Diabetes Update: What’s new? What does it matter?

Paul Callaway, MD
Professor, Department of Family & Community Medicine
University of Kansas School of Medicine-Wichita

Objectives:
- Discuss changing recommendations for care of the patient with T2DM
- Apply information re: new treatment options to the patient population you care for
- Discuss patient-centered care of the patient with T2DM

T2DM: Natural History
- Chronic disorder
- Progressive deterioration of pancreatic beta cells
- Available treatments don’t reliably alter natural history
  - Typical course: sequential addition of anti-diabetic drugs
  - Eventual addition of basal insulin
  - More complex regimens including basal/bolus
- Risks of hypoglycemia if glycemic targets are achieved
- Weight gain!....(side effect of insulin)
Burden of Disease

* ~ 26-29 million Americans affected
* Most common chronic disease
* Annual costs ~ $322 billion*
* Increase incidence coincides with increases in certain risk factors
  - Modifiable risk factors
  - Obesity & overweight

*American Diabetes Association, news release 11-20-2014

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2013 BRFSS: Center for Disease Control
Prevalence of Self-Reported Obesity Among U.S. Adults by State

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Modifiable Risk Factors

Photo courtesy of Dr. Ruth Weber

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Main Pathophysiological Defects in T2DM

Adapted from: Inzucchi SE, Sherwin RS in: Cecil Medicine 2011
T2DM: Landscape of Change

- New treatment options, novel mechanisms of action
- New and changing treatment recommendations
- New challenges re: the importance of glycemic control
- Varying opinions: BP & Lipid goals

Impact of Glycemic Control

- HbA1c – a metric
- Comprehensive CV risk reduction
  - BP, Lipids, Smoking Cessation, physical activity, anti-platelet tx, MNT
- Tight glucose control decreases microvascular disease
- Impact on macrovascular disease less clear (‘legacy effect’)
- Age of patient, duration of disease, patient in management, available resources
- Balancing risk vs. benefit
  - Drug cost, S.E. profile, hypoglycemia risk

Glycemic Goal?

Depiction of the elements of decision making used to determine appropriate efforts to achieve glycemic targets.
Initial Choice of Oral Glucose Lowering Medication for T2DM

- Large number of treatment agents, and ‘ed use of newer classes
- “Urgent need to clarify differences between available therapies”
- Aim: effect of the initial oral agent on subsequent tx intensification
- Secondary data analysis study; 15,516 pts met inclusion criteria


Initial Choice of Oral Glucose Lowering Medication for T2DM

- n = 15,516
- 57% metformin (24.5% required 2nd agent)
- 23% SU (37.1% required 2nd agent)
- 6.1% TZD (39.6% required 2nd agent)
- 13.1% DPP-4 inhibitor (36.2% required 2nd agent)
- SU assoc. with increased CV events (HR 1.16), CHF (HR 1.19)
- SU assoc. with increased hypoglycemia (HR 2.71)
- Other agents offer no compensatory benefit over metformin


SGLT2 Inhibitors

- Kidney reabsorbs filtered glucose thru SGLTs (proximal nephron)
- Blocking SGLT2 lowers BG by increasing urinary glucose excretion
- HbA1c reduction 0.5-1.5%
- Assoc. with decreased BP & weight, increased UTI’s, genital mycotic infection, LDL levels & risk of hypotension
- Canagliflozin (Invokana ®) -- 100-300 mg qd
  – FDA approved March 2013: ~$310
- Dapagliflozin (Farxiga ®) -- 5-10 mg qam
  – FDA approved January 2014: ~ $310
- Empagliflozin (Jardiance) -- 10-25 mg qam
  – FDA approved August 2014: ~$300

DPP-4 Inhibitors

- Slow the breakdown of naturally occurring incretins (GLP-1, GIP)
- Increasing experience in our practices
- A1c reductions ~ 0.6 (0.5 – 1.0)
- ** New concerns for increased hospitalizations for CHF
  – Saxagliptin (Onglyza ®)
- Use this class with caution in any CHF patient, until further studies published

** FDA announcement [2-11-2014]
GLP-1 RAs; Which one to use?

- Dulaglutide slightly better than exenatide and liraglutide
- Exenatide QW: slightly better than regular exenatide but slightly worse than liraglutide
  - *Diabetes Care*, Vol 33, No 6, June 2010
- Albiglutide slightly worse than liraglutide
- Overall, differences are modest

New GLP-1 Receptor Agonists

- Albiglutide (Tranzuem)
  - FDA approved April 15, 2014
- Dulaglutide (Trulicity)
  - FDA approved September 18, 2014
- Both are once weekly injections
- S.E.; nausea, diarrhea, vomiting, abd pain, decreased appetite, injection site reaction
Basal Insulin + GLP-1 RA

- GLP-1 RA usually added as 2nd or 3rd line treatment
  - Optimal role in management of T2DM; not established
- Interest in combining GLP-1 with basal insulin
  - Complementary mechanisms of action
  - Low hypoglycemic potential
- Meta-analysis of RCT’s [glycemic control (A1c & target), hypoglycemia, weight]
  - 2905 studies evaluated; 15 studies selected; 4348 participants
  - No commercial funding
  - Findings supportive of generalisability


Combining Basal Insulin & GLP-1 RA

- Combination therapy 92% more effective than ‘standard tx’
- Patients lost 7-13 lbs
- No increase in hypoglycemia compared to ‘standard tx’
- May fit into treatment algorithm sooner
- ‘Ideal trifecta’
  - Excellent control of BG
  - Little hypoglycemia risk
  - Limited or no weight gain
- Long term durability of tx is unknown
- Effective even for those late in the course of DM

Eng C, Kramer CK; et al, Lancet; Sept 12, 2014

Pioglitazone

- FDA approves Actos™ July 1999
- FDA approves generic pioglitazone; August 17, 2012
- More affordable option than $20/mo
- Bladder cancer risk?
- Continued concern re: CHF

Comprehensive Comparison of Tx’s

- Long term effects of various tx options is not known
- Glycemic Reduction Approaches in Diabetes (GRADE)
- A comparative effectiveness study
- Unmasked clinical trial
- Compares commonly used medications paired with metformin
  - Glycemia lowering effectiveness
  - Patient centered outcomes
- Begins recruitment at 37 U.S. centers in August 2013

Nathan D, Buse J, et al, Diabetes Care; Vol 36, Aug 2013
### Gout: A predictor of T2DM?

