Diabetes Mellitus and the Discharge Pharmacist

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Objectives

- Describe the pathophysiology, diagnosis, and complications of diabetes mellitus
- List the goals of diabetes mellitus management
- State recommendations regarding pharmacologic management of diabetes mellitus and associated complications
- Counsel patients on hypoglycemia recognition and management
- Utilize clinical counseling pearls

Diabetes Mellitus

Pathophysiology

- Increased insulin resistance
  - Decreased insulin sensitivity
- Progressive beta-cell dysfunction

Diabetes Mellitus Diagnosis

A1c
- ≥ 6.5%

FPG
- ≥ 126 mg/dL

OGTT 2-hr PG
- ≥ 200 mg/dL

Random PG
- ≥ 200 mg/dL
- Classic hyperglycemia symptoms present

Diabetes Mellitus Complications

Microvascular

- Nephropathy
- Neuropathies
- Retinopathy

Macrovascular

- Cardiovascular disease (CVD)
  - Diabetics are **2-4 times more likely to die** from *cardiovascular* complications that those without diabetes

Goals for Diabetes Mellitus Management

Qualitative

- Improve insulin resistance and glucose control
- Prevent and/or slow long term complications
- Prevent hypoglycemia
- Achieve blood pressure and lipid goals

Goals for Diabetes Mellitus Management

Quantitative

- A1c < 7.0 %
  - Reduces microvascular (and possibly macrovascular) complications
  - Mean PG = 154 mg/dL
  - < 6.5 % per AACE
- Pre-prandial PG 70–130 mg/dL
- Peak post-prandial PG < 180 mg/dL

Recommendations for the Management of Diabetes Mellitus

Medical Nutrition Therapy (MNT) & Therapeutic Lifestyle Changes (TLC)

- Lowers A1c up to 2 % over 3-6 months
  - Healthy eating
  - Weight loss
  - Increased physical activity (150 minutes/week)
- Moderate alcohol intake
  - 2 drinks/day MEN and 1 drink/day WOMEN
- 14 grams of fiber/1,000 kcal consumed

Recommendations for the Management of Diabetes Mellitus

ABCs of Diabetes

- Antiplatelet agents
- Blood pressure control
- Cholesterol control
- (Smoking cessation)

Recommendations for the Management of Diabetes Mellitus

Antiplatelets

- **Aspirin 81 mg daily**
- Primary prevention of CVD
  - Increased CV risk (10-year risk >10 %)
    - Most men > 50 years or women > 60 years
    - At least 1 additional major risk factor (family Hx of CVD, hypertension, smoking, dyslipidemia, or albuminuria)
- Secondary prevention with existing CVD

Recommendations for the Management of Diabetes Mellitus

Blood Pressure Control

- Treat hypertension to a blood pressure goal of **<140/80**
- BP >120/80: initiate therapeutic lifestyle changes (TLC)
- BP >140/80: initiate TLC + pharmacological therapy

Pharmacological Therapy

- **ACE inhibitors (ACEIs)/Angiotensin receptor blockers (ARBs)** preferred
- 2+ agents usually required (*administer ≥ 1 at bedtime)
- Monitor SCr and potassium levels

Recommendations for the Management of Diabetes Mellitus

Cholesterol Management

- TLC
- TLC + **Statin** (regardless of lipid levels)
  - Overt CVD
  - Without CVD who are > 40 and have $\geq$ 1 other CVD risk factors (see antiplatelets)
- Combination pharmacological therapy has no benefit over statins alone

Recommendations for the Management of Diabetes Mellitus

Statin Therapy per 2013 ACC/AHA

- 40 to 75 years of age
- LDL-C 70-189 mg/dL
- Moderate-intensity statin therapy
  - If ≥ 7.5% estimated 10-year ASCVD risk, use *high-intensity* statin therapy, unless contraindicated
- Maximum tolerated statin intensity is key

Recommendations for the Management of Diabetes Mellitus

Smoking Cessation

- Counsel to quit smoking/using tobacco products to decrease CVD risk
- #1 modifiable risk factor to prolong life

Recommendations for the Management of Diabetes Mellitus

Nephropathy

- Persistent albuminuria = urinary albumin excretion > 30 mg/24 hours
  - **ACEI or ARB** recommended

Neuropathy

- Lyrica (pregabalin) & Cymbalta (duloxetine) FDA approved
- Venlafaxine, amitriptyline, gabapentin, valproate, opioids may also be effective

Standards of Medical Care in DM

- Published annually in January
- Medication Reconciliation recommendations
  - "The patient's medications must be cross-checked to ensure that no chronic medications were stopped and to ensure the safety of new prescriptions.
  - Prescriptions for new or changed medication should be filled and reviewed with the patient and family at or before discharge."

