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CASE REPORT

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Multimodal strategy to protect lean mass in people using semaglutide for obesity – case report

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Abstract

Introduction: Semaglutide, a glucagon-like peptide-1 analogue (aGLP-1), has emerged as a pivotal therapy for managing obesity by significantly reducing caloric intake through central nervous system modulation. Beyond appetite control, it demonstrates efficacy in diminishing visceral fat and improving metabolic markers. However, concerns arise regarding its potential to induce lean mass loss, highlighting the need for adjunctive strategies. **Objective:** This study aims to assess the effects of a multimodal intervention combining semaglutide therapy with nutritional supplementation and resistance training on body composition, particularly lean mass preservation. **Case Description:** A 38-year-old male with obesity underwent semaglutide treatment alongside a structured protocol integrating a ready-to-drink nutritional supplement, resistance exercise, and dietary intervention. Over six months, changes in weight and body composition were evaluated using DXA, bioimpedance, and plicometry. The patient experienced a significant weight loss of 14.6 kg, with body fat reduction of 8.5 kg, 9.7 kg, and 10.4 kg, depending on the measurement method. Notably, lean mass loss was minimized, supporting the efficacy of adjunctive strategies in mitigating muscle depletion during weight loss. **Final considerations:** These findings underscore the need for mitigation strategies to be started together with any aGLP-1 when treating a person with obesity including but not limited to diet, exercise and a metabolic-friendly ready to drink nutritional supplement - a non-pharmacological strategy frequently forgotten by endocrinologists.

Keywords: Case Report. Semaglutide Therapy. Corporal Composition. Nutritional Supplement.

Introduction

Semaglutide, a glucagon-like peptide-1 analogue (aGLP-1), has emerged as an effective therapy for the management of obesity. Clinical studies indicate that its mechanism of action involves modulating appetite through interactions with receptors in the central nervous system, especially in the arcuate nucleus of the hypothalamus, resulting in a significant reduction in caloric intake [1].

In addition to appetite reduction, semaglutide has shown promising effects in reducing body fat, particularly visceral fat, which is directly associated with increased cardiovascular and metabolic risk. This diminution in visceral fat contributes not only to aesthetic improvement, but also to the mitigation of systemic inflammation and metabolic dysfunctions associated with excess adipose tissue [2,3]. These results have proven effective for obese patients with or without diabetes [4].

However, despite the positive results, semaglutide-induced weight loss is not limited to fat reduction alone. A recent systematic review of the effect of semaglutide on lean mass, in the treatment of obesity, revealed that weight reduction was predominantly driven by loss of body fat. However, there was considerable variability in the reduction in lean mass, which ranged from 0% to 40% of total weight loss—underscoring the need to add muscle mass and function also as critical endpoints in future clinical trials **[5]**.

According to Prada et al., aGLP-1 requires strategic use to optimize body composition changes, suggesting that simultaneous nutrition and exercise interventions to mitigate muscle loss are extremely important, as muscle tissue not only serves mechanical functions but also plays vital endocrine and physiological roles **[6]**.

In view of the above, to protect lean mass in individuals using semaglutide for obesity, some strategies have been suggested based on recent research results. Regular assessments of body composition using bioimpedance analysis, for example, can help track changes in lean and fat mass during semaglutide treatment **[7]**. Identifying early signs of lean mass reduction allows timely interventions.

In this context, resistance exercise and a high-protein diet are among the potential options. Ensuring adequate protein intake is crucial, as high-protein diets have been shown to help preserve lean mass during weight loss[5]. Nutritional counseling can guide patients in maintaining a balanced diet that supports muscle health. Likewise, incorporating resistance training into your exercise regimen can significantly help preserve and even increase lean mass during weight loss **[8]**.

Based on this, the description of this clinical case is relevant to deepen the understanding of strategies for preserving muscle mass in patients treated with second-generation anti-obesity drugs, considering the significant loss of lean mass observed with these treatments and the need to validate interventions such as nutritional supplements in the clinical context.

Thus, this case report aimed to describe an obese patient who was treated with semaglutide and for whom a ready-to-drink (RTD) nutritional supplement was used with the intention of protecting against muscle mass loss, with the purpose of evaluating whether the use of a specific nutritional supplement for diabetes mellitus (DM), associated with the practice of exercise, is capable of preventing the loss of lean mass induced by treatment with aGLP-1.

