

# SULFONYLUREAS

FLAME LECTURE: 4

FAIN 10.25.18

# LEARNING OBJECTIVES

- ▶ To describe the mechanism of action of SULFONYLUREAS
- ▶ To counsel the patient regarding the benefits, risks, and uses for sulfonylureas
- ▶ Prerequisites:
  - ▶ NONE
- ▶ See also – for closely related topics
  - ▶ Flame Lecture: on Type 2 DM
  - ▶ Flame Lectures regarding other medications for treatment of DM

# OVERVIEW

- ▶ 1 of 2 classes of drugs that directly stimulate release of insulin from pancreatic beta cells
  - ▶ Thus, they are useful only in pts with some beta cell function (aka not Type 1 DM)
- ▶ Sulfonylureas include:
  - ▶ 1<sup>st</sup> Generation: Acetahexamide, Chlorpropamide, Tolbutamide
    - ▶ 1<sup>st</sup> gen are no longer used due to increased CV risk
  - ▶ 2<sup>nd</sup> Generation: Glipizide, Glyburide, Glimepiride

# MECHANISM OF ACTION

- ▶ Sulfonylureas inhibit the K-ATP channel in the pancreatic basal cells → alters cellular resting potential → calcium influx into the cell → stimulation of insulin secretion
- ▶ Increases sensitivity of beta cells to both glucose and amino acids
- ▶ May also increase tissue sensitivity to insulin

# INDICATIONS/BENEFITS

- ▶ 2<sup>nd</sup> line treatment for non-obese T2DM patients that cannot tolerate metformin or in whom metformin is contraindicated
- ▶ Lower glucose concentration by approx 20% and A1C by 1-2%

# CONTRAINDICATIONS/PRECAUTIONS

- ▶ Sulfonylureas should not be used in Type 1 DM
- ▶ Caution in patients >75 y/o, patients with renal impairment, and patients with liver disease
- ▶ Increased risk for allergic reactions to sulfonylureas in patients with a history of "sulfa allergies"
- ▶ Can be used in pregnancy, but should be discontinued >2 weeks before expected delivery date
  - ▶ Though long-term safety data still pending

# ADVERSE EFFECTS

- ▶ Hypoglycemia is the most worrisome side effect with a higher incidence in chlorpropamide and glyburide and a lower incidence in glipizide and glimepiride
- ▶ All sulfonylureas also are associated with weight gain
- ▶ Other side effects include GI upset and skin reactions

# MONITORING

- ▶ Sulfonylurea metabolites are renally excreted
- ▶ Kidney function should be assessed prior to starting sulfonylurea
- ▶ Risk of hypoglycemia is greater in patients with CKD

# KEY INFO

- ▶ Sulfonylureas should be used for 3-6 months to achieve adequate glycemic control
- ▶ If glycemic control cannot be achieved with sulfonylureas, other medications may be added to regimen
- ▶ If combo of sulfonylureas and other medications is not sufficient, insulin therapy should be initiated

# REFERENCES

1. Am Fam Physician. 2001 May 1;63(9):1747-56.
2. Sola D, Rossi L, Schianca GP, et al. Sulfonylureas and their use in clinical practice. *Arch Med Sci*. 2015;11(4):840-8.
3. "Sulfonylureas and Meglitinides in the Treatment of Diabetes Mellitus - UpToDate." Accessed October 27, 2018.