Evidence-Based Strategies to Improve Glycemic Control in Type 2 Diabetes

Saturday, June 23, 2012
New York, NY
Session 3: Evidence-Based Strategies to Improve Glycemic Control in Type 2 Diabetes

Learning Objectives

1. Apply current data from clinical trials for A1C goal setting and individualization of treatment.
2. Recognize the importance of timely initiation of drug therapy including the early insulin initiation in reducing the complications of type 2 diabetes.
3. Describe interdisciplinary team and collaborative care approaches that can improve clinical outcomes.
4. Identify and implement strategies for overcoming the barriers to insulin initiation and medication adherence.

Faculty

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Professor of Medicine
Yale University School of Medicine
Director, Yale Diabetes Center
Clinical Chief, Endocrinology
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A native New Yorker, Dr Inzucchi received his undergraduate degree from Fordham University in the Bronx and his MD degree from Harvard Medical School in Boston. He completed his residency in internal medicine and his post-doctoral fellowship in endocrinology and metabolism at Yale-New Haven Hospital, in New Haven. He is currently professor of medicine at the Yale University School of Medicine in New Haven, where he serves as clinical director of the section of endocrinology and program director of the endocrinology & metabolism fellowship. He also directs the Yale Diabetes Center at Yale-New Haven Hospital.

Dr Inzucchi has authored or co-authored more than 300 manuscripts, chapters, and abstracts, some published in the foremost medical journals, including the New England Journal of Medicine and JAMA. His practical booklet “The Yale Diabetes Center Diabetes Facts & Guidelines” has an annual circulation in excess of 100,000 copies. A former member of the editorial board of Diabetes Care, Dr Inzucchi is currently an associate editor of the Journal of Clinical Endocrinology and Metabolism.

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Professor of Medicine, Division of Endocrinology
Brody School of Medicine, East Carolina University
Medical Director, East Carolina University Diabetes and Obesity Institute
Medical Director, Inpatient Diabetes Program, Pitt County Memorial Hospital
Greenville, North Carolina

Dr Tanenberg is a professor of medicine, division of endocrinology, Brody School of Medicine, East Carolina University in Greenville, North Carolina and serves as medical director of the E.C.U. Diabetes and Obesity Institute and director of the clinical diabetes fellowship. Dr Tanenberg is also the medical director of the Inpatient Diabetes Program at Pitt County Memorial Hospital in Greenville, NC.

In addition, Dr Tanenberg directs the East Carolina University-Diabetes Research Center for Clinical Trials where he has been a principal investigator for over 60 diabetes research studies. Dr Tanenberg is board certified in internal medicine, and in endocrinology and metabolism.

With special interests including insulin therapy, Type 1 diabetes, and treatment of patients with diabetic neuropathy, severe insulin resistance, and metabolic syndrome, Dr Tanenberg has over 100 publications including articles, book chapters, and abstracts. He has been published in scientific journals including Diabetes, Metabolism, Endocrine Practice, Diabetes Technology and Therapeutics, Mayo Clinic Proceedings, and the New England Journal of Medicine. He has been endocrinology editor for Hospital Physician and is an editor of the lay journal, Diabetes Health. He lectures throughout the country on the treatment of diabetes and the prevention and treatment of diabetic complications.
Faculty Financial Disclosure Statements
The presenting faculty reports the following:

Dr Inzucchi has served as a consultant for Boehringer Ingelheim, Merck, and Takeda; as a speaker for Novo-Nordisk; and in a research study funded by Eli Lilly Co. on behalf of Yale University.
Dr Tanenberg serves on speakers’ bureaus for Boehringer Ingelheim, Lilly, and sanofi-aventis, U.S., and has conducted clinical trials supported by Johnson & Johnson, Lilly, Novo-Nordisk, and sanofi-aventis, U.S.

Education Partner Financial Disclosure Statement
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Brian Lee, PharmD, Elizabeth Wilkerson, CHES, and Cara Williams, PharmD, have no financial relationships to disclose.