Methods

This case study involves a male patient with grade I obesity who was followed by a multidisciplinary team (physician, nutritionist and physical educator) for a period of 6 months. A baseline assessment was conducted that included the identification of the patient's baseline characteristics, such as sex, age and other relevant comorbidities.

Anthropometric, laboratory and imaging measurements were conducted at the beginning of the study and after six months, including weight, BMI and body composition. Body composition was assessed by plicometry (ISAK - level 2) and bioimpedance (In Body 570), in addition to dual energy X-ray absorptiometry (DXA) (General Electric / Lunar Prodigy Advance - Software version 17). Biochemical tests were also performed to measure blood glucose, glycated hemoglobin, inflammatory markers, among other laboratory parameters.

The intervention consisted of administering Semaglutide, with an initial dose of 0.25 mg subcutaneously once a week, following a protocol of escalation of 0.25 mg every month until reaching the full dose for obesity (2.4 mg/week), according to the Brazilian label **[9]**. In addition, nutritional supplementation with Nutren Control® - RTD (Nestlé Health and Science Brazil) was prescribed, with a recommendation of 1 to 2 bottles per day as a meal replacement for breakfast and/or dinner (composition in Figure 1), associated with a balanced diet.

Figure 1. Nutritional composition of Nutren Control®.

Amount per 100mL		% DV (*)	Amount per 100ml		% DV (*)
Energy Value	104 kcal = 437 kJ	5%	Energy Value	104 kcal = 437 kJ	5%
Carbohydrates, of which:	7.2 g	2%	Copper	0.16 µg	18%
Sugars****	2.3 g	**	Selenium	6.9 µg	20%
Glucose	0 g	**	Zinc	1.3 mg	19%
Galactose	0 g	**	Molybdenum	9.0 µg	20%
Fructose	0 g	**	Chromium	6.5 µg	19%
Lactose	0 g	**	Vitamin A	76 µg RE	13%
Sucrose	0 g	**	Vitamin D	32.0 UI	16%
Proteins	7.5 g	10%	Vitamin E	4.8 mg α-TE	48%
Total fats, of which:	5 g	9%	Vitamin K	8.9 µg	14%
Saturated Fats	0.4 g	2%	Vitamin C	22 mg	49%
Trans Fats	0 g	**	Vitamin B1	0.09 mg	8%
Monounsaturated Fats	2.8 g	**	Vitamin B2	0.13 mg	10%
Polyunsaturated Fats	1.4 g	**	Niacin	1.6 mg	10%
Alpha-linolenic Acid	260 mg	**	Vitamin B6	0.16 mg	12%
Cholesterol	1.6 g	**	Vitamin B12	0.45 µg	19%

Fibers	2.0 g	8%	Folic Acid	22 µg	6%
Sodium	60 mg	3%	Pantothenic Acid	0.30 mg	6%
Calcium	120 mg	12%	Biotin	2.7 µg	9%
Iron	1.4 mg	10%	Choline	46 mg	8%
Phosphorus	86 mg	12%	Inositol	24 mg	**
Magnesium	36 mg	14%	Taurine	6.8 mg	**
Manganese	320µg	14%	L-Carnitine	9.1 mg	**
Iodine	26 µg	20%			

*% Daily Values are based on a 2,000 kcal or 8,400 kJ diet. Your daily values may be higher or lower depending on your energy needs. **DV not established. ***Contains sugars naturally present in the ingredients.

Source: Nutren Control® - RTD (Nestlé Health and Science Brazil).

The physical exercise protocol included three weekly sessions of resistance training, lasting 60 to 80 minutes per session. Each session comprised eight exercises, performed in three sets of 8 to 10 maximum repetitions, with one minute of rest between sets, covering upper and lower muscle groups. The training program was prescribed by an experienced physical education professional at the beginning of the study and reassessed/improved after 12 weeks.

The results measured included changes in anthropometric and body composition parameters over time, the effects of supplementation and exercise on the preservation of lean mass, as well as impacts on laboratory and imaging tests, in addition to the patient's overall evolution.

Ethical aspects were ensured through the submission and approval of the project by the Research Ethics Committee (approval number: 7.353.838), in accordance with current ethical guidelines. The patient's anonymity and the obtaining of the Free and Informed Consent Form (FICF) were guaranteed.

This case report was prepared in accordance with the CARE (CAse REport) guidelines, to ensure transparency, scientific rigor, and international standardization in the reporting of clinical cases.

