Insulin Therapy for Optimizing Glycemic Control in Type 2 DM

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Case 1

- A 45 years-old Thai female with T2DM for 3 years
- HT, Dyslipidemia, no DR, no DN
- BW 60 kg., BMI 24.9 kg/m²
- **Current therapy**: metformin 850 mg tid, glipizide 10 mg bid, losartan 50 mg od and simvastatin 10 mg od
- Last FPG 270 mg/dl, HbA1c 9.4%

What is the target of HbA1c?
How to get the HbA1c target??
Case 2

• A 65 years-old Thai male with T2DM for 15 years
• HT, Dyslipidemia, post PCI at LAD for 1 year
• BW 75 kg., BMI 27.5 kg/m²
• **Current therapy** : metformin 850 mg bid, glipizide 10 mg bid, basal insulin 34 unit sc hs, simvastatin 20 mg/d, clopidrogel 75 mg/d, losartan 100 mg/d
• Last FPG 115 mg/dl, HbA1c 9.0%, creatinine 1.4 mg/dl (GFR 65)

What is the target of HbA1c?

How to get the HbA1c target??
Outlines

• Glycemic control in type 2 DM
• Insulin and type 2 DM
• Starting insulin therapy in type 2 diabetes
• Insulin regimens for type 2 diabetes
• Barriers to insulin therapy
Glycemic control in type 2 DM
Legacy Effect in Long-Term UKPDS

Intensive vs conventional treatment

1977–1991 Randomization
1997 20 years (Trial end)
2007 30 years

10-year Post Trial Follow-up (non-interventional)

12%* 16%** 25%*
16%** 6% 9%*
24%*

Any diabetes-related endpoint
Myocardial infarction
Microvascular disease
All-cause mortality

*p<0.05 **p=0.052 for intensive vs conventional treatment

NEJM 2008;359:1577–89
## Implications of recent trial outcomes

<table>
<thead>
<tr>
<th>Variables</th>
<th>VADT (n=1,700)</th>
<th>ACCORD (n=10,250)</th>
<th>ADVANCE (n=11,140)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HbA(_{1c}) (%)</strong></td>
<td>8.4 vs 6.9</td>
<td>7.5 vs 6.4</td>
<td>7.3 vs 6.5</td>
</tr>
<tr>
<td><strong>Primary outcome</strong></td>
<td>MI, stroke, CV death, new or worsening CHF, revascularisation and inoperable CAD, amputation for ischemic gangrene</td>
<td>Non-fatal MI, non-fatal stroke, CVD death</td>
<td>Non-fatal MI, non-fatal stroke, CVD death</td>
</tr>
<tr>
<td><strong>HR (95% CI) for primary outcome</strong></td>
<td>0.87 (0.730–1.04)</td>
<td>0.90 (0.78–1.04)</td>
<td>0.94 (0.84–1.06)</td>
</tr>
<tr>
<td><strong>HR (95% CI) for mortality</strong></td>
<td>1.07 (0.80–1.42)</td>
<td><strong>1.22 (1.01–1.46)</strong></td>
<td>0.93 (0.83–1.06)</td>
</tr>
</tbody>
</table>

Implications of these studies

• Targeting A1C levels in T2DM is < 7 %
• Physicians should *aggressively manage hyperglycemia during the earliest phases* in order to minimize microvascular and macrovascular complications.
• A1C levels < 7 % in high risk patients with T2DM **does NOT** reduce cardiovascular risk.
• A1C goals and targets in high risk patients with T2DM should be *individualized.*

Guidelines provide HbA$_{1c}$, FBG and PPBG targets

<table>
<thead>
<tr>
<th></th>
<th>Healthy$^1$</th>
<th>ADA$^1$</th>
<th>AACE$^2$</th>
<th>IDF$^3$</th>
<th>THAI$^4$</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA$_{1c}$* (%)</td>
<td>&lt;6.0</td>
<td>&lt;7.0$^+$</td>
<td>≤6.5</td>
<td>&lt;7.0</td>
<td>&lt;7.0$^+$</td>
</tr>
<tr>
<td>FBG, mg/dl</td>
<td>&lt;100</td>
<td>90–130</td>
<td>&lt;110</td>
<td>&lt;115</td>
<td>90–130</td>
</tr>
<tr>
<td>PPBG, mg/dl</td>
<td>&lt;140 $^*$</td>
<td>&lt;180 $^{**}$</td>
<td>&lt;140 $^{**}$</td>
<td>&lt;160 $^{**}$</td>
<td>&lt;180 $^{**}$</td>
</tr>
</tbody>
</table>