Acronym List

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
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</thead>
<tbody>
<tr>
<td>ACCORD</td>
<td>Action to Control Cardiovascular Risk in Diabetes (clinical trial)</td>
</tr>
<tr>
<td>ADVANCE</td>
<td>Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation</td>
</tr>
<tr>
<td>AF</td>
<td>(physical exam) afebrile</td>
</tr>
<tr>
<td>ALT</td>
<td>alanine aminotransferase</td>
</tr>
<tr>
<td>BG</td>
<td>blood glucose</td>
</tr>
<tr>
<td>BMI</td>
<td>body mass index</td>
</tr>
<tr>
<td>BUN/Cr</td>
<td>blood urea nitrogen/creatinine ratio</td>
</tr>
<tr>
<td>CAD</td>
<td>coronary artery disease</td>
</tr>
<tr>
<td>COPD</td>
<td>chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td>CVD</td>
<td>cardiovascular disease</td>
</tr>
<tr>
<td>DCCT/EDIC</td>
<td>Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications database</td>
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<tr>
<td>DPP-4</td>
<td>dipeptidyl-peptidase-4</td>
</tr>
<tr>
<td>ECG/EKG</td>
<td>electrocardiogram</td>
</tr>
<tr>
<td>eGFR</td>
<td>estimated glomerular filtration rate</td>
</tr>
<tr>
<td>FPG</td>
<td>fasting plasma glucose</td>
</tr>
<tr>
<td>GFR</td>
<td>glomerular filtration rate</td>
</tr>
<tr>
<td>GLP-1</td>
<td>glucagon-like peptide-1</td>
</tr>
<tr>
<td>HCTZ</td>
<td>hydrochlorothiazide</td>
</tr>
<tr>
<td>HR</td>
<td>heart rate</td>
</tr>
<tr>
<td>HSM</td>
<td>hepatosplenomegaly</td>
</tr>
<tr>
<td>JVD</td>
<td>jugular venous distention</td>
</tr>
<tr>
<td>LAD</td>
<td>left anterior descending</td>
</tr>
<tr>
<td>LBBB</td>
<td>left bundle branch block</td>
</tr>
<tr>
<td>NAD</td>
<td>no apparent distress</td>
</tr>
<tr>
<td>NPH</td>
<td>neutral protamine Hagedorn</td>
</tr>
<tr>
<td>OSA</td>
<td>obstructive sleep apnea</td>
</tr>
<tr>
<td>PPG</td>
<td>postprandial glucose</td>
</tr>
<tr>
<td>RR</td>
<td>respiration rate</td>
</tr>
<tr>
<td>RRR</td>
<td>relative risk reduction</td>
</tr>
<tr>
<td>s/p</td>
<td>status post</td>
</tr>
<tr>
<td>SEM</td>
<td>systolic ejection murmur</td>
</tr>
<tr>
<td>SMBG</td>
<td>self-monitored blood glucose</td>
</tr>
<tr>
<td>SU</td>
<td>sulfonylurea</td>
</tr>
<tr>
<td>(T2)DM</td>
<td>(type 2) diabetes mellitus</td>
</tr>
<tr>
<td>TG</td>
<td>triglycerides</td>
</tr>
<tr>
<td>TSH</td>
<td>Thyroid Stimulating Hormone</td>
</tr>
<tr>
<td>TZD</td>
<td>thiazolidinedione</td>
</tr>
<tr>
<td>UKPDS</td>
<td>United Kingdom Prospective Diabetes Study</td>
</tr>
<tr>
<td>VADT</td>
<td>Veterans Affairs Diabetes Trial</td>
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Suggested Reading List


Overcoming Challenges in Treatment Intensification for Type 2 Diabetes

Medication List (1 of 2)

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>acarbose</td>
<td>Precose</td>
</tr>
<tr>
<td>amlodipine</td>
<td>Norvasc</td>
</tr>
<tr>
<td>atenolol</td>
<td>Senormin, Tenormin</td>
</tr>
<tr>
<td>atorvastatin</td>
<td>Lipitor</td>
</tr>
<tr>
<td>bendroflumethiazide</td>
<td>Carvet, Farlabet</td>
</tr>
<tr>
<td>bezafibrate</td>
<td>Welchol</td>
</tr>
<tr>
<td>buvorpril</td>
<td>Rembec, Vasotec</td>
</tr>
<tr>
<td>bumetanide</td>
<td>Delone, Furocot, Lasix, Lo-Aqua</td>
</tr>
<tr>
<td>buspirone</td>
<td>Amazyl</td>
</tr>
<tr>
<td>cilostatide</td>
<td>Gliquisol</td>
</tr>
<tr>
<td>flurbiprofen</td>
<td>Diabeta, Glycine, Glynase, Micronase</td>
</tr>
<tr>
<td>insulin aspart</td>
<td>NovoLog</td>
</tr>
<tr>
<td>insulin detemir</td>
<td>Levemir</td>
</tr>
</tbody>
</table>

Medications List (2 of 2)

