Primary Care
Type 2 Diabetes Update

May 16, 2014

Presented by:
Barb Risnes APRN, BC-ADM, CDE

Objectives:

• Discuss strategies to address common type 2 diabetes patient management challenges

• Review new pharmacological treatment for type 2 diabetes and recommendations for their use

• Identify when to initiate insulin in type 2 diabetes
Diabetes Care: a team approach

Diabetes Educators, RN’s, RD’s, Pharmacists
Community resources as available

- Diabetes prevention
- Self Management Support & Education
- Lifestyle coaching / Motivational interviewing
- Therapy management
- Insulin pump and sensor therapies

Key Points

- Screen all at risk—family hx, overweight, cardiovascular disease, elevated lipids/BP…

- Discuss prevention, refer to a Diabetes Prevention Program as available.

- CV risk reduction – manage blood pressure and lipids.

- Discuss importance of weight management, active lifestyles and tobacco cessation.

- Glucose toxicity accelerates beta cell failure. Treat early and aggressively.
1 in 4 US Adults have Pre-Diabetes
Without change likely to develop T2D within 10 years

• Lifestyle therapy is twice as effective in reducing development of diabetes than medical therapy.

• National Diabetes Prevention Program currently offered at EH East & Central Regions

• Free 16 week program for people with pre-diabetes (fasting blood glucose 100-125 or A1c 5.7-6.4%)

• Focus on healthy lifestyle changes: weight loss, increasing activity, healthy eating and lower fat diets

Since my husband developed diabetes, I've lost thirty pounds following his diet!
Individualize Glycemic Targets for Adults with Diabetes

More stringent (less than 6.5%)
- Short Diabetes duration
- Long life expectancy
- No significant CVD

Less stringent (less than 8%)
- Severe hypoglycemic history
- Limited life expectancy
- Advanced macrovascular or microvascular complications
- Extensive comorbidities
- Long term diabetes in whom general A1c target difficult to obtain*

ADA 2014 Guidelines

Pharmacological Therapy

First line therapy ► Metformin (lowers A1c 1-2%)
if no contraindications
Start low dose & titrate

Second choice ► no clear evidence what’s best
- Treat the main defect
- Minimize hypoglycemia
- Minimize weight gain
- Protect remaining beta-cell function
- Consider cost
Proposed use of Metformin based on eGFR

<table>
<thead>
<tr>
<th>eGFR</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greater than 60</td>
<td>No renal contraindication, monitor renal function annually</td>
</tr>
<tr>
<td>45-60</td>
<td>Continue use, monitor renal function every 3-6 months</td>
</tr>
<tr>
<td>30-45</td>
<td>Prescribe with caution, use lower dose (e.g. half normal dose), monitor renal function Do not start new patient on metformin</td>
</tr>
<tr>
<td>Less than 30</td>
<td>Stop Metformin</td>
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</tbody>
</table>

A New Look at an Old Drug: Metformin 2013
Gregg Simonson, PhD, Director, Professional Training and Consulting
International Diabetes Center

GLP-1 receptor agonists:

Byetta / Bydureon (exenatide), Victoza (liraglutide)

Coming this summer Albiglutide—no renal adjustment required

- Gut (incretin) hormone – targets post prandial glucose
- Increased postprandial insulin, reduces glucagon, slows gastric emptying
- Promotes weight loss about 3kg
- Low risk for hypoglycemia
- Injectable (byetta & victoza virtually painless)
- Nausea increased with large or high fat meals or when starting – need to titrate
- Caution if history or high risk for pancreatitis (causation inconsistent with current data)
- Avoid if family or personal history of medullary thyroid cancer
- Costly
- Moderate to high A1c reduction (0.8-2.0%)
DPP-4 inhibitors:

Januvia (sitagliptin), Onglyza (saxagliptin),
Tradjenta (linagliptin), Neshina (alogliptin)

- Increases GLP-1
- Once daily oral medication
- No hypoglycemia, consider reducing sulfonylureas
- Well tolerated
- Weight neutral
- Use with caution if history of Pancreatitis
- Lower dose with renal impairment (except no restriction with tradjenta)
- Costly
- Modest A1c reduction (0.5-0.9%)

SGLT2 inhibitors:

Invokana (canagliflozin), Farixga (dapagliflozin)

- Blocks glucose reabsorption by the kidneys
- No beta cell function required
- Generally well tolerated, once daily pill
- Weight reduction 2-3 kg in 12 weeks
- May lower blood pressure 3-5 mmHg, caution in elderly, with anti-hypertensives
- Contraindicated (less effective) if eGFR less than 60
- Monitor creatinine, use Invokana with caution if GFR 45-60
- Increased urination, risk of dehydration, yeast or UTI
- Monitor potassium, may cause hyperkalemia esp if renal impairment, ACE, ARBS or potassium sparing diuretics
- Costly with limited long term safety
- Lowers A1c 0.5-1.5%
**Thiazolidinediones (TZD’s)**
*Actos (pioglitizone), Avandia (rosiglitizone)*