*DCCT referenced assays: normal range 4–6%; **1–2 hours postprandial; $^+$ADA and ADA/EASD guidelines recommend HbA$_{1c}$ levels as close to normal (<6%) as possible without significant hypoglycaemia$^{1,5}$
AACE=American Association of Clinical Endocrinologists; ADA=American Diabetes Association; EASD=European Association for the Study of Diabetes; IDF=International Diabetes Federation

1. ADA recommendations 2012.
2. AACE. Recommendations 2011.
3. IDF. Recommendation 2012.
### Percentage of Patients Who Reach Glycemic Targets (DiabCare 2008)

<table>
<thead>
<tr>
<th></th>
<th>ADA n ( %)</th>
<th>AACE/IDF n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FPG</td>
<td>967 (45.6%)</td>
<td>457 (21.6%)</td>
</tr>
<tr>
<td>HbA1c</td>
<td>670 (35.5) %</td>
<td>368 (19.5 %)</td>
</tr>
</tbody>
</table>

**ADA target for FPG < 7.2 mmol/L, HbA1c < 7 %**

**AACE/IDF target for FPG < 6.1 mmol/L, HbA1c < 6.5 %**
Insulin and Type 2 DM
Natural History of Type 2 Diabetes

<table>
<thead>
<tr>
<th>Obesity</th>
<th>IGT</th>
<th>Diabetes</th>
<th>Uncontrolled Hyperglycemia</th>
</tr>
</thead>
</table>

- **Glucose (mg/dl)**
  - **Fasting Glucose**
  - **Post Meal Glucose**

- **Relative β-cell function (%)**
  - **Insulin Resistance**
  - **Insulin Level**

### Insulin requirements in T2DM: disease duration and HbA$_{1C}$ target

<table>
<thead>
<tr>
<th>Study</th>
<th>Baseline age (yr)</th>
<th>T2DM duration (yr)</th>
<th>HbA$_{1C}$ target (%)</th>
<th>% Requiring insulin at end of study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Standard</td>
<td>Intensive</td>
</tr>
<tr>
<td>VADT</td>
<td>60.4</td>
<td>11.5</td>
<td>&lt; 9.0</td>
<td>&lt; 6.0</td>
</tr>
<tr>
<td>ACCORD</td>
<td>62.2</td>
<td>10.0</td>
<td>&lt; 7.0-7.9</td>
<td>&lt; 6.0</td>
</tr>
<tr>
<td>ADVANCE</td>
<td>66.0</td>
<td>7.9</td>
<td>Local standard</td>
<td>&lt; 6.5</td>
</tr>
</tbody>
</table>

VADT: Veterans Affairs Diabetes Trial  
ACCORD: Action to Control Cardiovascular risk in Diabetes  
ADVANCE: Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation

Insulin and Type 2 Diabetes

• Insulin deficiency is an important part in the pathogenesis of type 2 diabetes

• Insulin remain the most potent anti-hyperglycemic agent available for uncontrolled type 2DM patients
Starting insulin therapy in T2DM
Early insulin therapy in T2DM
Effect of intensive insulin therapy on β-cell function and glycemic control in newly diagnosed-T2DM

• **Subjects:**
  – 382 aged 25–70 yrs, with FPG of 126–300 mg/dl from 9 centers in China

• **Intervention:**
  – Randomly assigned to CSII or MDI or OHD.
  – Rx was stopped after normoglycaemia was maintained for 2 weeks and FU on diet and exercise alone.

• **Measurement:**
  – IVGTT and blood glucose, insulin, and proinsulin were measured 0, after Rx and at 1-year follow-up.

• **Primary endpoint:**
  – time of glycaemic remission and remission rate at 1 yr of Rx

Remission rates at one year in three groups

Remission rates after 1 year were significantly higher in the insulin groups (CSII and MDI) than in the OHD group.

51.1% (68 of 133) in the CSII group
44.9% (53 of 118) in MDI group
26.7% (27 of 101) in OHD group

P=0.012

Increased acute phase insulin response in CSII and MDI than OHD

- \(\beta\)-cell function represented by acute insulin response was sustained in the insulin groups but significantly declined in the OHD group at 1 year in the remission group.