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
</tr>
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<tbody>
<tr>
<td>insulin glargine</td>
<td>Lantus</td>
</tr>
<tr>
<td>insulin glulisine</td>
<td>Apidra</td>
</tr>
<tr>
<td>insulin lispro</td>
<td>Humalog</td>
</tr>
<tr>
<td>exenatide</td>
<td>Victoza</td>
</tr>
<tr>
<td>lasix</td>
<td>Zetia</td>
</tr>
<tr>
<td>metformin</td>
<td>Fortamet, Dulagludase, Actos, Symlin, Prandia, Daiveslea, Qvaro,</td>
</tr>
<tr>
<td>liraglutide</td>
<td>NovoLog</td>
</tr>
<tr>
<td>metformin</td>
<td>Fortamet, Glucophage, Glimetia, Rozan</td>
</tr>
<tr>
<td>nateglinide</td>
<td>Starlix</td>
</tr>
<tr>
<td>pioglitazone</td>
<td>Actos</td>
</tr>
<tr>
<td>rosvastatin</td>
<td>Zocor</td>
</tr>
<tr>
<td>tamoxifen</td>
<td>Soltamox</td>
</tr>
<tr>
<td>valsartan</td>
<td>Diovan</td>
</tr>
<tr>
<td>valsartan</td>
<td>Diovan</td>
</tr>
<tr>
<td>valsartan</td>
<td>Diovan</td>
</tr>
</tbody>
</table>

Pre-Activity Assessment

Pre-Activity Questions 1 of 5

How confident are you in your ability to identify barriers to insulin initiation and implement solutions in your patients with type 2 diabetes? (based on a scale of 1 to 5, with 1=“Not at all confident” and 5=“Very confident”)

1. 1 - Not at all confident
2. 2
3. 3
4. 4
5. 5 - Very confident

Pre-Activity Questions 2 of 5

How often do you currently develop and implement strategies to overcome patient specific barriers to insulin initiation in individuals with type 2 diabetes? (based on a scale of 1 to 5, with 1=“Never” and 5=“Always”)

1. 1 - Never
2. 2
3. 3
4. 4
5. 5 - Always
Pre-Activity Questions 3 of 5

The National Diabetes Education Program (NDEP) has identified all of the following potential benefits of utilizing a collaborative, multidisciplinary team care approach for the treatment of patients with diabetes EXCEPT?

1. Improved glycemic control
2. Reduced hospitalizations
3. Improved overall survival
4. Decreased health care costs

Pre-Activity Questions 4 of 5

In a 75-year-old female patient with a 18-year history of type 2 diabetes and CVD who reports having increasing difficulty reading her prescription labels, which of the following A1C targets might be most appropriate for this patient?

1. <6.5%
2. <7.0%
3. <8.0%
4. <9.0%

Pre-Activity Questions 5 of 5

In a type 2 diabetes patient on optimal doses of metformin and glipizide with an A1C of 8.6 and goal of < 7%, which of the following might be the best approach to getting him to goal?

1. Add NPH insulin twice a day
2. Add a basal insulin analogue at bedtime
3. Add insulin premix insulin analog 70/30 twice daily & stop oral agents
4. Add pioglitazone

Learning Objectives

• Apply current data from clinical trials for A1C goal setting and individualized treatment
• Recognize the importance of timely initiation of drug therapy including the early insulin initiation in reducing the complications of type 2 diabetes
• Identify and implement strategies for overcoming the barriers to insulin initiation and medication adherence.
• Describe interdisciplinary team and collaborative care approaches that can improve clinical outcomes

A1C goal setting and individualized treatment

Pathophysiologic Progression and Vascular Complications of Type 2 Diabetes

IFG = impaired fasting glucose; IGT = impaired glucose tolerance.
Glycemic Burden

T2DM patients were exposed to an A1C >8% for nearly 5 years and an A1C >7% for about 10 years from diagnosis before initiating insulin.

<table>
<thead>
<tr>
<th>Mean Number of Months with A1C &gt;7%</th>
<th>Diet &amp; Exercise</th>
<th>Metformin Monotherapy</th>
<th>Sulfonylurea Monotherapy</th>
<th>Metformin &amp; Sulfonylurea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Months</td>
<td>22.5</td>
<td>33.5</td>
<td>41.5</td>
<td>58.3</td>
</tr>
</tbody>
</table>


SOLVE: Baseline A1C Distribution at Insulin Initiation


Clinical Inertia

Failure of health care providers to initiate or intensify therapy when indicated

Are Patients with T2DM Reluctant to Start Insulin Therapy?

