis
- The only oral antidiabetic agent approved for use in children with T2DM
Insulin therapy for Type 2 DM in children

Pros:
- effective
- overcomes glucotoxicity
- experience in use among pediatricians

Cons:
- risk of hypoglycemia
- weight gain
- injections

Type 1 Diabetes Mellitus (T1DM)

Demographics
- State of absolute insulin deficiency caused by immunologically based destruction of the islets of Langerhans
- 2nd most common chronic disease in childhood
- 1:350 children by age 18
- Increasing 3 – 4% per year < in under age 5

Type 1 Diabetes Mellitus

Genetic Risk
- Diabetes risk is influenced by DQA and DQB, DR3 and DR4 genes
- Family members can be assessed for risk by genetic evaluation
- But, no known treatment to halt the autoimmune process and prevent the onset of T1DM exists

Type 1 Diabetes Mellitus

Antibodies

- Inflammatory process against the islets is accompanied by the development of serum antibodies:
  - Islet cell antibody (ICA512)
  - Glutamic acid decarboxylase antibody (GAD65)
  - Insulin antibody

Type 1 Diabetes Mellitus

Clinical Presentation

Management of Diabetes in children

Goals of medical therapy for children/adolescents
- normal growth and development
- optimal glycemic control
- positive psychosocial adjustment
- minimize short and long-term complications

Children/adolescents with Diabetes differ from adults in many aspects, we need to consider the unique aspects of care for this population:
- developmental stages
- family dynamics
- ability to provide self-care
- insulin sensitivity related to sexual maturity
- neurological vulnerability to hypoglycemia

**Tools for Achieving Blood Sugar Control**

- Medications
- Food (carbs)
- Physical activity
- Family/Health Care Team support

**Evolution of Diabetes Management Tools**

<table>
<thead>
<tr>
<th>Year</th>
<th>Tool</th>
</tr>
</thead>
<tbody>
<tr>
<td>1922</td>
<td>Discovery of insulin</td>
</tr>
<tr>
<td>1966</td>
<td>Urine glucose testing</td>
</tr>
<tr>
<td>1996</td>
<td>Insulin pump therapy</td>
</tr>
<tr>
<td>1996</td>
<td>Continuous glucose sensor</td>
</tr>
<tr>
<td>2003</td>
<td>Integrated systems: Pumps/Meters/Software</td>
</tr>
</tbody>
</table>
Insulin
Historical perspective

- Isolated 1921-1922 University of Toronto
- Before discovery of insulin, diabetic patients were treated with strict diets and died within a few years from starvation
- 1st patient successfully treated with insulin was a dog with DM

Insulin
Physiologic action

Stimulated by a rise in glucose levels in the peripheral bloodstream

Promotes lipid storage
Aborts uptake of glucose into cells of peripheral tissues

Stimulates glucose synthesis, inhibits glycogenolysis and gluconeogenesis

http://www.natap.org/2005/images/041105/TypeDia11.gif

Normal Insulin Action

Breakfast snack Lunch Basal insulin secretion
7 am 12 6 pm 10 pm 12 mid 7 am
24 hour normal insulin secretion. Serum insulin level increases in response to meals and snack. Continuous basal release occurs throughout the 24 hours.
PROFILES OF INSULIN ANALOGUES

*Novolog, Humalog, Apidra 3-4 hours

Regular 4-8 hours
NPH 12-20 hours
*Levemir 24 hours
*Lantus 24 hours

Pharmacology of commonly used insulins

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Onset (hr)</th>
<th>Peak (hr)</th>
<th>Duration (hr)</th>
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</thead>
<tbody>
<tr>
<td>Regular</td>
<td>0.5 - 1</td>
<td>2 - 3</td>
<td>3 - 6</td>
</tr>
<tr>
<td>Lispro (Humalog®)</td>
<td>0.25</td>
<td>1 - 2</td>
<td>3 - 4</td>
</tr>
<tr>
<td>Aspart (NovoLog®)</td>
<td>0.25</td>
<td>1 - 2</td>
<td>3 - 4</td>
</tr>
<tr>
<td>Glulisine (Apidra®)</td>
<td>0.25</td>
<td>1 - 2</td>
<td>3 - 4</td>
</tr>
<tr>
<td>NPH</td>
<td>2 - 4</td>
<td>6 - 10</td>
<td>10 - 16</td>
</tr>
<tr>
<td>Glargine (Lantus®)</td>
<td>1</td>
<td>none</td>
<td>20 - 24</td>
</tr>
<tr>
<td>Detemir (Levemir®)</td>
<td>1 - 2</td>
<td>5 - 14</td>
<td>14 - 23</td>
</tr>
</tbody>
</table>

Insulin Regimens

Total daily dose (short + long acting):
- 0.5-1.0 U/kg/day total, ~½ short, ½ long
- Generally lower dose in younger children, higher in adolescents (puberty)
- Less in honeymoon phase
- Split (2+ injections/day), mixed (combination of insulins) regimens
- Individualized- one size does not fit all!
**Insulin Delivery Systems**

