TYPE 2 DIABETES IN CHILDREN – DIAGNOSIS AND THERAPY

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Objectives:
1. To discuss epidemiology and presentation of Type 2 diabetes in children and adolescents,
2. To discuss common challenges in differential diagnosis of type 2 vs Type 1 diabetes
3. To discuss current guidelines for screening and treatment of Type 2 diabetes in children and adolescents
A 17-year old Hispanic female presents to ED with a history of a few days polyuria and polydipsia and a recent onset of nausea and feeling weak.

PE: BMI 31.2 kg/m^2, BP 125/79, mild acanthosis noted around the neck.

FH: Multiple family members on both sides have Type 2 diabetes.

Laboratory findings: BG of 590, urine 3+ ketones, metabolic acidosis.

Initial treatment: IV insulin with transition to SQ basal/bolus insulin treatment subsequently.
CASE 1- MONTH FOLLOW UP

- Patient returns to clinic; achieved normoglycemia on basal–bolus insulin regimen
- Additional laboratory findings available:
  - C-peptide 1.9 (nl 0.8-3.9)
  - Islet cell antibody, GAD-antibody – negative
  - Thyroid function: normal
  - Vitamin D level low (<10 25-OHD)
DIAGNOSIS: TYPE 1 OR TYPE 2

- Phenotype: consistent with Type 2; suggestive family history
- Negative antibodies and normal level of c-peptide suggestive of endogenous insulin production and absence of autoimmunity

- BUT

- Patient presented in DKA?
In the US currently 1 in 3 new cases of diabetes mellitus in youth younger than 18 years is Type 2 – strongly dependent of the ethnic composition of the patient population.

- **Non-Hispanic whites**: Type 2 represents 15% of all new cases of diabetes;
- **American Indians**: 86% of new cases
- **Asian-Pacific Islanders**: 70% of new cases
- **African-Americans**: 58% of new cases
- **Hispanics**: 46% of new cases

5.7-11.7% of new cases of Type 2 diabetes present in DKA vs 30% of Type 1 (SEARCH in DM group, Pediatrics, March 2014)
DIFFERENTIAL DIAGNOSIS:
TYPE1 VS TYPE 2

- Particularly complicated in patients that present sicker – in DKA
- Lab studies to consider:
  - 1. C-peptide – may be low at diagnosis if patient in DKA, as they are relatively insulinopenic. May need to be followed sequentially in order to clarify diagnosis
  - 2. Antibodies panel: GAD, insulin auto-antibody (obtain before starting treatment with insulin), islet-cell antibody, IAA. Current consensus is that presence of any antibody is diagnostic for autoimmune diabetes, even in the presence of phenotypic features of Type 2 diabetes (e.g. obesity, acanthosis).
CURRENT GUIDELINES: SCREENING

· **Overweight status**
  · Body mass index ≥85th percentile for age and gender
  · Weight for height ≥85th percentile
  · Weight ≥120 percent of ideal for height
· **Plus any two of the following risk factors:**
  · Family history of type 2 diabetes mellitus in a 1st or 2nd degree relative
  · High-risk race/ethnicity (Native American, African-American, Latino, Asian American, Pacific Islander)
  · Signs of insulin resistance on physical examination or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational age birthweight)
  · Maternal history of diabetes or gestational diabetes mellitus during the child's gestation
· **Screening frequency**
  · Begin screening at age 10 years, or at onset of puberty if this occurs less than 10 years old
  · Repeat screening every three years
CURRENT GUIDELINES: DIAGNOSIS OF DIABETES

- 1. HbA1c equal or higher than 6.5%; or
- 2. fasting plasma glucose equal or higher than 126 mg/dl; or
- 3. 2-hour plasma glucose equal or higher than 200 mg/dl during an OGTT performed as described by WHO by using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water; or
- 4. a random plasma glucose equal to or higher than 200 mg/dl with symptoms of hyperglycemia.

In the absence of unequivocal hyperglycemia, criteria 1-3 should be confirmed by repeat testing.
CURRENT GUIDELINES: TREATMENT OF TYPE 2 DIABETES

- Insulin therapy:
  - should be initiated for children and adolescents with T2DM who are ketotic or in DKA, in whom the distinction between types 1 and 2 is unclear and in patients who have random venous or plasma BG over 250 mg/dl or a HbA1c above 9%
  - there is more recent evidence that treatment with insulin for at least 2-4 weeks early in the disease may help preserve beta cell function
CURRENT GUIDELINES: TREATMENT OF TYPE 2 DIABETES

- In all other circumstances, clinicians should initiate a lifestyle modification program, including nutrition and physical activity, and start metformin as first-line therapy for children and adolescents at the time of diagnosis of Type 2 diabetes.