Willingness to Start Insulin/ Psychological Insulin Resistance

Factors Related to Psychological Insulin Resistance among Ambivalent or Unwilling Patients

- More negative and fewer positive beliefs about starting insulin
- More negative feelings about their current medications
- More diabetes-related distress

N = 1400.


Identify Patient Barriers

- Ask patient, listen to response, and confirm answer
  - "What is the hardest thing about taking care of your diabetes?"
  - "What concerns or worries do you have about using insulin to treat your diabetes?"

Patient Barriers to Insulin Initiation

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Addressing the Barriers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sense of failure</td>
<td>• Insulin is an inevitable step</td>
</tr>
<tr>
<td></td>
<td>• Discuss with patients early in the disease about insulin</td>
</tr>
<tr>
<td></td>
<td>• Do not use insulin as threat, but as solution</td>
</tr>
<tr>
<td>Insulin causes complications</td>
<td>• Acknowledge the patient’s fear</td>
</tr>
<tr>
<td></td>
<td>• Provide information about the provider’s experiences of the effectiveness of insulin.</td>
</tr>
<tr>
<td>Loss of independence</td>
<td>• Empower patient to take control of BG</td>
</tr>
<tr>
<td></td>
<td>• Provide self-management education</td>
</tr>
<tr>
<td></td>
<td>• Use insulin pens and insulin regimens that offer maximum flexibility</td>
</tr>
<tr>
<td>Insulin ineffectiveness</td>
<td>• Give &quot;limited&quot; trial with appropriate insulin doses</td>
</tr>
<tr>
<td></td>
<td>• Monitor for symptom improvement (nocturia, energy level, etc...)</td>
</tr>
</tbody>
</table>

Patient Barriers to Insulin Initiation

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Addressing the Barriers</th>
</tr>
</thead>
</table>
| Fear of injections   | • Insulin needles are small  
• Less painful than finger sticks for BG testing  
• Have patient give a dry injection in office  
• Insulin pen is less threatening |
| Fear of hypoglycemia | • Incidence is low, especially with basal analogs  
• Teach patient to recognize and treat (Rule of 15) |
| Weight gain          | • Meet with dietician before initiation of insulin  
• More physiologic insulin delivery may minimize weight gain  
• Minimize with metformin and GLP-1 receptor agonists |
| Cost                 | • Insulin is typically less expensive than using multiple oral medications  
• Use premix insulins or less expensive insulins |

Physician Barriers to Insulin Initiation

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Addressing the Barriers</th>
</tr>
</thead>
</table>
| Clinical inertia       | • Use systems to facilitate chronic disease care  
• EMR reminders to support real-time treatment and monitor results |
| Suboptimal insulin knowledge | • Education on insulin selection, initiation, and titration                             |
| Fear of hypoglycemia   | • Incidence is low, especially with basal analogs  
• Teach patient to recognize and treat |
| Weight gain            | • Have patient meet with dietician before initiation of insulin  
• More physiologic insulin delivery may minimize weight gain  
• Minimize with metformin and GLP-1 receptor agonists |

Insulin Non-adherence

• Common problem
  • More than 1 in 3 patients do not adhere to their insulin regimen
  • In insulin-naïve patients, 4.5% do not fill their insulin prescription and 25.5% do not continue their insulin

• Primary reasons for non-adherence
  • Plans to improve lifestyle in lieu of starting insulin
  • Loss of independence (negative impact on social and work life)
  • Fear of injection
  • Hypoglycemia
  • Sense of failure (self-blame)
  • Perception that insulin causes complications
  • Complex insulin regimen

Collaborative Care

Team Approach to Diabetes Care

- Discuss impact of diet on diabetes
- Formulate individualized meal plan
- Review treatment prescription with patient
- Evaluate & encourage adherence
- Assess patient understanding
- Address patient questions/concerns
- Initial and ongoing self-management education
- Follow-up patient
- Implement & revise treatment plan
- Review day-to-day management issues

Collaborative, Multidisciplinary Team Care

• Key function of Team Care is to provide continuous, supportive, and effective care for people with diabetes throughout the course of their disease

• Benefits of Team Care
  • Efficient patient education
  • Improved glycemic control
  • Increased patient follow-up
  • Higher patient satisfaction
  • Lower risk for the complications of diabetes
  • Improved quality of life
  • Reduced hospitalizations
  • Decreased health care costs


Starting Insulin

- Remains the most powerful tool we have to control blood glucose.
- Dosing potential and A1C reduction only limited by risk of hypoglycemia.
- Patients with type 2 diabetes are at lower risk for hypoglycemia than type 1 patients.