• Early intensive insulin intervention in patients with newly diagnosed T2DM have a favorable outcomes on
  – Recovery and maintenance of β-cell function
  – Prolonged glycemic remission compared with treatment with OHDs
Guideline recommendations for insulin therapy in T2DM
Thai guideline for glycemic control in T2DM

Thai guideline 2011
เมื่อวินิจฉัยโรค

- FPG < 180 และ HbA1C < 8 %
- FPG 180-250 mg/dl
- FPG 250-350 หรือ HbA1C > 9%

ปรับเปลี่ยนพฤติกรรม ออกกำลังกาย เรียนรู้บ้านาน และการดูแลตนเอง 1-3 เดือน ถ้าไม่ได้ตามเป้าหมาย ให้เริ่มยา

กินยาลดระดับน้ำตาล ฟื้นฟูร่างกายกลับสู่สุขภาพดี

Metformin
- ลักษณะดื้ออินซูลิน
- BMI >23 กก./ม² หรือ รอบเอวเกิน
- มี Acanthosis nigrican
- BP >130/80 หรือมี HT
- Elevated TG, low HDL

Sulfonylurea
- ลักษณะขาดอินซูลิน
- BMI <23 กก./ม² และ รอบเอวไม่เกิน
- มีอาการน้ำตาลสูงชัดเจน

ยาที่เป็นทางเลือก Glitazone, Repaglinide, AGI, DPP-4 inhibitors

พิจารณาใช้ยาร่วมกัน 2 ชนิด

ยาใช้ครั้งแรก ยาใช้เพิ่มเติม

ยาเม็ดลดน้ำตาล 3 ชนิด
- Metformin
- Sulfonylurea/Glinides
- TZDs
- DPP-4 inhibitors
- Basal insulin

ยาเม็ดลดน้ำตาล 2 ชนิด ร่วมกับอินซูลิน (NPH hs or LAA)

ยาเม็ดลดน้ำตาล 2 ชนิด ร่วมกับ metformin

Premixed insulin ac เช้าและเย็น ร่วมกับ metformin

Thai guideline 2011
FPG >300 mg/dl หรือ HbA1c > 11% ร่วมกับอาการน้ำตาลในเลือดสูง

- ฉีดอินซูลินวันละหลายครั้ง เลียนแบบการตอบสนองคนปกติ
  - RI-RI-RI-NPH or LAA
  - หรือ RAA-RAA-RAA-LAA or NPH
  - ปรับขนาดโดยดูน้้าตาลหลังอาหารแต่ละมื้อ
  - หรือ ส่งต่อผู้เชี่ยวชาญโรคเบาหวาน

RAA = rapid acting insulin analog, LAA = long acting insulin analog
Basal insulin: NPH start 0.1-0.15 unit/kg/day

Thai guideline 2011
ADA/EASD Management Algorithm 2012

Healthy eating, weight control, increased physical activity

Metformin
- high
- low risk
- neutral/loss
- GI / lactic acidosis
- low

If needed to reach individualized HbA1c target after ~3 months, proceed to two-drug combination (order not meant to denote any specific preference):

- Metformin + Sulfonylurea
- Thiazolidinedione
- DPP-4 Inhibitor
- GLP-1 receptor agonist
- Insulin (usually basal)

If needed to reach individualized HbA1c target after ~3 months, proceed to three-drug combination (order not meant to denote any specific preference):

- Metformin + Sulfonylurea + TZD
- Thiazolidinedione + SU
- DPP-4 Inhibitor + TZD
- GLP-1 receptor agonist + Insulin
- Insulin (multiple daily doses)

- More complex insulin strategies

ADA/EASD guideline: April 2012.
IDF Treatment Algorithm for T2DM 2012

1. **Lifestyle measures**

2. **Then, at each step, if not to target (generally HbA$_1c$ < 7.0%)**
   - **Consider first line**
     - Metformin
     - 
       - Sulfonylurea
       - or
       - α-Glucosidase inhibitor
   - **Consider second line**
     - Sulfonylurea
     - Metformin (if not first line)
     - or
     - α-Glucosidase inhibitor or DPP-4 inhibitor or Thiazolidinedione
   - **Consider third line**
     - Basal insulin or Pre-mix insulin
     - or
     - α-Glucosidase inhibitor or DPP-4 inhibitor or Thiazolidinedione
   - **Consider fourth line**
     - Basal + meal-time insulin
     - or
     - Basal insulin, or Pre-mix insulin (later basal + meal-time)

