Chlorpropamide and Tolbutamide (Orinase) (1st Generation Sulfonylureas)

Chlorpropamide and tolbutamide are first generation sulfonylureas that promote insulin release. This action increases the amount of circulating insulin to maintain normal blood glucose levels in the body. These drugs are indicated for patients with type 2 diabetes who have the ability to produce insulin (refer to Picmonic "Insulin"). However, first generation sulfonylureas are rarely used due to their lower potency and significant drug-drug interactions. Side effects of these medications include hypoglycemia and cardiovascular toxicity. These drugs should not be used while pregnant, breastfeeding, consuming alcohol, or taking beta blockers. Use of these sulfonylureas alongside other oral hypoglycemic drugs is usually discouraged due to its increased risk of hypoglycemia, however, sometimes it is clinically appropriate to use these medications together. Monitor patients closely for hypoglycemic effects if these agents are combined.



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Mechanisms

1st Generation Sulfonylureas

(1) Wand Sulfur-funnel-U-rainbow

First generation sulfonylureas are the first oral hypoglycemics developed. However, they are rarely used and have been replaced by second generation sulfonylureas based on fewer drug-drug interactions and increased potency. Sulfonylureas can also be used in combination with other oral hypoglycemic drugs in patients who fail initial therapy with lifestyle intervention and metformin. Use caution to avoid severe hypoglycemia. Important to note that sulfonylureas generally are not used in combination with insulin.

Stimulate Release of Insulin

Releasing Insect-syringes

First generation sulfonylureas stimulate the pancreatic islet cells to release insulin. These medications bind to ATP-sensitive potassium channels and cause depolarization of the cell membrane. Calcium enters the cells while insulin is released into the bloodstream.

Indications

Type 2 Diabetes

Dyed-bead-pancreas in (2) Tutu

First generation sulfonylureas stimulate insulin release and are indicated for patients with type 2 diabetes with the ability to produce insulin. These drugs are ineffective in patients with type 1 diabetes, since they are unable to produce insulin. Medications such as chlorpropramide and tolbutamide may be used alone or in conjunction with other drug therapy. However, these drugs should be used along with proper diet and exercise for glucose management in patients with type 2 diabetes.

Side Effects

Hypoglycemia

Hippo-glue-bottle

First generation sulfonylureas increase insulin release and may cause hypoglycemia. Since these drugs are metabolized in the liver and excreted by the kidneys, dysfunction in either organs may cause drug toxicity and fatal hypoglycemia. Refer to Picmonic "Hypoglycemia Assessment" for more information.

Possible Cardiovascular Toxicity

Heart with Vessels and Toxic-green-glow

Several research studies have linked tolbutamide, the first sulfonylurea medication available, with increased risk of cardiovascular toxicity, i.e., sudden cardiac death. Inform patients about the increased risk of adverse cardiovascular reactions.

Weight Gain

Up-arrow Weight-scale

Weight gain is one of the side effects of sulfonylureas, making them less preferable options for managing diabetes in obese patients.

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Considerations

Exacerbated Hypoglycemia with Beta-blockers

Hippo-glue-bottle Made Worse by Beta-fish with Blocks

Combining sulfonylureas with beta-blockers should be avoided due to an increased risk of severe hypoglycemia. Beta-blockers can also conceal the symptoms of hypoglycemia, particularly tachycardia.

Avoid During Pregnancy and Breast Feeding

Avoid-sign Pregnant-woman Breast-feeding

First generation sulfonylureas are teratogenics and should be avoided during pregnancy. Newborn exposure to sulfonylureas at the time of delivery can result in severe hypoglycemia lasting up to 10 days. Nursing mothers should not take sulfonylureas, since these drugs are excreted into the breast milk and cause hypoglycemia in the infant. Insulin should be substituted for glucose control.

Avoid Alcohol

Avoid-sign Alcoholic-martini

Warn the patient to avoid alcohol while taking first generation sulfonylureas. The combination of these two substances may cause a disulfiram-like reaction manifesting with flushing, palpitations, and nausea. Alcohol potentiates the hypoglycemic effects of the sulfonylurea medications. The reaction may be more of a nuisance than of any significant clinical importance. Be sure to warn patients of the potential for developing this reaction as it may cause embarrassment or anxiety.

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