Time Profiles of Human Insulins and Analogs

<table>
<thead>
<tr>
<th>Insulin Type</th>
<th>Onset</th>
<th>Peak, h</th>
<th>Duration of Action, h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin lispro, aspart, glulisine</td>
<td>10-15 min</td>
<td>0.5-1.5</td>
<td>2-4</td>
</tr>
<tr>
<td>Short acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular human insulin</td>
<td>30-60 min</td>
<td>2-3</td>
<td>3-6</td>
</tr>
<tr>
<td>Intermediate-acting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human NPH insulin</td>
<td>2-4 h</td>
<td>4-10</td>
<td>10-16</td>
</tr>
<tr>
<td>Long acting (basal)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin glargine</td>
<td>1-2 h</td>
<td>No pronounced peak</td>
<td>24</td>
</tr>
<tr>
<td>Insulin detemir</td>
<td>1-2 h</td>
<td>Relatively flat</td>
<td>Up to 24</td>
</tr>
</tbody>
</table>


Physiologic Insulin Secretion


When To Start Insulin in T2DM

- When combination oral/injectable agents become inadequate.
- Unacceptable side effects of other agents
- Patient with advanced hepatic or renal disease.
- Special circumstances (i.e. steroids, infection, pregnancy.)
- Patient with hyperglycemia in the hospital.
- “ Severely” uncontrolled diabetes*

*Defined as fasting glucose > 200 mg/dl, random glucose > 300 mg/dl, A1C > 10%, ketonuria, or symptomatic polyuria, polydipsia, and weight loss by ADA 2009 Consensus Statement. After glucose controlled, oral agents can be safely and insulin withdrawn if patients.


Summary of Comparative Insulin Trials

1. Any insulin will lower glucose and A1C; the more injections and the higher the dose, the better the control.
2. All insulins result in weight gain and increase the risk of hypoglycemia.
3. Generally, insulin analogues reduce the incidence of hypoglycemia over human insulins - but generally do not result in better overall glycemic control.
4. Insulin strategies that include prandial dosing (i.e., basal-bolus; premixed) will generally reduce A1C to a greater extent than basal-only, but at the expense of more weight gain, hypoglycemia.

Initial Insulin Strategies in Type 2 Diabetes

• Basal insulin therapy
  – NPH at bedtime or long-acting insulin analog (glargine, detemir) once daily
  – Start 10 units daily or 0.2 units/kg/day
  – Adjust 2-4 units every 3 days based on fasting BG

• Premixed insulin
  - Once or twice daily (before breakfast and/or dinner)
  - Adjust every 3 days based on fasting & pre-dinner BG

Premixed vs Basal-Bolus

Premixed Basal-bolus

<table>
<thead>
<tr>
<th>Patients to Target A1C &lt;7.0 (%)</th>
<th>Premixed</th>
<th>Basal-bolus</th>
</tr>
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<tbody>
<tr>
<td>Liebl et al., 2009</td>
<td>50</td>
<td>60</td>
</tr>
<tr>
<td>Hirao et al., 2007</td>
<td>32</td>
<td>33</td>
</tr>
<tr>
<td>Rosenstock et al., 2008</td>
<td>54</td>
<td>69</td>
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</tbody>
</table>

Premixed vs Basal Insulin Analogs in T2DM

<table>
<thead>
<tr>
<th>A1C (%)</th>
<th>9.7</th>
<th>2.8*</th>
<th>9.8</th>
<th>2.4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premixed</td>
<td>Basal</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| A1C<7% | 66%* | 40% |
| Hypoglycemia (events/yr) | 0.4* | 0.7 |
| Weight (kg) | 5.4* | 3.5 |
| Insulin dose (units/day) | 79±40 | 51±27 |

*P < 0.01 vs glargine.


Advancing Basal Insulin

Baseline Characteristics of T2DM Prior to Initiating Insulin Therapy

<table>
<thead>
<tr>
<th>Basal hyperglycemia</th>
<th>Postprandial hyperglycemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4.5%</td>
<td>10.5-15%</td>
</tr>
<tr>
<td>Basal A1C Category (%)</td>
<td>Total A1C (%)</td>
</tr>
<tr>
<td>4.5-5.5%</td>
<td>5.5-6.0%</td>
</tr>
<tr>
<td>7-8%</td>
<td>8-9%</td>
</tr>
<tr>
<td>9-10%</td>
<td>10-12%</td>
</tr>
<tr>
<td>12-14%</td>
<td>≥14%</td>
</tr>
</tbody>
</table>

Data from Riddle et al. Diabetes Care. 2011;34:2608-2614.
Relative Contribution to A1C after Treatment (24-28 wks)

Basal insulin

Premix, lispro or OAD

A Recommendation for Starting and Adjusting Basal Insulin

Bedtime or morning long-acting insulin
OR
Bedtime intermediate-acting insulin
Daily dose: 10 units or 0.2 units/kg

Increase dose by 2 units every 3 days until FPG is 70-130 mg/dL.
If FPG is >180 mg/dL, increase dose by 4 units every 3 days.