IDF guideline 2012
When to Start Insulin in T2DM:

• **Insulin initiation is indicated**
  
  – Signs of severe insulin deficiency
    
    • ketosis, uncontrolled DM with multiple OHD, severe weight loss
  
  – Fasting plasma glucose (FPG) levels are frequently above 250 mg/dl
  
  – Random glucose levels are consistently above 300 mg/dl
  
  – Or HbA1c > 10%

• **Insulin should be considered**
  
  – Whenever the HbA1c > 8.5% with one or more OHD
Insulin regimens for T2DM
Physiological Serum Insulin Secretion Profile

Total daily insulin requirement = 0.5-1 unit/kg/D

The 50/50 Rule
## Characteristics of current available insulin

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Onset of action*</th>
<th>Peak action*</th>
<th>Duration*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lispro, aspart, glulisine</td>
<td>0.1-0.25</td>
<td>0.5-1.5</td>
<td>3-5</td>
</tr>
<tr>
<td>Regular</td>
<td>0.5-1.0</td>
<td>2.0-3.0</td>
<td>5-8</td>
</tr>
<tr>
<td>NPH</td>
<td>1-3</td>
<td>4.0-10</td>
<td>10-20</td>
</tr>
<tr>
<td>Glargine</td>
<td>2-4</td>
<td>No peak</td>
<td>20-24</td>
</tr>
<tr>
<td>Determir</td>
<td>2</td>
<td>No peak</td>
<td>16-24</td>
</tr>
<tr>
<td>Lispro75/25</td>
<td>0.25-0.5</td>
<td>5.8 (1.3-12)</td>
<td>12-24</td>
</tr>
<tr>
<td>Lispro 50/50</td>
<td>c/w lispro</td>
<td>1.0</td>
<td>c/w lispro 75/25</td>
</tr>
<tr>
<td>Aspart 70/30</td>
<td>0.17-0.33</td>
<td>2.4</td>
<td>12-24</td>
</tr>
</tbody>
</table>

*Time (hr)

Common Insulin Regimens: Type 2 DM

• Basal Insulin (plus oral agents)
  – Single dose glargine, detemir, NPH

• Conventional “Mixed” Insulin Therapy
  – NPH plus short-/rapid-acting insulin

• Multiple Daily Injections (MDI)
  – Long-acting insulin + mealtime insulin
4-T: Treating to Target in Type 2 Diabetes study

First Phase
One year
- Add biphasic insulin* twice a day
- Add prandial insulin* three times a day
- Add basal insulin* once (or twice) daily

Second Phase
year 2\textsuperscript{nd}-3\textsuperscript{rd}
- Add prandial insulin at midday
- Add basal insulin before bed
- Add prandial insulin three times a day

* Intensify to a complex insulin regimen in year one if unacceptable hyperglycaemia

From one year onwards, if HbA\textsubscript{1c} levels were >6.5%, sulfonylurea therapy was stopped and a second type of insulin was added

4-T: HbA$_{1c}$ Values Over 3 Years

Median ±95% confidence interval

Glycated haemoglobin (%)

Years since randomization

Overall 6.9% (6.8 to 7.1)

Biphasic ± prandial
Prandial ± basal
Basal ± prandial

4-T: Relative Changes over 3 Years and Hypoglycemia

Mean ± 1SD

- Glycated Haemoglobin: Baseline value 8.5%, Baseline prevalence of hypoglycaemia grade 2 or 3 <0.001
- Fasting Plasma Glucose: Baseline value 9.6 mmol/l (173 mg/dl)
- Postprandial Glucose: Baseline value 12.6 mmol/l (227 mg/dl)
- Body Weight: Baseline value 85.8 kg

ADA/EASD 2012: insulin therapy guidelines for T2DM
Insulin Initiation for T2DM

Oral hypoglycemic drugs failure

Add Basal Insulin

ADA/EASD guideline: April 2012.
Starting with BASAL INSULIN ADVANTAGES

• 1 injection
• Safe and simple titration
• Low dosage
• Effective improvement in glycemic control
• Limited weight gain
Type of Basal Insulin

