

The Intersection of GLP-1 Therapy and Ocular Health: What Clinicians Need to Know

2 hours

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Description

Glucagon-like peptide-1 (GLP-1) agonists are a class of medications utilized to treat type 2 diabetes mellitus (T2DM) and obesity. This course offers a comprehensive exploration of the relationship between GLP-1 receptor agonists and ocular health including emerging evidence on their impact on ocular conditions, such as diabetic retinopathy, nonarteritic ischemic optic neuropathy, and glaucoma.

Objectives

- Deepen their knowledge of how GLP-1 agonists work, their pharmacological effects, and their role in managing Type 2 Diabetes Mellitus (T2DM) and other metabolic conditions
- Gain insights into the expression of GLP-1 receptors in ocular tissues, the potential protective effects of these agonists on the retina and optic nerve, and possible clinical treatment options in the future
- Understand how GLP-1 agonists may influence ocular health, including their potential effects on diabetic retinopathy and other ocular conditions, such as NAION

Overview (10 min)

- The role of endogenous glucagon-like peptide 1
 - Endogenous incretin hormone
 - Produced by L-cells in the small intestine in response to food intake
- Physiological Functions
 - Stimulates glucose-dependent insulin secretion from pancreatic β -cells
 - Inhibits glucagon release from α -cells
 - Slows gastric emptying, leading to reduced postprandial glucose spikes
 - Promotes satiety, contributing to reduced food intake
- GLP-1 in Glucose Homeostasis
 - Role in Blood Glucose Regulation
 - Facilitates glucose uptake and storage by enhancing insulin secretion
 - Balances glucose production and utilization
 - Degradation by DPP-4 Enzyme
 - GLP-1 is rapidly inactivated by the enzyme dipeptidyl peptidase-4 (DPP-4)
 - The short half-life of endogenous GLP-1 limits its therapeutic potential

Discovery and Development of GLP-1 Agonists

- Challenges of Native GLP-1
 - Limited therapeutic utility due to rapid degradation
 - Need for longer-acting analogs to harness GLP-1's benefits
- Development of GLP-1 Receptor Agonists
 - Synthetic analogs designed to resist DPP-4 degradation
 - Mimic the action of GLP-1 with extended half-lives
 - Examples Exenatide, Liraglutide, Semaglutide, Dulaglutide
- Introduction to GLP-1 agonists
 - Activation of GLP-1 Receptors
 - GLP-1 agonists bind to and activate GLP-1 receptors on pancreatic β -cells
 - Augment insulin secretion in a glucose-dependent manner, reducing the risk of hypoglycemia
 - Inhibition of Glucagon Secretion
 - Suppress inappropriate glucagon release, especially in hyperglycemic states
 - Effects on Gastric Emptying and Appetite
 - Delay gastric emptying, reducing postprandial glucose excursions
 - Promote satiety, leading to weight loss in patients with T2DM

Clinical Applications of GLP-1 Agonists

- Type 2 Diabetes Mellitus (T2DM)
 - Primary indication for GLP-1 agonists
 - Effective in lowering HbA1c, particularly in patients with high cardiovascular risk
- Obesity Management
 - GLP-1 agonists such as Semaglutide are approved for obesity treatment
 - Significant weight loss benefits observed in clinical trials
- Cardiovascular Benefits
 - Reduction in major adverse cardiovascular events (MACE) observed in long-term studies
 - Potential use in patients with established cardiovascular disease
- Emerging Applications
 - Investigation into potential benefits in non-alcoholic fatty liver disease (NAFLD)
 - Research into neuroprotective effects and use in Alzheimer's disease

GLP-1 medications

- Semaglutide
 - Brand Names
 - Ozempic (injectable)
 - Rybelsus (oral)

- Can be used with other glucose-lowering agents such as metformin or basal insulin

Comparative Efficacy and Safety

- Comparison with Other Antidiabetic Agents
 - GLP-1 agonists vs insulin, SGLT-2 inhibitors, DPP-4 inhibitors
 - Positioning in diabetes treatment algorithms
- Safety Profile
 - Common side effects nausea, vomiting, diarrhea
 - Risk of pancreatitis and thyroid C-cell tumors (in animal studies)
 - Monitoring and managing adverse effects

Clinical Evidence and Research

- Impact on Diabetic Retinopathy
 - Review of studies investigating the effects of GLP-1 agonists on diabetic retinopathy progression
 - Discussion of significant findings
 - Initial worsening of DR but improvement in DR over time
 - Reduced progression rates
 - Improvement in retinal health
- Recommendations for Monitoring
 - Guidelines for regular eye examinations in patients on GLP-1 agonists
 - Consideration of accelerated monitoring upon initiation
 - Presence of DR
 - Early detection strategies for managing potential ocular complications

GLP-1 Receptors in the Eye

- Expression in Ocular Tissues
 - Presence of GLP-1 receptors in retinal ganglion cells, endothelial cells, and Müller cells
 - Potential role in neuroprotection and anti-inflammatory effects within the eye
- Mechanistic Insights
 - How GLP-1 agonists might influence ocular tissues through anti-apoptotic and anti-oxidative pathways
- Animal Studies and Preclinical Research
 - Insights from preclinical models on GLP-1's protective effects on the retina
 - Mechanisms explored in animal studies
 - Reduction of oxidative stress
 - Reduction of inflammation
- Future treatments in Glaucoma

- Review of studies investigating the effects of GLP-1 agonists on open angle glaucoma
- Possible treatment targets in neurodegenerative diseases

Q&A / Discussion