In the event of hypoglycemia or FPG level <70 mg/dL:
Reduce bedtime insulin dose by 4 units, or by 10% if >40 units.

Continue regimen and check A1C every 3 months.

“Basal Only” Insulin Therapy

When Basal Alone is Not Enough

When is Basal Alone Not Enough?

When A1C values are still not at target AND...

• Basal insulin dose titrated to 0.4-0.6 units/kg/day
• Fasting BG levels at or approaching target
• Post-prandial BG values remain above target

Mimicking Physiologic Insulin Secretion: “Basal-Bolus” Insulin Therapy

B = breakfast; D = dinner; hs = at bedtime; L = lunch.
Progressive Insulin Strategies in T2DM

1 Injection
'Basal only'
• NPH
• Detemir
• Lantus

2 Injections
PreMix
• Human 70/30
• Aspart 70/30
• Lispro 75/25

3 Injections
PreMix
• TID AC
• Basal + Rapid
• Basal/Bolus Lite

4 Injections
PreMix
• TID AC
• Basal + Rapid
• Basal/Bolus Lite

How to intensify using the basal plus approach

• Choose the “target” meal to initiate prandial coverage
  – Breakfast or the largest meal of the day
• Start 4-6 units of a rapid-acting insulin analog 10-15 minutes before the meal
• Adjust prandial insulin dose based on
  – 2-h PPG -> target < 180 mg/dl
  – Next pre-prandial or HS BG -> target < 130 mg/dl
• If A1C remains above target add 2nd prandial dose
  – Usually need about 8-12 units of prandial insulin to cover meal(s)

Insulin Pens

• More convenient than traditional vial and syringe
• More accurate, repeated doses
• Easier to use for those with visual or fine motor skill impairments
• Less injection pain (Needles are not dulled by insertion into vial diaphragm before a second insertion into the skin)
• Most insurance companies are covering insulin pens
• But more expensive! (2 X)

Summary

• Identify appropriate candidates for intensive diabetes management
• Address barriers to treatment intensification
• Make use of multidisciplinary approach to diabetes management
• Start and optimize basal insulin
  – Involve patient in insulin dose adjustments
• Intensify by adding prandial coverage in a simplified manner

Premixed (Biphasic) Insulin Analogs

Humalog 75/25, 50/50
Novolog 28/72
Humulin 70/30
Novolin 70/30

• Premixed insulin may be appropriate
  – When basal/bolus cannot be used
• For those with regular lifestyles, who eat similar amounts at similar times each day
• Those who wish only 2 injections/day

Patient Case Discussion
Case 1: Presentation

- A 54-year-old man with a 6-year history of Type 2 diabetes presents in your office for routine evaluation.
- At first visit, patient presented with polyuria, polydipsia, weight loss and fatigue and had a blood glucose in the 400 mg/dl range and A1C of 12.2%.
- He was prescribed the combination of metformin and glipizide at the outset, and with gradual dose titration over the first year, his A1C decreased to 10.1%. At that time, you recommended that the patient transition to insulin therapy, but he strongly preferred oral agents.

Case 1: Evaluation

- His physical exam shows:
  - Weight 339 lbs  BP 142/86  HR 84  RR 14  Afebrile
  - Acanthosis nigricans
  - Normal thyroid
  - Lungs clear
  - Heart normal
  - Abdomen obese; no organomegaly or masses
  - Extremities trace edema, full distal pulses; no neuropathy
- His labs as follows:
  - BG 178 mg/dl  A1C 8.3%
  - LDL-C 133  HDL 38  TG 218
  - BUN 22  Cr 1.2

Case 1: Medications

- His current medications are:
  - Metformin 850 mg twice daily
  - Glipizide 10 mg twice daily
  - Pioglitazone 30 mg daily
  - Atorvastatin 40 mg daily
  - Lisinopril / HCTZ 20/35 mg daily
  - Atenolol 50 mg daily

Case 1: Question 1

What would you recommend at this point regarding his glucose control?

