Objectives

• Present newer types of insulin
• Review advancements in insulin delivery devices
• Discuss new insulin pump technologies
Disclosures

- No relevant financial disclosures
- May discuss some technology that is not yet FDA approved

Case 1

- 56 yr old M with T2DM- 14 yrs
- Complications include retinopathy and mild neuropathy
- Has met with diabetes education and RD in past, continues to eat high-carb diet and frequent fast food
- Medical History: T2DM, HTN, hyperlipidemia, OSA, BMI 42
- Family History: +T2DM in mother
- Current regimen:
  - Glargine 75 units BID
  - Aspart 30 units TID with meals plus correction
  - Metformin 1000 mg BID
  - Glipizide XL 10 mg daily
- Labs:
  - A1c = 9.2% (has been 8.6-9.8% recently)
  - eGFR >60, TGs slightly elevated
What is the next best step to manage his diabetes?

A. Start GLP-1 agonist
B. Stop glipizide and add GLP-1 agonist
C. Change glargine and aspart to U-500 insulin with meals
D. Stop glipizide since it is not working, and increase glargine and aspart doses
E. Refer for insulin pump and CGM

Recent Advancements in Insulin

• Within the last few years, we now have...
  – Concentrated insulins
  – Ultra-long basal insulin
  – Inhaled insulin
  – “Biosimilar” insulin
  – Faster-acting rapid insulin
Concentrated insulins

- Historically, insulin has been U-100
  - 100 units per ml
- Concentrated insulin can be used for:
  - Giving high doses of insulin in extreme insulin resistance
  - Reducing number of injections
  - Reducing the volume of the insulin injected
  - Fewer insulin pens needed per month

U-500 insulin

- U-500 = 5 times concentrated (500 units/ml)
- Requires clear education for the patient
- In vial form, U-100 syringe is needed
  - no U-500 syringe
- Prescription should be very clear to avoid confusion--a major limitation of U-500
  - For example, a prescription should read: U-500 concentrated insulin, Inject 100 units (drawn to 20 units or 0.2 ml on a U-100 syringe) TID with meals
U-500 insulin

• Humulin R U-500 KwikPen now approved, available April 2016
  – Dials in actual units, so no conversion needed
  – Each pen holds 1500 units of insulin (3 ml)
  – Dosed in 5 unit increments, up to a maximum single dose of 300 units
  – Different color to avoid confusion – still requires education

Candidates for U-500 insulin

• Type 2 DM with obesity and/or severe insulin resistance
• Patients with insulin requirements > 200 units per day
• Post-operative or post-transplant state
• High-dose glucocorticoid state
• Severe systemic infection
• Insulin resistant syndromes

Using U-500

- In our case, glargine 75 units BID and aspart about 100 units/day = TDD of 250 units
- 60% (150 u) before breakfast, 40% (100 u) before dinner
- Give 30 minutes before meal
- Rx: 150 units (drawn to 30 units on U100 syringe) before breakfast, 100 units (drawn to 20 units on U100 syringe) before dinner
- Titrate from there (Stress diet, lifestyle as well!)
**U-500 Profile**

- U-500 profile is similar to regular insulin, with a longer “tail”
- Usually dosed 2-3 times/day with meals
- Acts as both mealtime and basal insulin

**U-300 Glargine**

- U-300 Glargine (Toujeo)
  - Same insulin as Lantus (initiate 1:1 from lantus)
  - Given once daily, around the same time
  - ONLY comes in pen
    - Pen dial is actual units, so patients do not need to calculate any volume changes
  - 450 units per pen (dispensed in box of 3 pens)
  - Can inject up to 80 units at a time
  - Less nocturnal hypoglycemia than Lantus
  - *For Lantus BID users, this can be an option for the same dose to be given just once daily*
### Humalog U-200

- The only rapid-acting concentrated insulin
- Comes in pen, units shown are actual units (no need to covert volume)
- Bioequivalent to U-100 Humalog
- Pen holds 600 units, can give up to 60 units per injection
- Fewer pen changes per month

### Degludec (Tresiba)

- Daily basal insulin
- Comes in 2 concentrations: U-100 and U-200 pens
- The pen is in actual units, no volume conversion needed by patient
- U-200 pen: can give up to 160 units in 1 injection (600 units per pen, 3 pens per box)
- Duration of action up to 42 hours, *so timing of the daily dose can be flexible*
- Less overnight hypoglycemia
Degludec Pharmacology

Degludec with Aspart

- Ryzodeg 70/30
- FDA approved, however no plan currently to market in the US
Afrezza (inhaled insulin)

- Box comes with 2 inhaler devices
- Cartridges inserted into inhaler; come in 4, 8 and 12 unit cartridges
- Contraindicated in smokers
- Must monitor spirometry (FEV1) at baseline, 6 months, then annually
- Unclear future

