

Oral Medications and Type II Diabetes

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Glycemic control for Type II diabetes has always been thought of as a three-pronged attack: diet, exercise, and medications. The medication was typically a single pill that stimulated the pancreas to produce more insulin. Advances in pharmacotherapy have increased the number of options available to the healthcare provider and widened the array of medicines available for glycemic control.

There are currently four groups of oral diabetes medications. Although they all help in lowering blood glucose levels because they work in different ways, they are often used in combination with insulin to achieve optimal control of blood sugar. Secretagogues stimulate the production of insulin by the pancreas (not for use by Type I diabetics); sensitizers increase cellular sensitivity to insulin; alpha-glucosidase inhibitors delay absorption of glucose from the gastrointestinal tract; and combination medications combine metformin and medication from one of the other groups.

Insulin Secretagogues

Sulfonylureas

In use since 1942, sulfonylurea medications stimulate the beta cells of the pancreas to make more insulin. Sulfonylureas are indicated as an adjunct therapy to lower the blood glucose levels in patients with Type II diabetes whose hyperglycemia cannot be controlled by diet and exercise alone. Sulfonylureas tend to be ineffective in patients with little residual capacity to produce insulin, severely obese patients, or patients with a fasting glucose >270. All sulfonylureas can cause severe and long-lasting hypoglycemia. They can also cause some weight gain. Sulfonylureas are renally excreted.

There are two categories of sulfonylureas: first generation and second generation. First-generation sulfonylureas include Acetohexamide; chlorpropamide (Diabinese®); tolazamide (Tolinase®); and tolbutamide (Orinase®). Diabinese is the only first-generation sulfonylurea still in use today, but it should be used with caution especially in the elderly population due to its extended half-life.

Second-generation sulfonylureas include glipizide (Glucotrol® and Glucotrol® XL), glyburide (Micronase®, Glynase®, and Diabeta®) and glimepiride (Amaryl®).

Sulfonylureas can interact with several other types of drugs. Interactions with nonsteroid antiinflammatory drugs (NSAIDs), anticoagulants, and tricyclic antidepressants can cause hypoglycemia. Hyperglycemia may occur because of interactions with thiazide diuretics, corticosteroids, thyroid agents, and calcium channel blockers. Blood glucose levels should always be monitored during initiation, cessation, or changes in therapy with any of these agents. Also, there is about a 40-minute delay in the absorption of glipizide when it is taken with food. For this reason, glipizide is much more effective when taken 30 minutes before a meal. The other sulfonylureas may be taken with food.

Patients who have renal or hepatic insufficiency, older adults, and people who are debilitated or malnourished may be at an increased risk of hypoglycemia with these medications. Therefore, blood glucose levels should be monitored appropriately.

Metiglinides

Metiglinides (repaglinide [Prandin®] and nateglinide [Starlix®]) also stimulate pancreatic production of insulin. They were deliberately developed with a shorter half-life than sulfonylureas in order to increase insulin response to meals. Because there is a rise in blood glucose levels when eating a meal, metiglinides are taken 15–30 minutes prior to the start of a meal to help regulate the sudden increase in glucose levels. If a meal is skipped or delayed, this medication must be skipped or delayed. This class of medications is less likely to cause hypoglycemia than the sulfonylureas.

As with most medications, drug interactions also occur with metiglinides. Due to inhibition of metiglinide's metabolism by ketoconazole and macrolide antibiotics, hypoglycemia may occur when they are given concurrently. Barbiturates and carbamazepine may cause hyperglycemia due to rapid induction of metabolism of the metiglinides.

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Insulin Sensitizers

Biguanides

Biguanides (Metformin [Glucophage®, Glucophage® XL, Riomet®]) work by shutting off the liver's excess glucose production and making muscles more sensitive to insulin. Metformin does not affect insulin production and requires the presence of insulin to work. It is also renally excreted. Metformin can be used alone or in combination with sulfonylureas, thiazolidinediones, and insulin. Metformin may lower cholesterol levels. It does not cause weight gain and therefore may be an ideal agent for an obese patient.

