

ALPHA-GLUCOSIDASE INHIBITORS AS AGENTS IN THE TREATMENT OF DIABETES

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Although the gastrointestinal tract does not play a significant role in the pathogenesis of either type 1 or type 2 diabetes, modification of its physiological activities can be used to improve glycemic and lipid control in these disorders. alpha -Glucosidase inhibitors are drugs that delay digestion of complex carbohydrates by acting as competitive inhibitors of the intestinal alpha -glucosidase enzymes that hydrolyze oligosaccharides into monosaccharides.

This decreases rises in postprandial plasma glucose, As a consequence of their pharmacological action, alpha - glucosidase inhibitors also cause a concomitant decrease in postprandial plasma insulin and gastric inhibitory polypeptide and a rise in late postprandial plasma glucagon-like peptide 1 levels. In individuals with normal or impaired glucose tolerance with hyperinsulinemia, alpha -glucosidase inhibitors decrease hyperinsulinemia and improve insulin sensitivity. In patients with type 2 diabetes, alpha -glucosidase inhibitors when added to a high carbohydrate diet treatment lower fasting plasma glucose by a mean of 24 mg/dl, postprandial plasma glucose by a mean of 54 mg/dl, and HbA(1c) by a mean of 0.90%. When added to the treatment of type 2 diabetic patients on insulin, metformin, or sulfonylureas, there is an additional decrease in HbA(1c), of 0.54, 0.73, and 0.85%, respectively. In type 1 diabetic patients, alpha -glucosidase inhibitors can be used to reduce postprandial glycemic excursions and decrease postprandial hypoglycemia.

Additional benefits of alpha -glucosidase inhibitors in the treatment of patients with type 2 diabetes are a lack of hypoglycemia with monotherapy, an excellent safety profile, and a modest decrease in postprandial plasma triglyceride levels. The major adverse events associated with alpha -glucosidase inhibitor treatment are flatulence, abdominal discomfort, and bloating. These effects are the consequences of undigested carbohydrate reaching the colon, where it is fermented by the bacteria. Appropriate dosing - which includes starting with a very low dose of the drug, titrating the dose upwards very slowly and not increasing the dose beyond that which maximally benefits glycemic control - will significantly decrease these gastrointestinal side effects. The alpha -glucosidase inhibitors available in the U.S. are acarbose and miglitol.