Antiglycemic Agents

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KEYWORDS

• Diabetes mellitus • GLP-1 receptor agonists • DPP-4 inhibitors • SGLT2 inhibitors • Insulin

HOSPITAL MEDICINE CLINICS CHECKLIST

1. Incretins are hormones produced by cells in the gastrointestinal tract that increase secretion of insulin from pancreatic β cells after ingestion of a meal.
2. Glucagon-like peptide-1 (GLP-1) receptor agonists increase secretion of insulin from pancreatic β cells, slow gastric emptying, and increase satiety to control hyperglycemia while promoting weight loss.
3. Dipeptidyl peptidase inhibitor-4 (DPP-4) inhibitors block the activity of a peptidase enzyme that degrades endogenous incretin hormones.
4. Although cases of acute pancreatitis and pancreatic cancer have been reported in patients treated with GLP-1 receptor agonists and DPP-4 inhibitors, cohort studies have not identified a higher risk.
5. Further studies must be conducted to determine if GLP-1 receptor agonists and DPP-4 inhibitors can be safely used to treat hospitalized patients.
6. Sodium-glucose co-transporter 2 (SGLT2) inhibitors increase urinary glucose excretion by blocking the activity of a membrane protein that mediates glucose reabsorption in the proximal tubule.
7. Treatment with SGLT2 inhibitors may be associated with an increased risk of genitourinary infections, symptomatic hypotension, and diabetic ketoacidosis.
8. Under the right circumstances, a patient using an insulin pump may be allowed to continue to manage it to control hyperglycemia during hospitalization.
9. A preparation of microparticle-bound insulin inhaled through a special device can be used to deliver rapid-acting prandial doses.
10. U-500 is a concentrated preparation of regular insulin that can be used to treat patients with insulin resistance who require greater than 200 units daily to control hyperglycemia.

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What are incretins, and what is the incretin effect?

The incretin effect refers to the observation that orally administered glucose elicits a higher insulin secretory response than a similar amount of glucose administered intravenously. Incretins are gastrointestinal peptide hormones that mediate this effect by regulating pancreatic β-cell function and postprandial insulin secretion.[1]

The two best-characterized incretins are gastric inhibitory polypeptide (GIP) and glucagon-like peptide-1 (GLP-1). GIP and GLP-1 are secreted within minutes after food is ingested. Together they act to mediate approximately 70% of postprandial insulin secretion. GIP produced by K cells in the duodenum and the proximal jejunum stimulates glucose-dependent insulin release from pancreatic β cells. In patients with type 2 diabetes mellitus (T2DM), GIP's effects on stimulating insulin production are impaired.[2] GLP-1 produced by L cells in the ileum and the colon stimulates glucose-dependent insulin release from pancreatic β cells, slows gastric emptying, and increases satiety to reduce food intake. In contrast to GIP, which stimulates glucagon release, GLP-1 inhibits glucagon release. This inhibitory activity can reduce the inappropriate postprandial increase in glucagon that occurs in patients with T2DM. Unlike GIP, GLP-1 retains its ability to promote insulin secretion in patients with T2DM.[2]

What are GLP-1 receptor agonists?

GLP-1 receptor agonists are a class of injectable agents that activate the GLP-1 receptor, reducing postprandial hyperglycemia. Endogenous GLP-1 has a half-life of about 2 minutes due to the combined effects of rapid degradation by dipeptidyl peptidase inhibitor-4 (DPP-4) and renal clearance of intact and degraded GLP-1 fragments. Synthetic GLP-1 receptor agonists resist degradation by DPP-4, allowing for twice-daily, once-daily, or once-weekly dosing by subcutaneous injection. There are currently 5 formulations of GLP-1 receptor agonists approved for use by the US Food and Drug Administration (FDA) (**Table 1**).

How are GLP-1 receptor agonists used in clinical practice?

GLP-1 receptor agonists have emerged to become first-line agents used in the treatment of T2DM. They exhibit a robust glucose-lowering effect, typically decreasing hemoglobin A1c (HbA1c) by about 1%. As a class, they are associated with a low risk of hypoglycemia and have been shown to have a favorable effect on weight control

Table 1
Glucagon-like peptide-1 receptor agonists

Agent	Brand Name	Concentration	Dose	Available Forms
Exenatide	Byetta	250 μg/mL	5 μg subcutaneously (SQ) twice daily	1.2 mL prefilled pen
			10 μg SQ twice daily	2.4 mL prefilled pen
	Bydureon	—	2 mg SQ weekly	2 mg prefilled pen
Liraglutide	Victoza	6 mg/mL	0.6 mg, 1.2 mg, or 1.8 mg SQ daily	3 mL prefilled pen
Albiglutide	Tanzeum	—	30 mg SQ weekly	30 mg prefilled pen
			50 mg SQ weekly	50 mg prefilled pen
Dulaglutide	Trulicity	—	0.75 mg SQ weekly	0.75 mg prefilled pen
			1.5 mg SQ weekly	1.5 mg prefilled pen