NPH insulin
Onset: 1 1/2 hr  Peak: 4-12 hr  Duration: 16-24 hr

Long-acting analogue insulin
Onset: 2-3 hr  Peak: none  Duration: 24 hr

Insulin Level

Hours

0 2 4 6 8 10 12 14 16 18 20 22 24

Intermediate (NPH)

Long (Glargine)

Long (Detemir)
How to Start Basal Insulin in T2DM:

• Initiate insulin with single injection of basal
  – Bedtime or morning long-acting insulin or
  – Bedtime intermediate-acting insulin
  – Daily dose: 10 units or 0.2 unit/kg

• Target range of FBG 70 -130 mg/dl
How to Adjust Basal Insulin in T2DM:

• Check FBG and increase dose until in target range:
  - Typical dose increase is 2 units every 3 days,
  - If FPG >180 mg/dl: increase by 4 units every 3 days

• If hypoglycemia occurs or if fasting glucose (<70 mg/dL)...
  Reduce bedtime dose by ≥4 units or 10% if dose >60 units

• If HbA₁c is <7%  - Continue this regimen
  - Check HbA₁c every 3 months

• If HbA₁c is ≥7% - Adjust insulin regimens
WHEN TO CONSIDER MORE COMPLEX INSULIN REGIMENS?

• FPG is acceptable, but HbA1C is still high after 3-6 months of basal titration
• Significant postprandial glucose excursions (> 180 mg/dl)
• When aggressive titration is limited by hypoglycemia
• The need for prandial insulin therapy when the daily dose exceeds 0.5 u/kg/day because of weight gain and increase risk of hypoglycemia

ADA/EASD guideline: April 2012.
Insulin Intensification for T2DM

1. Oral hypoglycemic drugs failure
2. Add Basal Insulin
   - Add Prandial Insulin
   - Switch to Premixed Insulin

ADA/EASD guideline: April 2012.
**Type of Prandial Insulin**

Rapid (Lispro, Aspart, Glulisine)

- Onset: <1/2 hr
- Peak: 1 hr
- Duration: 3-4 hr

Regular insulin

- Onset: 1/2 hr
- Peak: 1-3 hr
- Duration: 6-8 hr
Adding Prandial Insulin

• **Adding prandial insulin**: precise and flexible

• **Starting dose**
  - 4 u/meal, 10% of total daily dose, or 0.05-0.1 u/kg
  - Monitor pre-prandial glucose of next meal or 2h postprandial glucose
  - Target pre-prandial < 90-130 mg/dl & 2h post-prandial 140-160 mg/dl

• **Titration**: 1-2 unit every few days

Adding Prandial Insulin

• When prandial insulin is initiated, *insulin secretagogues should be discontinued, or tapered and discontinued*

• Further prandial injections can be added, progressing towards **basal–bolus therapy**

Insulin Lispro with Bedtime NPH vs NPH BID in T2DM: Study Design

- Treatment targets: Lispro + NPH = 2-hr PPG ≤ 8 mmol/L, NPH BID = fasting and predinner BG ≤ 6 mmol/L

Insulin Lispro with Bedtime NPH vs NPH (BID) in Type 2 Diabetes

- Total daily insulin dose (Mean ± SD; U/kg):
  Lispro 0.4 ± 0.1 vs NPH 0.5 ± 0.1, $P<.05^1$

- D-glucitol is a biomarker that is inversely correlated with glucose fluctuations$^2$

- Between-group hypoglycemia incidence was NS$^1$

NS = not significant; SD = standard deviation.

Insulin Intensification: switch to premixed insulin

- Fixed combination of intermediate insulin with RI or rapid analog
- More convenient but less adaptable methods
- Administered twice daily, before morning and evening meals
- Reduced HbA$_{1C}$ when compared to basal insulin alone
- Inflexible but may be appropriated for patients who eat regularly
  - Human insulin 70/30, 50/50
  - Insulin analog 75/25, 70/30, 50/50

Effect of mixtures of NPH and RI

- May experience late morning or nocturnal hypoglycemia because of excessive levels of insulin at these times

Starting dose: Premixed insulin

• Start total daily dose: 0.2-0.4 units/kg/day

• Usually conventional initial approach to dosing premixed insulins in general practice is to prescribe
  – a ratio of 2/3 of the total daily insulin dose in the morning before breakfast
  – and 1/3 in the evening before dinner.
Adjusting dose: Premixed insulin