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Moderate reduction in A1c 0.7-1.2%</td>
<td>• Edema / CHF</td>
</tr>
<tr>
<td>• Reduces insulin resistance</td>
<td>• Weight gain</td>
</tr>
<tr>
<td>• Low hypoglycemia potential</td>
<td>• Fracture</td>
</tr>
<tr>
<td>• Possible CVD benefit</td>
<td>• Patient perceptions</td>
</tr>
<tr>
<td>• Protective of beta-cell</td>
<td>• Delayed onset</td>
</tr>
<tr>
<td></td>
<td>• Association with bladder cancer unresolved</td>
</tr>
</tbody>
</table>

FDA Drug Safety Communication November 2013: Data does not show increased risk of heart attack

**Sulfonylurea**
*Glipizide, Glimepiride, Glyburide*

- Lack durability
- Modest weight gain
- Hypoglycemia Risk
- Low cost
- Reduces A1c 0.4-1.2%
Insulin

• Use in combination with oral & injectable therapies
• Oral medications should not be abruptly discontinued when starting insulin therapy because of the risk of rebound hyperglycemia
• Less weight gain when combined with Metformin

Risks:
• Hypoglycemia
• Weight gain
• Training required
• Glucose monitoring
• Costly in higher doses

Despite the valiant efforts of the research group, the insulin suppository still had one major drawback.

Currently recruiting for
GRADE Study sponsored by the NIH
Glycemic Reduction Approaches in Diabetes:
a comparative Effectiveness study

GRADE will directly compare the 4 most commonly used types of glucose-lowering medications second to metformin

- Glimepiride
- Sitagliptin
- Liraglutide
- Basal insulin glargine

ADA & EASD
Diabetes Care, vol 35, June 2012
Patient Centered Care = Shared Decision Making

**Diabetes Decision Aide Cards**

- Shareddecisions.mayoclinic.org

7th card addresses **Cost** of therapy

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**Start Basal Insulin**

- Initially if A1c over 9% with significant symptoms
- A1c over target on 2 other agents
- A1c over 10-11%
- Fasting glucoses elevated despite other therapies

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INSULIN ACTION TIMES

<table>
<thead>
<tr>
<th></th>
<th>BEGINS TO WORK</th>
<th>WORKING HARDEST</th>
<th>STOPS WORKING EFFECTIVELY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PRANDIAL &amp; CORRECTION</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rapid-acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lispro (Humalog)</td>
<td>5-15 minutes</td>
<td>1-2 hours</td>
<td>3-4 hours</td>
</tr>
<tr>
<td>Aspart (Novolog)</td>
<td>5-15 minutes</td>
<td>1-2 hours</td>
<td>3-4 hours</td>
</tr>
<tr>
<td>Glulisine (Aprida)</td>
<td>5-15 minutes</td>
<td>1-2 hours</td>
<td>3-4 hours</td>
</tr>
<tr>
<td>Short-acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular (Novolin, Humulin)</td>
<td>30-45 minutes</td>
<td>2-3 hours</td>
<td></td>
</tr>
<tr>
<td><strong>BASAL</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate-acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NPH</td>
<td>2-4 hours</td>
<td>4-8 hours</td>
<td>10-16 hours</td>
</tr>
<tr>
<td>Long-acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glargine (Lantus)</td>
<td>2 hours</td>
<td>No peak</td>
<td>Up to 24 hours</td>
</tr>
<tr>
<td>Detemir (Levemir)</td>
<td>2 hours</td>
<td>No peak</td>
<td>Up to 24 hours</td>
</tr>
</tbody>
</table>

Adapted by B. Risnes from prescribing literature

Select a Starting Basal Dose
(Lantus or Levemir)

<table>
<thead>
<tr>
<th></th>
<th>A1c less than 8%</th>
<th>A1c 8-10%</th>
<th>A1c greater than 10%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal Insulin</td>
<td>0.1 units/kg</td>
<td>0.2 units/kg</td>
<td>0.3 units/kg</td>
</tr>
<tr>
<td>(added to oral agents or initiated in hospital due to elevated fasting glucoses)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Start with one dose; take at same time each day</td>
<td></td>
<td></td>
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IDC 2006

Basal Insulin Adjustment Guidelines

- Adjust for lows first
- Adjust for highs next
- Adjust by 3 units every 3 days (or 10% of dose)
- Enable patient to self adjust as appropriate
- Careful not to over basal-insulinize (replaces about 50% insulin needs)
- Consider addition of mealtime insulin if TDD exceeds 0.5 units/kg

Decrease basal dose if:
- Low fasting glucose
- Glucose drops more than 50 points from bedtime to wake up

Increase basal dose if:
- High fasting glucose
- Glucose rises without carb intakes from bedtime to wake up
Based on the patient’s blood glucose record, how would you evaluate current basal insulin dose?

