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Synergy Between GLP-1 Receptor Agonists, Nutritional Therapy, and Physical Exercise in Optimising Body Composition and Cardiometabolic Health

Rodolfo Melo Raiol

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Comunicações curtas

ABSTRACT

Therapy with glucagon-like peptide-1 (GLP-1) receptor agonists has revolutionized the treatment of obesity and metabolic dysfunctions. However, the rapid weight loss induced by these drugs raises clinical concerns regarding depletion of fat-free mass and reductions in bone mineral density. This short communication synthesizes the recent literature on the physiology of GLP-1 receptor agonists, highlighting the non-negotiable need for multidisciplinary interventions. The integration of appropriate nutritional management with periodized resistance training emerges as the gold standard to mitigate the risk of secondary sarcopenia and to potentiate systemic adaptations to treatment.

Keywords: GLP-1, Weight Loss, Sarcopenia.

Affiliated institution – Scientific Director, Brazilian Diabetes Society (Pará Regional Chapter).
Dean of the Postgraduate Program in Therapeutic Resistance Training and Exercise Physiology Applied to Special Populations, Centro Universitário do Estado do Pará.

Corresponding author: *Rodolfo Melo Raiol*

1 Introduction and cardiometabolic physiology

GLP-1 receptor agonists constitute a landmark in the management of metabolic disorders, given their pleiotropic actions across multiple physiological systems. Initially developed to improve glycaemic control in type 2 diabetes, these agents have subsequently demonstrated robust cardiometabolic benefits, including direct modulation of hepatic and renal signalling pathways [1]. Within an obesogenic context, GLP-1–mediated central mechanisms promote early satiety and delay gastric emptying, thereby reducing spontaneous energy intake [2,3].

While a sustained energy deficit remains the principal driver of adipose tissue reduction, chronic appetite suppression may substantially perturb physiological homeostasis. Accordingly, the contemporary clinical challenge extends beyond inducing weight loss to ensuring the qualitative preservation of metabolically and functionally relevant tissues during the catabolic process. Addressing this challenge requires an advanced understanding of the anatomical, functional, and biomechanical adaptations elicited throughout treatment.

2 The critical role of clinical nutrition in tissue preservation

Pharmacotherapy-induced appetite suppression is consistently associated with clinically relevant alterations in dietary intake patterns, particularly with respect to macronutrient distribution and total protein consumption [5]. Contemporary position statements and clinical guidelines from medical and nutrition societies increasingly underscore that diet therapy should be regarded not as an adjunct, but as a central, preventive component of care aimed at attenuating the adverse sequelae of rapid, medication-mediated weight loss [4].

Within this framework, insufficient protein intake during treatment with GLP-1 receptor agonists may exacerbate losses of lean soft tissue by amplifying skeletal muscle catabolism. Accordingly, individualized nutritional prescription is essential to support myofibrillar protein synthesis and to ensure adequate substrate availability for the

maintenance of functional capacity and tissue integrity. In the absence of a structured lifestyle intervention grounded in the adequacy of macro- and micronutrient intake, the sustainability of therapeutic outcomes may be undermined, with concomitant increases in the risk of frailty and other complications over the long term [6].

3 Biomechanical responses and the imperative for physical training

The unintentional loss of fat-free mass associated with the use of GLP-1 receptor agonists has direct and clinically meaningful implications for musculoskeletal health. Reductions in muscle volume, concomitant with potential declines in bone mineral density resulting from decreased mechanical loading during weight loss, may increase susceptibility to orthopaedic dysfunction and accelerate functional decline [8].

In this context, resistance training, particularly within a therapeutic strength-training approach, constitutes a primary and non-substitutable intervention to attenuate catabolic processes [7]. The mechanical tension generated by resistance exercise activates anabolic signalling pathways, including mTORC1, which, in synergy with adequate protein intake, supports the maintenance of muscle architecture and physical performance. Randomised controlled trials indicate that the systematic integration of structured exercise into GLP-1 receptor agonist therapy yields superior improvements in metabolic syndrome severity, visceral adiposity, and the modulation of systemic inflammatory markers when compared with pharmacotherapy alone [9]. Additionally, training periodisation, by strategically and progressively organising load variables, appears to optimise insulin sensitivity and enhance glycaemic control, bringing it closer to physiological homeostasis more effectively than pharmacological monotherapy [10].

4 Conclusion

The efficacy of GLP-1 receptor agonists in inducing clinically significant reductions in body weight is well established; however, the qualitative profile of the weight lost warrants rigorous clinical and scientific monitoring. The attenuation of protein catabolism and the prevention of osteomyoarticular deterioration depend on an

integrated, multidisciplinary approach that aligns high-protein nutritional planning with resistance exercise prescription grounded in mechanotransductive principles. Accordingly, the systematic implementation of these combined interventions should be considered a standard-of-care strategy for healthcare professionals aiming to promote sustainable weight management and long-term cardiometabolic health.

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