1. No change in regimen
2. Add a DPP-4 inhibitor
3. Add a GLP-1 receptor agonist
4. Add a basal insulin at bedtime
5. Add a premix insulin twice daily
Case 1: Question 2
If you chose a basal insulin regimen for this patient, what initial dose would you choose?

1. 10 units
2. 50 units
3. 0.2 units/kg
4. 0.5 units/kg
5. 1.0 units/kg

Case 1: Question 3
If you chose a basal insulin regimen for this patient, how would you titrate the dose?

1. 2-4 units every 3 days until FBG <130 mg/dl
2. 1 unit every week until FPG <130 mg/dl
3. 5 units every 3 days until PPG < 180 mg/dl
4. 15-20% increase every 3 months until A1C<7%
5. No titration, dose is fixed

Case 2
67-year-old African American woman has an extensive history of Type 2 Diabetes

Case 2: Presentation
• A 67-year-old African American woman presents in your office.
• She has an extensive history of Type 2 Diabetes.
• Initially treated with oral agents, but for the past 5 years has been on insulin.
• Her control has been deteriorating over the past 2 years, during which time her A1C has been consistently >8%. Home glucose meter readings in the fasting state are in the low 100s.
• She has developed several urinary tract infections over the past year and has been hospitalized once for community acquired pneumonia.

Case 2: Evaluation
• Past medical history:
  − COPD
  − Diverticulitis
  − Breast cancer
  − Multinodular goiter
• Her physical examination shows:
  − Elderly appearing woman in NAD.
  − BP 156/92 HR 102 RR 18 Afebrile
  − Mild JVD; enlarged lobulated thyroid; no cervical nodes
  − Mild wheezes upper lung fields bilaterally
  − S1 S2 II/VI SEM
  − Obese abdomen. No HSM.
  − 1+ edema; bunion deformities; decreased distal pulses; decreased monofilament sensation in the feet.
• You obtain the following labs:
  − FPG 143 mg/dl
  − A1C 9.1%
  − BUN 44 Cr 1.2 (eGFR 75)
  − K+ 5.6
  − LDL-C 106 HDL-C 52 TG 175
  − EKG LBBB
  − SMBG Log: FPG 120-150 mg/dl
  − Post-prandial BGs 200-320 mg/dl
**Case 2: Medication**

- Her current medication are:
  - Glargine insulin 54 units at bedtime
  - Metformin 850 mg twice daily
  - Glimepiride 4 mg daily
  - Rosuvastatin 10 mg daily
  - Amlodipine 5 mg daily
  - Valsartan 160 mg daily
  - Furosemide 40 mg daily
  - Tamoxifen 20 mg daily
  - Sertraline 100 mg daily

**Case 2: Question 1**

What is the most likely explanation for the discrepancy between her A1C and her FPG?

1. Hemoglobinopathy
2. Inaccurate glucose meter
3. Post-prandial hyperglycemia
4. Reduced hepatic glucose production

**Case 2: Question 2**

What is the best therapeutic option at this time?

1. Add a GLP-1 receptor agonist.
2. Increase glargine dose to target FPG < 100 mg/dl.
3. Switch glargine to BID dosing.
4. Add prandial insulin injections with a rapid-acting analogue.
5. Change glargine to pre-mixed insulin BID.

**Case 2: Question 3**

Assuming that a basal-bolus insulin regimen is chosen, what would you recommend she do with her oral agents?

1. Stop both metformin and glimepiride
2. Continue metformin, stop glimepiride
3. Continue both metformin and glimepiride
4. Continue metformin, stop glimepiride, add pioglitazone

**Case 2: Question 4**

How would you titrate the mealtime insulin component to an advanced, basal-bolus regimen?

1. Based on fasting BG
2. Based on 2-hr post-prandial BG
3. Based on carbohydrate counting
4. No titration; dose is fixed

**Post-Activity Assessment**
Post-Activity Questions 1 of 5
After participating in this activity, how confident are you now in your ability to identify barriers to insulin initiation and implement solutions in your patients with type 2 diabetes? (based on a scale of 1 to 5, with 1=“Not at all confident” and 5=“Very confident”)

1. 1 - Not at all confident
2. 2
3. 3
4. 4
5. 5 - Very confident

Post-Activity Questions 2 of 5
After participating in this activity, how often do you now plan to develop and implement strategies to overcome patient specific barriers to insulin initiation in individuals with type 2 diabetes? (based on a scale of 1 to 5, with 1=“Never” and 5=“Always”)

1. 1 - Never
2. 2
3. 3
4. 4
5. 5 - Always

Post-Activity Questions 3 of 5
The National Diabetes Education Program (NDEP) has identified all of the following potential benefits of utilizing a collaborative, multidisciplinary team care approach for the treatment of patients with diabetes EXCEPT?

