THE FUTURE OF GLP-1 AGONISTS AND GROWTH HORMONE COMBINATION: WEIGHT LOSS WITH MUSCLE PRESERVATION

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INTRODUCTION: GLP-1 receptor agonists (e.g., semaglutide, tirzepatide) have revolutionized the treatment of obesity and type 2 diabetes, achieving unprecedented weight loss of 15–20%. However, a major limitation is that approximately 25–40% of lost weight comes from lean muscle mass, not fat. This muscle loss can lead to functional decline, metabolic slowdown, and weight regain. Growth hormone (GH) is a potent anabolic hormone that stimulates muscle protein synthesis and lipolysis. However, GH is also known to induce insulin resistance. The interaction between GLP-1 and GH remains poorly understood. This abstract aims to analyze the crosstalk between GLP-1 and GH and evaluate the potential of combined therapy for quality weight loss.

METHODS: A targeted literature review was conducted using PubMed and Google Scholar databases. Key studies published between 2020 and 2025 were selected, including: Abdulla et al. (2020) – GLP-1 infusion and muscle protein synthesis in older adults; Hjelholt et al. (2020) – GH-induced insulin resistance mechanisms; Cignarelli et al. (2022) – GLP-1 and GH/IGF axis review; and Kristensen (2025) – long-acting GH plus GLP-1 combination therapy. Data extraction focused on muscle metabolism, insulin sensitivity, and fat oxidation outcomes.

RESULTS: The analysis revealed three main findings. First, GLP-1 independently stimulates muscle synthesis. Abdulla et al. (2020) demonstrated that GLP-1 infusion increased muscle protein synthesis rate from 0.058% to 0.102% per hour ($p<0.05$) in older adults, suggesting direct anabolic effects beyond insulin secretion. Second, GH induces insulin resistance via lipolysis. Hjelholt et al. (2020) showed that GH increases free fatty acid release from adipose tissue, which suppresses pyruvate dehydrogenase activity in skeletal muscle, reducing glucose uptake by approximately 30%. Third, combination therapy preserves muscle while minimizing insulin resistance. Kristensen (2025) found that co-administration of long-acting GH with a GLP-1 agonist resulted in preservation of lean muscle mass (no significant loss), accelerated fat oxidation (20–25% increase), and minimal insulin resistance (only transient, resolved within 2–4 weeks).

DISCUSSION: The findings indicate that GLP-1 and GH have bidirectional crosstalk rather than opposing actions. GLP-1 may enhance GH secretion via hypothalamic pathways, while GH amplifies GLP-1's lipolytic effects. The key clinical implication is that adding low-dose GH to GLP-1 therapy could solve the "muscle loss problem" of current obesity treatments. However, limitations include small sample sizes, short follow-up periods, and potential long-term safety concerns of GH (e.g., acromegaly, tumor risk).

CONCLUSION: The combination of GLP-1 plus low-dose growth hormone represents a promising new strategy for "quality weight loss" – losing fat while preserving muscle. This approach could transform obesity pharmacotherapy. Large-scale, long-term randomized controlled trials are urgently needed to confirm efficacy and safety. Keywords: GLP-1 receptor agonists, growth hormone, muscle preservation, insulin resistance, obesity, quality weight loss.

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Abstract:

GLP-1 receptor agonists achieve 15–20% weight loss, but 25–40% of lost weight is lean muscle, causing metabolic and functional decline. Growth hormone (GH) stimulates muscle synthesis but induces insulin resistance. This review analyzed GLP-1 and GH crosstalk using key studies (2020–2025). Findings show that GLP-1 independently increases muscle protein synthesis (0.058→ 0.102%/h, $p<0.05$). GH reduces glucose uptake by ~30% via free fatty acid-induced PDH suppression. Importantly, combining long-acting GH with a GLP-1 agonist preserves lean mass, increases fat oxidation by 20–25%, and causes only transient insulin resistance (2–4 weeks). Adding low-dose GH to GLP-1 therapy is a promising strategy for quality weight loss (fat loss with muscle preservation), though long-term safety trials are needed.

Kerwords: GLP-1 receptor agonists, growth hormone, muscle preservation, insulin resistance, obesity.