Use of New Medications to Treat Type 2 Diabetes: Case Studies

Anne Peters, MD
Professor, USC Keck School of Medicine
Director, USC Clinical Diabetes Programs

1. Patient-Centered Approach

"...providing care that is respectful of and responsive to individual patient preferences, needs, and values - ensuring that patient values guide all clinical decisions.”

- Gauge patient’s preferred level of involvement.
- Shared decision making – final decisions re: lifestyle choices ultimately lies with the patient.
- Explore, where possible, therapeutic choices.
- Utilize decision aids.

ADA/EASD Recommendations for HbA1c

Less stringent (7.5% - 8%)< 7%
More stringent (as close to 6% as possible)

- Long diabetes duration
- Short life expectancy
- Complications, comorbidities
- History of severe hypoglycemia
- Short diabetes duration
- Long life expectancy
- No CVD

Case #1

- MC is an 87 yo female with a 10 – 20? year history of type 2 diabetes.
- She is a very poor historian and when she came to see me two years ago she had an HbA1c = 12% with symptoms.
- She was blind in her left eye and had severe retinopathy in her right eye and wanted tight BG control.
- She had had colon and urethral cancer, was getting steroid injections into her knees, could barely walk and had CHF, RI, renal stones, PUD, asthma, HTN, GERD, liver disease…etc

Case #1

- Her meds were levoxyl and losartan.
- She stated she couldn’t take TZD’s, metformin, Januvia.
- She did no SMBG and refused to learn. She would not give an injection. She could not attend clinic often due to transportation difficulties.
- Of note, she weighed 10 pounds at birth and is of French Sephardic Jewish descent. She grew up in Algeria.
- What is her target and what do you do?
Case #1

- More data: her C-peptide level = 9.4 ng/ml with a BG level = 244 mg/dl. Creatinine = 1.6 mg/dl, eGFR = 39
- She had chronic LE edema and a nonhealing left foot abscess.
- I started her on glimepiride 1 mg/day. Discussed lifestyle changes. Uptitrated to 2 mg based on a lack of symptoms of hypoglycemia (phone follow-up).
- At her next visit 3 months later her HbA1c = 8.1%

Case #2

- SR is a 76 yo male with type 2 DM and ESRD on dialysis
- He had been on 70/30 insulin twice daily which caused frequent episodes of hypoglycemia, especially when he didn’t eat.
- Changed to an MDI regimen with Lantus and premeal rapid acting insulin but this was too complicated for him to adhere to.
- Goals: reduce hypoglycemia, lower complexity, improve quality of life
- Added sitagliptin 25 mg, reduced premeal insulin dose by 50%, continued his basal insulin
- Eventually his premeal insulin was stopped, his basal insulin was continued and his SMBG reduced to once daily

Case #3

- 54 year old white man newly diagnosed with poorly controlled type 2 diabetes
- Notable in his history was weight gain since a back injury and “light duty” at work
- Decreased exercise due to pain
- PMH: HTN, disc disease, no known CVD
- Metformin (MET) 500 mg BID
- On no other medications at first visit
Case #3

- General
  - Healthy white male
  - Weight 302 lbs (137 kg)
  - Height 6’1’’
  - BMI 39.8
- Cardiac
  - Pulse 100 and regular
  - Blood pressure (BP) 142/100 mm Hg
- Vision
  - No retinopathy

Case #3

- A1C 9.2%
- Blood glucose 216 mg/dL (12 mmol)
- Creatinine 1.0 mg/dL
- Total cholesterol 302 mg/dL
  - Triglycerides (TG) 846 mg/dL
  - Low-density lipoprotein (LDL) – not calculated due to elevated TG
  - High-density lipoprotein 42 mg/dL
- Thyroid function within normal limits

Case #3

- Increase Metformin to 1000 mg BID; glimepiride added
- BP treated with ACE-I and Beta Blocker
- Lipids treated with statin
- Patient worked on weight loss with no change
- A1C improved to 8.1%

Case #3

- Exenatide was started at 5 μg BID and increased to 10 μg BID after one month
- Glimepiride dose reduced by 50%
- Minimal nausea at the start of exenatide treatment

Case #3

- Patient began losing weight because of a decrease in his appetite
- Follow-up visit at 3 mo after initiation of exenatide
  - Weight fell from 302 to 292.4 lbs (137 to 133) (~ 9.6 lbs (~4.4 kg)
  - A1C decreased to 6.4%
  - Blood pressure 120/80, HR 72
  - Total cholesterol = 108, TG = 130, LDL = 54