Basal Insulin Dose is appropriate if:

- Fasting glucose are within the target range & blood glucose (BG) steady overnight
  - No greater than 50 mg/dl BG drop fasting

- The correct basal dose of insulin should usually keep blood glucoses in target when the patient is not consuming carbohydrates
Prandial Bolus = Mealtime Insulin

To control post-meal glucose rise

Give either as a **Set Dose** with a set amount of carbohydrate

*or*

Dosed according the amount of carbohydrate consumed at each meal = **Insulin to Carb Ratio**

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### Fitting Insulin to the Patient

*Lispro with Insulin Glargine*

- **Novolog**
- **Novolog**
- **Novolog**
- **Glargine**

**Serum insulin (mU/L)**

**Time of Day**

- Lantus (Glargine), Levemir (Detemir)
- Novolog (Aspart), Humalog (Lispro)

© 2004 International Diabetes Center
Mealtime Dosing Insulin Calculation

<table>
<thead>
<tr>
<th></th>
<th>A1c less than 8%</th>
<th>A1c 8-10%</th>
<th>A1c greater than 10%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mealtime (Bolus) Insulin Dosing: Novolog / Humalog</td>
<td>0.1 units/kg</td>
<td>0.2 units/kg</td>
<td>0.3 units/kg</td>
</tr>
<tr>
<td></td>
<td>Total basal/bolus insulin = 0.2 units/kg</td>
<td>Total basal/bolus insulin = 0.4 units/kg</td>
<td>Total basal/bolus insulin = 0.6 units/kg</td>
</tr>
<tr>
<td></td>
<td>add to basal insulin for elevated post-meal glucose levels</td>
<td>initially, mealtime dose divided evenly between meals</td>
<td></td>
</tr>
</tbody>
</table>

Adding Mealtime Insulin
Rapid acting insulin dosing calculation

- Add 10 units to total daily dose (TDD), give half as basal and half as bolus spread into 3 meals
- Titrate basal according to fasting glucoses, bolus according to post meal glucoses
Prandial Insulin Adjustment Guidelines

- Assess glucoses pre-meal versus 2-3 hours post meal or before next meal
- Post meal should be within 20-40 points of pre-meal
- Look for patterns
- Consider other variables: accuracy of carb counting, timing of doses in relation to meal, extra snacks not covered, insulin age & storage
- Adjust up or down by 10% of dose

How do you know if the Prandial Dose (insulin to carb ratio) is correct?
The Prandial Dose (insulin to carb ratio) is correct if …

- Pre-meal and 2-3 hour post-meal blood glucose readings are within 20-40 points
- Assumes accurate carbohydrate counting

Sliding Scales = Correction scale

- Not intended to cover food intake or basal needs
- Should not be used ongoing as sole means for glucose control if regular dosing required
- Used to correct or lower a high BG into target
- Correction dose based on total daily insulin dose (individualized)
- If required frequently, basal or prandial insulin may be needed
Determining Correction Factor
also referred to as the “Sensitivity”

1700 divided by Total daily insulin dose = mg/dl drop in BG

- Determine how much 1 unit will decrease BG
- Example: 1700 / 50 = 36
- One unit of Regular or rapid acting insulin will decrease BG by about 36 mg/dl
- Insulin Sensitivity = 36

Insulin Pen Devices

- 32 gauge 4 mm Nano pen needles proven just as effective as longer needles
- Needles do not come with pens, separate order (boxes of 100)
- 300 units insulin per pen (box of 5 = 1500 units) verses one vial of 1000 units
Insulin Pump Therapy

- Uses rapid-acting insulin only
- Infuses a continuous **basal rate** to maintain the blood glucose when not eating
- Patient administers a **bolus dose** of insulin when eating and/or **correction dose** if their blood glucose is high

Continuous Glucose Monitoring

![Graphs showing glucose levels over time](image)
“Control my diet, control my lifestyle, control my carbs…What are you, some kind of freak?”

Summary

- Glucose targets and therapy must be individualized
- Diet, exercise and education remain the foundation of any T2D treatment program
- Many patients will require insulin alone or in combination with other agents
- All treatment decisions, where possible, should be made in conjunction with the patient, focusing on his/her preferences, needs and values
- Comprehensive CV risk reduction must be a major focus of therapy
Questions?

References

- Diabetes decision aid cards. Shared decision making. Shared decisions.Mayoclinic.org