Metformin should be taken with food. Common side effects include nausea, diarrhea, and loss of appetite, all of which usually subside after several weeks of therapy. A rare side effect is lactic acidosis, which can be fatal. Renal and hepatic function should be checked at least annually.

Metformin must be discontinued before surgery or before any procedure which uses a contrast dye. The contrast dye along with metformin has led to acute renal failure in some patients; therefore metformin should be held 48 hours before administering the dye and 48 hours after the procedure to ensure that baseline renal function has resumed. Due to the induction of metformin's metabolism, cimetidine may increase the amount of metformin in the blood by up to 80%.

Metformin is not recommended for use in people with heart failure, renal dysfunction (creatinine >1.4 in males, >1.3 in females) or hepatic dysfunction, or in people who abuse alcohol. Metformin should be used with caution in those patients over age 80. The patient's creatinine clearance must be calculated and the dose adjusted accordingly.

Thiazolidinediones (TZDs)

The TZDs include rosiglitazone (Avandia®) and pioglitazone (Actos®), which help decrease insulin resistance by increasing sensitivity of insulin in the muscle and adipose tissue. They may be used alone or in combination with other oral hypoglycemic drugs and insulin. They

Continued on page 11

also facilitate an increase in high-density lipoproteins and mildly reduce diastolic blood pressure.

Hepatotoxicity is a risk with this class of medications, so liver function tests are recommended every 2 months during the first year, and periodically after that. Common side effects include peripheral edema, anemia, and weight gain. These drugs may be taken with or without a meal. If a meal is missed, the patient should be advised to take the medication with the next meal.

Alpha Glucosidase Inhibitors (AGIs)

Acarbose (Precose®) and miglitol (Glyset®) interfere with complex carbohydrate digestion in the small intestine. They delay carbohydrate absorption and decrease postprandial hyperglycemia. These medications are taken at every meal. Side effects include flatulence, abdominal pain, and diarrhea, which may lead to discontinuation of therapy.

These drugs are contraindicated in diabetic ketoacidosis, inflammatory bowel disease, and partial intestinal obstruction. These medications may decrease digoxin absorption; therefore digoxin levels should be monitored closely when administering these drugs. If hypoglycemia occurs, it must be treated with pure glucose, but not table sugar, because AGIs block absorption of complex carbohydrates.

Combinations

Avandamet® (rosiglitazone and metformin), Glucovance® (glyburide and metformin), and Metaglip® (glipizide and metformin) are three of the combination drugs in this class. Side effects of this class are the same as for the medications that make up each combination drug.

Nursing implications

Rehabilitation nurses can have a big impact on the success of their diabetic patients' medication regimen. Specific interventions include assessment, patient education, and social support.

Assessment

Assess which diabetic medications your patients are on. Review their entire medication list to be sure that there are not duplicates ordered by generic and brand names. Assess whether the dosage and timing of the medications are appropriate. Also assess your diabetic patients' current diet and activity, and whether there is a need for further education on these topics.

Patient education

Ensure that your patients are aware of the importance of adherence to prescribed diabetic medications. Teach them about the differences between the medications and how they work, the importance of timing of medications, and the side effects. Also teach about the interactions between diet, medications, and exercise.

Social support

Many medications are expensive, and the new Medicare D program may change how much many of your patients pay for their medications. If they express uncertainty about costs, consult a social worker or case manager to provide access to community resources for medication payments.

By addressing just these three areas, many serious problems with patient adherence to diabetic medication regimens could be avoided, and numerous complications prevented. 

Suggested Reading

- Drug Facts and Comparisons. (2005). *Facts and Comparisons*: St. Louis.
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- Willett, L.L., & Albright, E.S. (2004). Achieving glycemic control in Type 2 diabetes: A practical guide for clinicians on oral hypoglycemics. *Southern Medical Journal*, 97(11), 1088-1092.