**Syringe/needle and vial:**
- inexpensive, enables insulin to be mixed,
- syringes available with ½ unit markings
- 3ml and 10 ml
- Most good for 28 days at room temperature once opened, unopened refrigerate till expires

**Syringes and Pen Needles**

- **Gauge**
  - 29 to 32 – most kids use 30 or 31
- **Length**
  - 4 mm to 12.7 mm
  - Shorter needles require a longer holding time (5 to 10 seconds) in the tissue to prevent leakback

**Insulin Pens**

- Portable, preferred by many teens
- Can be used for 7 to 30 days once opened depending on insulin type
- Some deliver ½ unit
- 1.5 to 3 ml
Insulin Dosing at Meals

- Scale dosing based on blood glucose level, works best if the carb intake remains consistent
- Insulin to carbohydrate ratio with a correction dose, allows for more flexibility with carb intake
- The amount of flexibility a child has with his/her food plan is directly related to the insulin regimen they are using.

Insulin to Carbohydrate Ratio

The insulin dose (a “bolus”) is calculated to match the amount of carbohydrate to be consumed.

The bolus is delivered before, if given after the meal/snack you should be continually re-assessing if this practice is necessary because you are not matching the food and insulin action well.)
• NPH with a fast acting insulin
• Premix Insulin 75/25, 70/30
• Lantus with fast acting insulin
• Pump (Humalog or novolog)

• Less flexibility with portions and timing
• Less Flexibility with portions and timing
• More flexibility with portions and timing
• More flexibility with portions and timing

Sites for Insulin Injections

• Speed of absorption from sites: abdomen, arms, leg and buttocks
• Lantus can not be mixed with any other insulin and should be given into a body part that is only used to give Lantus

Lipohypertrophy

**Type 1 Diabetes Mellitus**

Preventing Complications

- The Diabetes Control and Complications Trial (DCCT): intensive therapy of type 1 diabetes mellitus reduces the risk of development and progression of microvascular complications.

- Epidemiology of Diabetes Interventions and Complications (EDIC) study: adolescents with type 1 diabetes should receive intensive therapy aimed at achieving glycemic control as close to normal as possible to reduce the risk of microvascular complications

**BG Testing**

- Before meals, at bedtime
- During the middle of the night
- After meals
- Before, during and after exercise
- Feeling low or feeling high
- During illness
Record keeping – Identifying Patterns

<table>
<thead>
<tr>
<th>Pre B</th>
<th>Pre L</th>
<th>snack</th>
<th>Pre D</th>
<th>Bed</th>
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<td>68</td>
<td>362</td>
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<td>401</td>
<td>183</td>
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Insulin adjustment
Hemoglobin A1c%

- Indirect indicator of the overall glycemic control
- Measurement of glycosylated hemoglobin gives a measure of the mean glucose concentration of the preceding 3 months (lifespan of a red blood cell)

Glycemic control: Age Specific

- Toddlers/Preschoolers (<6 years)
  BG Target Range 90 – 200
  HgbA1c - <8.5 but >7.5%
- School age (6 -12 years)
  BG Target Range 80 –180
  HgbA1c - <8.0%
- Adolescents/Young Adults (13 –19 years)
  BG Target Range 70 -150
  HgbA1c - <7.5%
Continuous Glucose Monitoring

Treatment of mild hypoglycemia

- BG < 70
- **Rule of 15**
  - Give 15 grams fast-acting carb (4 oz juice/soda, glucose tabs)
  - Wait 15 mins, then repeat BG.
  - If BG still < 70 Repeat 15 g fast-acting carb.
- Follow with complex carb snack (i.e. 15 g PB or cheese crackers, or meal, depending on timing)
Treatment of severe hypoglycemia

Glucagon (hormone secreted by α cells of the islets of Langerhans)
- given IM
- opposes the action of insulin
- activates hepatic glycogenolysis and gluconeogenesis
- patients with T1DM eventually develop glucagon deficiency
- contact parent and DM team if given

Management of hyperglycemia

- Assess cause of elevated BG, ? timing of test in relation to last meal/snack
  Ketone testing recommended for: signs of illness, missed insulin and bg levels of 240 to 300 or greater
- May need correction dose (i.e. if missed insulin)
- Contact parent/ diabetes team as needed

Management of hyperglycemia with ketones on pump

- Check ketones if BG > 240 mg/dl or ill
- Trace or small ketones
  - Push sugar-free fluids (~ 8 oz/hour for 2-3 hours)
- Moderate or large ketones
  - Give extra rapid acting insulin (10-20% of total daily insulin dose) in addition to usual dose by syringe/pen
  - Push sugar-free fluids
  - No exercise
  - Contact parent and DM team
  - Change site (possible site malfunction) and assess for possible pump malfunction
- Check BG and ketones q 2-3 hours