- Metformin should be started at a low dose (250-500 mg/day), increasing by 500 mg every 1 to 2 weeks, up to an ideal and maximum dose of 2000 mg daily in divided doses. Main GI adverse effects—abdominal pain, bloating, loose stools—present at initiation of metformin are often transient and disappear completely if medication is continued. Metformin is best tolerated when taken with food.
Therapeutic challenges: patients presenting with moderate hyperglycemia (BG 200-249); not achieving therapeutic goals (hemoglobin A1c <7%) on metformin therapy only:

- Option to add insulin to metformin or use insulin therapy alone

- Other antidiabetic agents not FDA approved for use in children, but sulfonylureas, thiazolidendiones and incretins are occasionally used in adolescents <18 years of age. Currently, trials of numerus antidiabetic medications ongoing in adolescent population.
CURRENT GUIDELINES: TREATMENT OF TYPE 2 DIABETES

- Frequency of blood glucose testing in patients with Type 2 diabetes: depends on following factors:
  - 1. Diagnosis: Fasting, premeal and bedtime testing recommended for all newly diagnosed patients, regardless of treatment, until reasonable metabolic control is achieved,
  - 2. Regimen used:
    - single insulin daily (bedtime) injection: fasting BG recommended,
    - oral agents: once therapeutic goal is achieved, some testing recommended, but frequency should be determined in clinical context,
    - oral agent and a single injection of a long lasting insulin: twice a day monitoring recommended (fasting and 2 hour post-prandial)
    - multiple daily injections: testing frequency similar to Type 1 diabetes: premeal and bedtime testing recommended
CURRENT GUIDELINES: TREATMENT OF TYPE 2 DIABETES

- Nutrition guidelines: recommended that clinicians incorporate the Academy of Nutrition and Dietetics’ pediatric Weight Management Evidence-Based Nutrition Practice Guidelines in the nutrition counseling of patients with T2DM

- http://www.adaevidencelibrary.com/topic.cfm?cat=2721
CURRENT GUIDELINES : TREATMENT OF TYPE 2 DIABETES

- Exercise prescription: current guidelines suggest that clinicians encourage children and adolescents with Type 2 diabetes to engage in moderate-to-vigorous exercise for at least 60 minutes daily and to limit nonacademic screen time to less than 2 hours per day.

- Individualization of that prescription most likely to result in success; family engagement is viewed as crucial.
It is currently recommended that primary care providers should endeavor to obtain the requisite skills to care for children and adolescents with Type 2 diabetes, and that they should communicate and work closely with a diabetes team of subspecialists when such consultation is available, practical and appropriate.

The frequency of consultations can vary, but in general should be obtained at diagnosis and then at least annually if possible. When treatment goals are not met, clinicians should consult with an expert trained in the care of children and adolescents with T2 DM.
TYPE 2 DIABETES IN CHILDREN: WHAT IS THE GOAL OF THERAPY

- In adult patients with T2DM, the goal is near-normoglycemia, and hemoglobin A1c < 6.5%. Consensus for pediatric patients right now puts that goal for children and adolescents to HbA1c of equal or less than 7%.

- Current research studies (TODAY study), point out that children with Type 2 DM tend to develop microvascular complications (nephropathy and retinopathy) at the same pace or even faster than patients with Type 1 DM, so screening for microalbuminuria and retinopathy should start shortly after the diagnosis in those patients.

- Patients with Type 2 DM are at higher risk for macrovascular complications, and careful management of additional morbidity (hyperlipidemia, hypertension, PCOS) is recommended, according to standard guidelines.
USEFUL REFERENCES:

• AAP Clinical Practice Guideline: Management of newly diagnosed Type 2 diabetes mellitus in children and adolescents. Pediatrics 2013;131(2) 364-80

• http://www.adaevidencelibrary.com/topic.cfm?cat=2721

• National Diabetes Education Program TIP sheets – can be ordered or downloaded from www.yourdiabetesinfo.org or ndep.nih.gov
• Thank you!

• Questions? Comments?
• Feel free to contact me at guttmann@ohsu.edu