Case #3

- Follow-up visit at 3 years after initiation of Exenatide
  - On exenatide 10 mcg BID plus metformin
  - Maintained his weight loss with a weight of 290 - 295
  - A1C ranges from 6.2 – 6.5%
  - Continues to be more physically active
RENAL HANDLING OF GLUCOSE

(180 L/day) (900 mg/L) = 162 g/day

90%

10%

NO GLUCOSE

The Prospect of SGLT2 Inhibition

SGLT2 Inhibitors Lower Renal Threshold for Glucose Excretion (RTG)

Canagliflozin and Dapagliflozin Warnings and Precautions

- Hypoglycemia: risk with secretagogues and/or insulin
- Genital mycotic infections
- Volume depletion/orthostatic changes
- Hypersensitivity
- Increased LDL
- Bladder cancer: don’t use if active; use with caution if prior history of bladder cancer (dapagliflozin only)

Adding an SGLT-2 Inhibitor

His words about the canagliflozin:

“This morning, I awoke early (4:45am) and tested and was feeling rested and raring to go. I was a 71. At 6:30am, without taking medication nor eating anything, I retested and I was a 96, which seemed normal based on my understanding of how blood glucose levels work at that time of the day. I took my Invokana, metformin (2000mg) and Glimipiride (2mg) at 7:00am and then ate breakfast. An hour after a well balanced breakfast I was at 117.”

Adding an SGLT-2 Inhibitor

“Yesterday, I tested a half dozen times with numbers between 96-136, with the exception of a 226 spike occurring one-hour after breakfast (it was a 114 at 7am) but it was also before taking my morning medication. I didn’t remember that the instructions strongly suggested taking the Invokana prior to breakfast. Last night, prior to dinner I was at 136 so I took 20cc of Lantus.

Today, taking the Invokana before breakfast, as prescribed, I’ve had one of those really good mornings where I don’t have a dullness following the first meal of the day.”
Case #4
- MT is a 69 yo male with a 15 year history of type 2 diabetes. He had CVD, HTN, chronic LBP, and psoriasis.
- He was referred to start on an insulin pump.
- He was on long acting insulin 100 units BID and premeal insulin at a dose of 50 – 75 units rapid acting insulin premeals. He also took 120 mcg pramlintide before meals, metformin and sitagliptin.
- He was 5’10” tall and weighed 276 pounds. His A1C = 7.3%.
- He had an extremely limited area where he could inject due to his skin issues and the 8 daily injections he was giving daily was causing marked skin irritation.
- Therefore, a once weekly GLP-1 RA was added to his regimen. The sitagliptin and pramlintide were stopped and his insulin doses were reduced by 20%.
- After 3 months his long acting insulin dose was reduced from 200 units per day to 60 units at bedtime. His mealtime insulin doses were reduced to 10 – 15 units per meal and he often gave no insulin for lunch.
- His weight fell by 24 pounds. He had no GI side effects or severe hypoglycemia.
- An SGLT-2 inhibitor was added and his diuretic dose was reduced and his premeal insulin tapered to zero
- On the combination of metformin, a once weekly GLP-1 RA, an SGLT-2 inhibitor and basal insulin 40 units at bedtime his A1C was 7.0% and his insulin injection burden changed from 8 injections per day to 1 daily and 1 weekly.

Final Case
- Over the next ten years we tried adding every therapy, from TZD’s to DPP4-I’s to insulin to all GLP-1 RA’s...occasionally his A1C would fall into the mid 7% range, but it would never stay there and was generally ~10%
- He “forgot” to do SMBG or self-titrator, he would miss appointments, he would gain and lose weight, stop and start exercise.
- His BMI ranged from 33 – 39 kg/m²
- We kept trying.
- After 11 years his A1C = 6.6% and his BMI = 27 kg/m².
- What happened?
- He had decided to change. His meds were now:
  - Metformin
  - Canagliflozin
  - Liraglutide
- All medications that helped with his lifestyle changes
Choosing the Appropriate Therapy

- SMBG?
- Side effects?
- Contraindication?
- Extra glycemic effects?
- Ease of use?
- Effectiveness?
- Weight?
- Cost?
- Patient Needs/Desires

There is No Such Thing as the Miracle Pill


THANK YOU