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Afrezza

- Nuffer et al, Ann Pharmacother, 2015
“Biosimilar” Insulins

- Basaglar, approved in US in January 2016
- Abasaglar already in several countries
  - 15-20% cheaper than Lantus
- Not considered “biosimilar” for regulatory purposes
- Other companies are creating their own “biosimilar” insulins

Case 2

- 26 year old female
- Type 1 diabetes since age 5
- Extremely difficult to control, with frequent, unpredictable highs and overnight hypoglycemia
- Shift worker, has variable schedule and often misses insulin doses
- Does not want a pump or CGM
- Medical history: T1DM
- Soc Hx: Smoker, some marijuana, no alcohol
- Current insulin:
  - Glargine 16 units QHS
  - Lispro 1:15 carb ratio, correction of 1:40
- Labs: A1c = 7.7%, normal TSH, eGFR
What is the next best step to help manage her T1DM?

A. Start an SGLT-2 inhibitor and reduce carb ratio to 1:18
B. Change glargine to degludec, given anytime of day (but 8 hours apart from last dose)
C. Tell her to only safe option is an insulin pump and CGM
D. Encourage her to change to a job with a regular day schedule

New Technologies in Insulin Delivery

- Patch Pumps
  - V-Go
  - Calibra
  - CeQur PaQ
  - Imperium
  - Others
V-Go: Disposable Insulin Delivery

- Patient uses once a day and then replaces with another the next day
- Patients fill V-Go with U-100 short-acting insulin (Novolog or Humalog)
- Patient applies V-Go, basal insulin flow begins after insertion
  - Gives basal rate of 20, 30, or 40 units total per day
- To deliver a bolus dose of insulin, patient presses Bolus Button (each “click” = 2 units)
  - Bolus up to 36 units per day (or up to 12 units per meal)
V-Go Dosing

<table>
<thead>
<tr>
<th>V-Go option</th>
<th>Preset basal rate</th>
<th>On-demand bolus dosing</th>
<th>Total available insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>VGo® 20</td>
<td>20 Units/24 hr (0.83 U/hr)</td>
<td>Up to 36 Units in 2-Unit increments*</td>
<td>56 Units</td>
</tr>
<tr>
<td>VGo® 30</td>
<td>30 Units/24 hr (1.25 U/hr)</td>
<td>Up to 36 Units in 2-Unit increments*</td>
<td>66 Units</td>
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<tr>
<td>VGo® 40</td>
<td>40 Units/24 hr (1.57 U/hr)</td>
<td>Up to 36 Units in 2-Unit increments*</td>
<td>76 Units</td>
</tr>
</tbody>
</table>

*You can only click the Bolus Delivery Button 18 times in every 24-hour period. Each click of the Bolus Delivery Button delivers 2 Units of insulin (1 click = 2 Units).

V-Go website: www.go-vgo.com

V-Go Workflow in our Clinic

- Order the prescription (V-Go 20, 30 or 40) and vial of rapid acting insulin
- Send to any diabetes educator for training
- Have patient pick up insulin for V-Go prior to the diabetes education visit, and bring to visit
  - If on Lantus, will need to hold Lantus night before or morning of V-Go start
- Do not tell patient to pick up the V-Go until AFTER seeing the diabetes educator, as the educator will give them a 6 day sample to make sure they like it
Calibra Finesse

• Insulin patch pump worn for 3 days
• Gives bolus insulin only
• Holds up to 200 units of rapid-acting insulin
• Boluses in 2 unit increments
• Can bolus through clothing
• FDA approved but not yet available in US

CeQur - PaQ

• 7 basal dose options: 16, 20, 24, 32, 40, 50, or 60 units per day
• On-demand bolus dosing
  – 2 units per dose
• Delivers up to 330 units of rapid-acting insulin over 3 days
• EU only
Imperium Patch Pump

- Not yet FDA approved
- Provides both basal and bolus
- Multi-day wear (not yet specified how long)
- Come pre-filled with insulin
  - Looking to partner with insulin makers, and potentially use concentrated insulins as well
  - Will then be sold by insulin company as their own (like insulin pens)
- Bluetooth connectivity to integrate with smartphone apps

Other Patch Pumps

<table>
<thead>
<tr>
<th>Device</th>
<th>Delivery</th>
<th>E or M</th>
<th>Days of wear</th>
<th>Reservoir size (units)</th>
<th>Basal rate increments (u/hr)</th>
<th>Bolus sizes (units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solo (Roche)</td>
<td>Basal+Bolus</td>
<td>E/M</td>
<td>3</td>
<td>200</td>
<td>0.05</td>
<td>0.05</td>
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<tr>
<td>Cellnovo</td>
<td>Basal+Bolus</td>
<td>E</td>
<td>3</td>
<td>150</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Jewelpump</td>
<td>Basal+Bolus</td>
<td>E/M</td>
<td>7</td>
<td>500-800</td>
<td>0.02</td>
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<tr>
<td>SteadyMed</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Medipacs pump</td>
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<td>NA</td>
<td>3</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Adapted from: Anhalt and Bohannon, Diabetes Technol Ther, 2010
Case 3