1. Improved glycemic control
2. Reduced hospitalizations
3. Improved overall survival
4. Decreased health care costs

Post-Activity Questions 4 of 5
In a 75-year-old female patient with a 18-year history of type 2 diabetes and CVD who reports having increasing difficulty reading her prescription labels, which of the following A1C targets might be most appropriate for this patient?

1. <6.5%
2. <7.0%
3. <8.0%
4. <9.0%

Post-Activity Questions 5 of 5
In a type 2 diabetes patient on optimal doses of metformin and glipizide with an A1C of 8.6 and goal of < 7%, which of the following might be the best approach to getting him to goal?

1. Add NPH insulin twice a day
2. Add a basal insulin analogue at bedtime
3. Add insulin premix insulin analog 70/30 twice daily & stop oral agents
4. Add pioglitazone

Your Curriculum Challenge

• A 48-year-old Puerto Rican male presents for evaluation of type 2 diabetes diagnosed 6 years ago.
• Past Medical History: HTN, Dyslipidemia; denies any recent episodes of hypoglycemia, occasional nocturia; no excessive thirst or urination during the day.
• Current Meds:
  – Metformin 1000mg twice daily
  – Glyburide 10 mg in the morning;
  – Enalapril 20 mg daily;
  – Simvastatin 20 mg daily (poorly adherent)
• Never injected insulin and is anxious about having to use “needles” to control his diabetes (relates his aunt went into kidney failure shortly after starting insulin injections).
Your Curriculum Challenge

• Social History: Does not exercise, but incorporates additional walking during activities of daily living; does not smoke; 2-3 glasses of wine per week, with dinner.

• Family History: Relevant for Type 2 diabetes in his mother (passed away at age 72 following a myocardial infarction), as well as his maternal aunt (currently on hemodialysis) and grandfather.

• Sporadic BG monitoring demonstrates range of 120-180 mg/dl in the morning and 90-220 mg/dl during the day.

Your Curriculum Challenge

Physical Exam

• Weight 220 lbs (100 kg)
• BMI 32 kg/m²
• BP 134/82
• Normal cardiac and vascular exam
• Liver slightly enlarged
• Normal 10-gram monofilament testing of lower extremities

Your Curriculum Challenge

Labs

<table>
<thead>
<tr>
<th>Labs</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1C</td>
<td>9.3%</td>
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<tr>
<td>Total cholesterol</td>
<td>172 mg/dL</td>
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<tr>
<td>Fasting glucose</td>
<td>212 mg/dL</td>
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<tr>
<td>TG</td>
<td>190 mg/dL</td>
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<tr>
<td>Creatinine</td>
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<td>GFR</td>
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<td>98 mg/dL</td>
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<td>ALT</td>
<td>58</td>
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<tr>
<td>Non-HDL-C</td>
<td>136 mg/dL</td>
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<tr>
<td>TSH</td>
<td>normal</td>
</tr>
<tr>
<td>Random urine albumin/creatinine ratio</td>
<td>35 mg/g</td>
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</tbody>
</table>

Tests

<table>
<thead>
<tr>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting ECG: Normal sinus rhythm</td>
</tr>
<tr>
<td>Fundoscopic exam: Mild nonproliferative DR (3 months before)</td>
</tr>
</tbody>
</table>

Pertaining to the patient just described, which of the following would you recommend? (1 of 2)

Choose all that apply!

1. Establish an initial A1C target of less than 7%.
2. Establish an initial A1C target of less than 6.5%.
3. Add a third oral agent to meet the target A1C.
4. Initiate basal insulin therapy to meet the target A1C.
5. Initiate BID premixed insulin therapy to meet the target A1C.

Pertaining to the patient just described, which of the following would you recommend? (2 of 2)

Choose all that apply!

1. If basal insulin is used, titrate carefully to achieve a fasting glucose target of <120-130 mg/dl.
2. If basal insulin is used, add prandial insulin if fasting glucose target met, but A1C still not at goal.
3. Titrate prandial insulin to achieve a fasting glucose target of <120-130 mg/dl.
4. Stop any insulin secretagogue (e.g. sulfonylurea) once insulin therapy beyond basal insulin is used.
5. Stop metformin once insulin is initiated.

Questions & Answers