Healthy eating, weight control, increased physical activity

Initial drug monotherapy

Metformin

	Metformin
Efficacy (↓ HbA_{1c})	high
Hypoglycemia	low risk
Weight	neutral/loss
Side effects	GI / lactic acidosis
Costs	low

If needed to reach individualized HbA_{1c} target after ~3 months, proceed to two-drug combination (order not meant to denote any specific preference):

Two-drug combinations

	Metformin + Sulfonylurea	Metformin + Thiazolidine-dione	Metformin + DPP-4 Inhibitor	Metformin + GLP-1 receptor agonist	Metformin + Insulin (usually basal)
Efficacy (↓ HbA_{1c})	high	high	intermediate	high	highest
Hypoglycemia	moderate risk	low risk	low risk	low risk	high risk
Weight	gain	gain	neutral	loss	gain
Major side effect(s)	hypoglycemia	edema, HF, Fx's	rare	GI	hypoglycemia
Costs	low	high	high	high	variable

If needed to reach individualized HbA_{1c} target after ~3 months, proceed to three-drug combination (order not meant to denote any specific preference):

Three-drug combinations

- Metformin + Sulfonylurea + TZD *or* DPP-4-i *or* GLP-1-RA *or* Insulin
- Metformin + Thiazolidine-dione + SU *or* DPP-4-i *or* GLP-1-RA *or* Insulin
- Metformin + DPP-4 Inhibitor + SU *or* TZD *or* Insulin
- Metformin + GLP-1 receptor agonist + SU *or* TZD *or* Insulin
- Metformin + Insulin (usually basal) + TZD *or* DPP-4-i *or* GLP-1-RA

If combination therapy that includes basal insulin has failed to achieve HbA_{1c} target after 3-6 months, proceed to a more complex insulin strategy, usually in combination with one or two noninsulin agents:

More complex insulin strategies

Insulin (multiple daily doses)

Standards of Medical Care in Diabetes 2014

Pearls

- Biguanides (Metformin)
  - Initial drug of choice for T2DM
  - Avoid in unstable or hospitalized patients with HF (increased risk of lactic acidosis)
  - Caution/avoid with SCr $\geq$ 1.5 MEN or $\geq$ 1.4 WOMEN
  - XR formulation decreases GI side effect from ½ to 1/10

Pearls

- Sulfonylureas
  - Create a “basal” insulin effect
  - Increased risk of hypoglycemia due to MOA
    - Avoid in hepatic impairment (insulin preferred in severe hepatic impairment)
  - Weight gain
  - Avoid combination with meglitinides
- Meglitinides (glinides)
  - Create a “bolus” insulin effect (must dose WITH meals)
  - Increased risk of hypoglycemia due to MOA
    - Avoid in hepatic impairment (insulin preferred in severe hepatic impairment)
  - Weight gain
  - Avoid combination with sulfonylureas

Pearls

- Thiazolidinediones (TZDs)
  - Avoid in heart failure
  - Edema, weight gain
  - Bone fractures
    - Caution in elderly
- Alpha-glucosidase inhibitors
  - GI side effects
- DPP-4 Inhibitors
  - ? Increased risk of pancreatitis

Pearls

- GLP-1 receptor antagonists
  - Weight loss
  - GI side effects
  - ? Increased risk of pancreatitis
- Amylin mimetics
  - Okay for use in T1DM
- SGLT-2 Inhibitors
  - Increased urinary glucose excretion
  - Yeast infections
  - **Hyperkalemia**

Pearls

- Insulins
  - Patient-specific choice
  - Basal + bolus regimen preferred
  - Sliding scale not recommended
  - Hypoglycemia

Hypoglycemia

Signs & Symptoms

- Sweating
- Shaking
- Dizziness
- Tachycardia
- Blurred vision
- Irritability

Treatment

- Check BG at 1st recognition of symptoms
- If BG < 70 mg/dL, treat with 15 grams of glucose
- Recheck BG in 15 minutes
- If < 70 mg/dL, repeat. If > 70 mg/dL, eat a well balanced snack.

QUICK Glucose Sources

- ½ can full sugar soda
- 4 oz. juice
- 3-5 hard candies, chewed
- Glucose tabs
- NOT a Snickers bar!

Pearls

- Fenofibrate > gemfibrozil, if a fibrate is necessary, to reduce risk of rhabdomyolysis
- Evaluate need for a Glucagon emergency kit prescription
  - High risk for hypoglycemia
- In general, vitamin or mineral supplements are not recommended unless a deficiency exists
  - Omega 3 fatty acids not recommended for CVD
- Remind/educate patients about complications of diabetes mellitus and the importance of taking the lead role in their own care

References

- American Diabetes Association. Standards of Medical Care in Diabetes 2014. Diabetes Care. Jan 2014. Volume 37, Supplement 1: S14-80.
- Pastors JG, Warshaw H, Daly A. The Evidence for the Effectiveness of Medical Nutrition Therapy in Diabetes Management. Diabetes Care 2002. 25(3):608-13.
- Inzucchi SE, Bergenstal RM, Buse JB, et al.;American Diabetes Association & European Association for the Study of Diabetes. Management of hyperglycemia in type 2 diabetes:a patient-centered approach. Position statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2012;35:1364–1379.