- Gout: common inflammatory arthritis
- Associated with obesity, HTN, metabolic syndrome, increased risk for major CV events
- Gout linked to risk of incident T2DM
  - Multivariate relative risk: 1.26
  - Men with high CV risk profile
  - Unknown whether generalizable


### Diabetes & Mental Health

- Depression: serious mental health comorbidity
- Rates of depression in DM is 2X the general population
- ‘Diabetes distress’ now recognized as separate entity from MDD
- All DM care involves ‘self management behavior’
  - Complex tasks that don’t take a vacation
  - Increased distress leading to poor self-care, non-adherence, higher complication rate, greater work disability
  - Diabetes distress: on-line education, problem solving coaching, health care team approach

DiabetesPro Quarterly, Summer 2014, pg 8

### Nutraceuticals & Complementary agents

- Oral chromium, cinnamon, caiapo (sweet potato skin extract), fenugreek, milk thistle and safflower oil
- Some reduction in HbA1c; studies of poor design; SOR C
- ADA states “no clear evidence of benefit from vitamin/mineral...”
- Pomegranate juice (1.5 ml/kg of bw)
  - Increase in beta cell function 3 hr. p consumption
  - Decrease in insulin resistance
  - Pomegranate in FG only occurred in ~ 80%

Shared Decision Making

- Acute Care: trained to be lifeguards
- Chronic Care: teach people to swim
- Choices that have the greatest effect are made by patients
- Patients are in control of their self-management
- Consequences of self-management impact the patient
  - Pts right and responsibility to be the primary decision maker
- Agenda setting, showing empathy, engaging, teach-back

Funnell M, et al, Consultant, May 2014

Putting it all together

T2DM UPDATE:

Diabetes Update: What’s New and Does It Matter?
Paul A. Callaway, MD
Family Medicine Winter Symposium
December 5, 2014

Our next patient
45 y.o. male postal worker with 4 year hx of T2DM. No hx of CVD. Active on job walking route. Denies tob or EtOH use. BMI 24.8

Current meds:
- Metformin 1000 mg BID
- Lisinopril 10 mg daily
- Simvastatin 20 mg daily

Over last 9 mo, A1c has increased from 7.0 to 7.9
Lifestyle issues are reinforced and diet is reviewed. Patient seems compliant. He does report an irregular eating schedule due to work and home responsibilities. BG log reveals avg. fasting @ 140, and 2 hr p largest meal @195.

What 2nd agent would you consider for glycemic control?

55 y.o. female with 12 yr. hx of T2DM. Has previous dx of CVD, with circumflex lesion of ~ 40% being tx’ed medically. Currently is free of CVD complaints/symptoms. Pt. exercises 3-4 times/wk riding a bicycle. Wt 190, BMI 29, B/P 130/75, HR 75
Recent A1c 8.0; HBG logs show fasting 95-110

Current meds:
- Metformin 850 BID,
- Insulin glargine 30 units daily,
- Atorvastatin 10 mg daily,
- Metoprolol XL 100 mg daily,
- ASA 81mg

Pt reports small breakfast and lunch portions with larger calorie intake with evening meal. What adjustment would you make in medical management?
38 y.o. female with recent dx of T2DM 8 months ago. She is in good health otherwise. Had elevated FPG at health screening at work leading to the dx of T2DM during F/U with you. States her weight has been a problem most of her adult life, and there is a strong FH of DM in her mom and maternal aunts. A1c @ dx was 7.8 which improved to 7.3 during the initial tx with metformin. Over the last 3 months, the A1c has deteriorated to 7.6.

At dx; wt 203, BMI of 31. Current wt 197, BMI 29

B/P, renal function & lipids are all WNL

Pt is engaged in tx, wants to do "whatever it takes" to manage this disease.

What are the issues; how will you decide the next agent?

**Update Summary: ‘Lecture in one slide’**

**What’s New?**

- Increasing disease burden
- Increasing pool of ‘at risk’ patient
  - Emphasis on ‘pre-diabetes’
- Expanding categories of pharmacologic agents
- Novel combinations of treatment
- Increased understanding of ‘diabetes distress’
- Importance of patient-centered care

**Does it Matter?**

- Customized approach for each patient
- Patient’s role/choice in tx selection as well as tx adherence
- New options of tx
- ID’ing ‘at risk’ patients
- Greater empathy for mental health
- Patients are overwhelmed with all the tasks
- GRADE trial: Much anticipated!

**T2DM Update:**

- “What we see depends mainly on what we look for.”
  -- John Lubbock, British banker, politician, naturalist and archaeologist

- “Life is not a matter of holding good cards, but of playing a poor hand well.”
  -- Robert Louis Stevenson, Scottish writer

**Diabetes Update: What’s new?**

**What does it matter?**

**Questions & Comments**