- < 70 mg/dl: decrease 1-3 units
- 140 - 250 mg/dl: increase 1-3 units
- > 250 mg/dl: increase 3-5 units or 10%

AM BG adjust PM premixed & PM BG adjust AM premixed

Move to basal/bolus insulin if

- Glycemic targets not reached with adjusting premixed insulin
- Patterns of hypoglycemia or hyperglycemia remain despite maximizing insulin therapy
- Total daily insulin dose exceed 1.5 units/kg
Twice Daily Lispro Mix25 vs Insulin Glargine in T2DM

- Randomized multicenter open-label, 32-weeks cross-over study
- Compare glycemic control of insulin lispro mixture (25% lispro and 75% NPL) twice daily with metformin VS once-daily insulin glargine plus metformin in T2DM

![Graph showing Mean HbA1c (%):]

- Baseline (N=93)
- Endpoint (N=93)
- Change from baseline 32-week crossover

**Daily insulin dose (Mean ± SD; U/kg)**
- Insulin glargine HS + Met: 0.36 ± 0.18
- Humalog Mix25 BID + Met: 0.42 ± 0.20

*P<.001 for between-group difference

Met = metformin.

Twice Daily Lispro Mix25 vs Insulin Glargine in T2DM

- Mean±SEM 7 points blood glucose profiles at the endpoint.
- FBG was higher with Lispro mixture, however 2-hr postprandial BG levels after each meal were lower with Lispro mixture, (p<0.001)

Insulin regimens should be designed taking lifestyle and meal schedules into account.
Barriers for insulin therapy
Insulin-induced hypoglycemia

- Hypoglycemia is frequent and rarely fatal complication of insulin therapy
- **Risk factors:** longer duration of DM, renal insufficiency, older age, lower HbA1c, cognitive dysfunction
- In the VADT, ADVANCE, and ACCORD trials, the **intensive therapy results in severe hypoglycemia 2.7-21.2%**, compared with 1.5-9.9% in standard therapy group
- Hypoglycemia may lead to increased mortality due to pro-arrhythmia by sympatoadrenal stimulation

Insulin-induced weight gain

• Insulin therapy associated with **modest weight gain which degree may vary by type of insulin such as**;
  – Less weight gain was seen with detemir than glargine as a basal, despite comparable glycemic control
  – Basal insulin added to OHD has less weight gain than either biphasic insulin aspart or prandial aspart insulin, despite similar HbA1c

• Variable effects on weight gain are seen when insulin combined with TZDs
Barriers for insulin therapy

• **Insulin-induced hypoglycemia**

• **Insulin-induced weight gain**

• Patients perceive their need for insulin as a failure to control their disease

• **Intentional insulin omission** which relates with:
  – older age,
  – lower income, lower education,
  – pain,
  – embarrassment
  – regimen complexity

Case 1

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What is the target of HbA1c?
HbA1c < 7%

How to get the HbA1c target?
Add basal insulin before bedtime
or
Add 3rd OHD: TZDs, DPP-4 inhibitors
Case 2

- A 65 years-old Thai male with T2DM for 15 years
- HT, Dyslipidemia, post PCI at LAD for 1 year
- BW 75 kg., BMI 27.5 kg/m²
- Current therapy: metformin 850 mg bid, glipizide 10 mg bid, basal insulin 34 unit sc hs, simvastatin 20 mg/d, clopidrogeol 75 mg/d, losartan 100 mg/d
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What is the target of HbA1c?

HbA1c < 7%

How to get the HbA1c target?
Case 2

How to get the HbA1c target?

Advice SMBG .. and intensified with
- Add bolus insulin at main meal
  or
- Change to premixed insulin twice daily

Increase dose bedtime basal insulin ?
  or
Add 4th OHDD: TZDs, AGIs ??

>> Less benefits
Summary

• Insulin therapy is frequently required during the course of DM to maintain glycemic control and prevent complications
• Initiating insulin therapy by adding basal insulin.
• Intensified insulin therapy by adding prandial insulin (basal bolus regimens) or switching to premixed insulin
• Targets of glycemic control are HbA$_{1C}$ 7%, FPG < 130 mg/dl and PPG < 180 mg/dl which can be individualized
• The larger the doses and more aggressive titration, the lower the HbA$_{1C}$, but often with a greater adverse effects
Thank you for your attention.