Successful Type 2 Diabetes Management in Primary Care

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Objectives

- Pathophysiology of Type 2 diabetes
- Current guidelines in Type 2 diabetes management
- Explore different classifications of pharmacological management
- Explore non-pharmacological interventions

Pathophysiology

- Diabetes - Group of metabolic disorders of fat, carbohydrates, and protein metabolism that results from defects in insulin secretion, insulin action (sensitivity), or both.

Current Guidelines

- American Diabetes Association (ADA)
- American Association of Clinical Endocrinologists (AACE)

Ominous Octet

Hyperglycemia in Type 2 Diabetes

American Diabetes Association: General recommendations.
Pharmacological Management of Type 2 Diabetes

- Biguanides
- Sulfonylureas
- Thiazolidinediones (TZD)
- Dipeptidyl peptidase-4 inhibitors (DPP-4)
- Glucagon-like peptide-1 agonist (GLP-1)
- Sodium glucose co-transporter-2 (SGLT2)
- Insulin

Biguanides: Metformin

- Decreases hepatic glucose production and intestinal glucose absorption; increases insulin sensitivity
- Metformin (Glucophage), Metformin XR (Glucophage XR)
- Usually first choice in Type II DM
- Used in pre-diabetes (HbA1c 5.7-6.4)
- Usually does not cause hypoglycemia
- GI upset – start low and titrate up
- XR forms have less GI effects
- Can cause decrease in Vit. B12
- Avoid in renal impairment
- Hold before iodinated contrast study, may resume 48 hours after if renal function normal

(DiPiro, 2017)
### Sulfonylureas

- Binds to the beta-cells of the pancreas and stimulates insulin secretion
- Metabolized CYP450: 2C9
- Glimepiride (Amaryl)
- Glipizide (Glucotrol, Glucotrol XL)
- Glyburide (DiaBeta)

#### Main characteristics
- Mainly metabolized CYP450: 2C9
- Associated with photosensitivity
- Hypoglycemia is common side effect
- Weight gain
- Renal insufficiency and liver disease patients have higher risk of hypoglycemia

#### Examples
- Glimepiride (Amaryl)
- Glipizide (Glucotrol, Glucotrol XL)
- Glyburide (DiaBeta)

#### Side effects
- Weight gain
- Renal insufficiency and liver disease patients have higher risk of hypoglycemia
- Associated with photosensitivity
- Hypoglycemia is common side effect

#### References
- DiPiro, 2017

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### TZD

- Enhances insulin sensitivity in muscle and fat by increasing glucose transporter expression and suppressing hepatic glucose production
- Pioglitazone (Actos)
- Rosiglitazone (Avandia)

#### Main characteristics
- Weight gain seen
- First generation thiazolidinediones associated with hepatotoxicity. Newer TZDs used with caution in liver insufficiency
- Black box warning: thiazolidinediones cause or exacerbate CHF – especially if given with insulin
- Associated with photosensitivity
- Hypoglycemia is common side effect
- Weight gain
- Renal insufficiency and liver disease patients have higher risk of hypoglycemia

#### References
- DiPiro, 2017

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### DPP-4

- Inhibits dipeptidyl peptidase-IV, enzyme that breaks down GLP-1, thus enhancing GLP-1 effects of glucose-dependent insulin secretion and suppression of glucagon secretion.
- Sitagliptin (Januvia)
- Alogliptin (Nesina)
- Saxagliptin (Onglyza)
- Linagliptin (Tradjenta)

#### Main characteristics
- Weight neutral
- No GI effects
- Linagliptin (Tradjenta) interacts with ACE-1 causing increased risk of angioedema

#### Examples
- Sitagliptin (Januvia)
- Alogliptin (Nesina)
- Saxagliptin (Onglyza)
- Linagliptin (Tradjenta)

#### Side effects
- Weight neutral
- No GI effects
- Linagliptin (Tradjenta) interacts with ACE-1 causing increased risk of angioedema