- 46 year old female, T2DM for 10 years (had GDM at age 29)
- Has been on MDI insulin for last 5 years (glargine/lispro)
- Has strong aversion to bolusing in public or outside of home
- Often misses lunch and dinner doses
- Fasting BG usually ok, then higher later in the day

- Medical history: T2DM, obesity (BMI 34), microalbuminuria. Rare hypoglycemia, none severe
- Non-smoker
- Labs: A1c 8.2%, (had been in the 6.8-7.6% range until the last year)

How would you approach her difficulty with getting all her multiple daily injections (MDI) insulin does?

A. Change to insulin 75/25 given breakfast and dinner (to avoid lunch dose)
B. Stop prandial lispro and switch to oral repaglinide before meals
C. Tell her to inject insulin pen discreetly through her clothing when eating out
D. Stop her basal/bolus MDI and use a V-Go patch pump
New Insulin Pump Technology

- MiniMed 530G, 640G and 670G
- “Smart Meters”
- Dexcom Share
- Minimed Connect

Towards the artificial pancreas?

A. Kowalski, JDRF
Medtronic MiniMed 530G with Enlite

- Uses Enlite sensor
- Only pump/CGM with threshold suspend function
- Range of 6 feet (1.8 m)
- Calibrate every 12 hrs
- Sensor lasts 6 days
- Works with CareLink software
- 180 or 300 unit reservoir

MiniMed 640G

- Pending approval by FDA
- Similar to the 530G sensor augmented pump but will suspend insulin 30 minutes before it predicts a low
- After 2 hours or when glucose starts to increase, insulin delivery will resume
- Will have new design
MiniMed 670G

• MiniMed 670G with Enlite 3 CGM
• “Hybrid closed loop”
• Not FDA approved, may be on market in US in 2017
• The pump software automatically increases/decreases insulin delivery to target a blood glucose of 120 mg/dl
• “Hybrid” means patients still must carb count to bolus

New Glucose Meters

• In the US, decision driven mainly by insurance
• Rapidly advancing technology
• Examples:
  – Tests ketones on same meter (Novocare)
  – Downloads data to cloud (Solus, Accuchek Connect, Telcare)
  – Subscription-based programs (Livongo, One Drop)
  – All-in-one: lancing/strips/meter/app (Dario)
Bolus Calculators

- FreeStyle Insulinx and Accucheck Aviva Connect
  - Program carb ratios, correction factors
  - Will calculate active insulin as well
  - Can be downloaded at home and remotely shared to healthcare team

Continuous Glucose Monitoring (CGM) Technology – Home Use

- DexCom GS™
  - 7-day sensor
  - Calibrated q 12hrs by manual entry, any meter
  - 20 ft range of transmission
  - Upload to DexCom Share
  - Integrated with Animas, Tandem pumps

- Medtronic Guardian REAL-Time™
  - 3 or 6-day sensor
  - Calibrated q 12hrs with any meter
  - Wireless transmission of data from transmitter to receiver
  - Upload to Medtronic CareLink
  - Integrated with insulin pump (Revel or 530G)

- Abbott Freestyle Libre
  - 14 day sensor
  - Factory calibrated
  - Wireless transmission of data from transmitter to receiver
  - No alarms
  - Relatively inexpensive
  - Can download to AGP
  - Not available in US (FDA approval pending)
Clinical Use: Medtronic iPro2

iPro2 simplifies starting a patient on a Professional CGM study and improves clinical efficiencies

Clinical Use: Dexcom Professional

- Blinded or Unblinded
- Up to 7 days
Case 4

- 36 year old male with T1DM since age 2
- Currently on detemir and aspart
  - Detemir 18 units BID and aspart 1:10 carb ratio with correction
- Has 1-2 episodes per month of hypoglycemia at night
- Has several glucose >300 mg/dl during the week
- Eats a variable diet, does not miss insulin doses
- Eats a snack (30g carb) before bed to avoid lows, reduces levetir 50% if under 120 mg/dl at bed
- Social Hx: Lives alone, non-smoker, occasional EtOH
- Family Hx: +CAD in father
- Labs: A1c 6.9%, runs 6.5-7.3% consistently

What would you recommend to help better control his wide glucose excursions?

A. Change to an insulin pump with threshold suspend and CGM functionality
B. Start a CGM
C. Change insulin detemir to U-300 glargine
D. Recommend a glucose meter that can calculate a bolus dose of insulin based on his carb count and correction
E. His A1C is at goal, no changes needed
Example of the future: Encapsulated Insulin?

- Human embryonic stem cells
- Semi-permeable barrier product (not a medical device per se)
- Unknown dosing or optimal subcutaneous implant location
- Presumed no autoimmunity

Questions?