#### References
- DiPiro, 2017

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### GLP-1

- Binds to and activates GLP1 receptors resulting in glucose-dependent insulin secretion, slowed gastric emptying*, suppression of glucagon secretion and promotion of satiety.
- Daily administration
- Exenatide (Byetta)
- Liraglutide (Victoza)
- Lixisenatide (Adlyxin)
- Dulaglutide (Trulicity)
- Semaglutide (Ozempic)

#### Main characteristics
- Used in DMI
- Promotes weight loss
- Do not use with renal impairment
- Higher risk for genitourinary yeast and bacterial infections
- Once weekly administration
- Exenatide Er (Bydureon)
- Dulaglutide (Trulicity)
- Semaglutide (Ozempic)

#### Examples
- Exenatide (Byetta)
- Liraglutide (Victoza)
- Lixisenatide (Adlyxin)
- Dulaglutide (Trulicity)
- Semaglutide (Ozempic)

#### Side effects
- Weight neutral
- No GI effects
- Linagliptin (Tradjenta) interacts with ACE-1 causing increased risk of angioedema

#### References
- DiPiro, 2017

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### SGLT-2

- Inhibits Na-Glucose cotransporter 2 in the proximal tubule, reducing glucose reabsorption and increasing urinary glucose excretion.
- Dapagliflozin (Farxiga)
- Canagliflozin (Invokana)
- Empagliflozin (Jardiance)
- Ertugliflozin (Steglatro)

#### Main characteristics
- Used in DMI
- Promotes weight loss
- Do not use with renal impairment
- Higher risk for genitourinary yeast and bacterial infections

#### Examples
- Dapagliflozin (Farxiga)
- Canagliflozin (Invokana)
- Empagliflozin (Jardiance)
- Ertugliflozin (Steglatro)

#### Side effects
- Used in DMI
- Promotes weight loss
- Do not use with renal impairment
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#### References
- DiPiro, 2017

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### Insulin

#### Basal insulins (long acting)
- Insulin glargine (Lantus, Basaglar, Toujeo*)
- Insulin detemir (Levemir)
- Insulin degludec (Tresiba)

#### Bolus insulins (short or rapid acting)
- Insulin lispro (Humalog)
- Insulin aspart (Novolog)

#### References
- DiPiro, 2017

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**Note:**
- * indicates higher MI rates seen with rosiglitazone (Avandia) but not higher risk of mortality.
- Black box warning: thiazolidinediones cause or exacerbate CHF – especially if given with insulin.
- Higher risk for genitourinary yeast and bacterial infections.
At Risk

- Identify those at risk for developing diabetes
- Overweight BMI >=25 kg/m² with one or more of the following risk factors
  - First-degree relative
  - History of CVD
  - HTN >140/90
  - HDL level <35 mg/dL and/or triglyceride level >250 mg/dL
  - Physical inactivity
  - Women with PCOS
  - Women with history of gestational diabetes
  - Acanthosis nigricans

(ADA, 2019)

Non Pharmacological

- Lifestyle modifications
  - Diet
  - Exercise
  - Smoking cessation
- Additional support
  - Dietician
  - Organizations
  - Support groups
  - Group visits
- Prevention
  - Blood pressure control
  - Lipid management
  - Chronic kidney disease
  - Retinopathy

Key Points

- HgbA1c is not just average blood glucose, can tell when the glucose is rising most and where the “problem” area is
  - Look at fasting and postprandial glucose levels
  - Closer HgbA1c is to goal – more of the HgbA1c is postprandial glucose
  - HgbA1c < 7.3% - 70% of the number accounts for postprandial glucose

(Monnier & Coleta, 2006)

Key Points

- Post prandial glucose levels most appropriate in determining cardiovascular risks
  (Cabalot et. al, 2006)
- ASCVD – coronary heart disease, cerebrovascular disease or peripheral arterial disease – leading cause of morbidity and mortality for individuals with diabetes

(ADA, 2019)
Key Points

- Most success comes from an agreed, thoughtful, individualized plan between provider and patient.
- May be some compromise
- Must explore patient’s willingness and ableness with:
  - Disease Process
  - Prevention
  - Medications
  - Food
  - Activity

References