Results

Case Report

A 38-year-old sedentary male patient living with grade 1 obesity (starting BMI of 31,8 kg/m^2) came to our clinic on May 27, 2024, reporting "difficulty in controlling his weight", and "recurrent weight fluctuation". He also has a personal history of systemic arterial hypertension (SAH), hyperlipidemia (elevated LDL-cholesterol levels), metabolic dysfunction-associated steatotic liver disease (MASLD) and primary hypothyroidism (etiology: Hashimoto thyroiditis). He was then started in a multidisciplinary program for obesity treatment. The nutrition plan prescribed by our registered dietitian was according to Brazilian Diabetes Society recommendations **[9]** and was intentionally defined with focus on loss of body fat but also preserving muscle mass. It included Nutren Control® 3 doses per day during the first four weeks, reducing to 1-2 doses per day thereafter. Regarding the exercise plan it was centered in resistance physical activity as described above. The drug treatment included semaglutide 2,4 mg/week. It is worth mentioning that both SAH and hypothyroidism were well controlled over the 6 months period of this trial. The evolution of biochemical data can be seen in Table 1.

Table 1. Patient´s biochemical data.

Parameter	Baseline	Sixth month
Blood glucose (mg/dL)	93	92
Glycated hemoglobin (%)	5.5	5.2
Triglycerides (mg/dL)	65	67
Total cholesterol (mg/dL)	271	194
HDL cholesterol (mg/dL)	51	40
LDL cholesterol (mg/dL)	203	138
Creatinine (mg/dL)	0.95	1.01
Total testosterone (ng/dL)	458	811
Free testosterone (ng/dL)	9.47	14.68
Bioavailable testosterone (ng/dL)	222	344
25 hydroxy vitamin D (ng/dL)	27.1	29.7
Transaminase Glutamic-Pyruvic (U/L)	45	50
Glutamic-Oxaloacetic Transaminase (U/L)	28	26

Source: Own Authorship.

The results indicate a significant improvement in the lipid profile, with a reduction in total cholesterol and LDL, suggesting a positive impact of the treatment in reducing cardiovascular risk. However, there was a decrease in HDL (from 51 mg/dL to 40 mg/dL), which may reinforce the need to include aerobic exercise in prescription of the person who lives with obesity (PWO).

Glycemia remained stable, while glycated hemoglobin showed a slight reduction (5.5% to 5.2%), indicating an improvement in glycemic control. The hormonal profile showed a significant increase in total testosterone (458 ng/dL to 811 ng/dL), free testosterone and bioavailable testosterone, possibly related to the loss of visceral body fat. Vitamin D levels also showed a slight increase, probably related to the composition of Nutren Control® - which has vitamin D in its formula.

Liver enzymes showed discrete changes, with no clear indication of liver impairment as shown by the comparison of baseline and 6 months post treatment elastography. Creatinine remains within the normal range.

A significant reduction in the patient's anthropometric parameters was observed over the

6month follow-up period. The initial body weight of 113.5 kg decreased to 98.9 kg, representing a total weight loss of 14.6 kg. Consequently, the BMI also showed a reduction, going from 31.8 kg/m² at baseline to 28.6 kg/m² at follow-up, reflecting a shift from obesity to overweight. In addition, waist circumference reduced from 116.7 to 103 cm (-13.7 cm). These findings indicate a substantial improvement in anthropometric parameters, suggesting a reduction in the metabolic risk associated with excess weight.

Table 2 summarizes the measurements performed at baseline and after 6 months using different methods of assessing body composition. The results demonstrate a substantial loss of body fat mass over 6 months, regardless of the method used, ranging from -8.5 kg by DXA and -9.7 kg by BIA. In addition, lean mass was reduced to a lesser extent, with a decrease of -2.8 kg of lean soft tissue and SMM, and a minimal variation of -0.1 kg in skin fold measurements. These results suggest that the treatment had a positive effect on reducing body fat, with an important impact on preserving lean mass.

Table 2. Evolution of body compartments through 3 body composition devices.

Device	Baseline	Follow Up (6m)	ΔDelta
DXA			
Fat Mass (kg)	42.4	33.9	-8.5
Lean Soft Tissue (kg)	66.8	64.0	-2.8
BIA			
Fat Mass (kg)	40.8	31.1	-9.7
Skeletal Muscle Mass (kg)	41.1	38.3	-2.8
Skin Folds			
Fat Mass (kg)	39.6	29.2	-10.4
Skeletal Muscle Mass (kg)	37.1	37.0	-0.1

Source: Own Authorship.

Discussion

The use of aGLP-1 has been associated with approximately 10% lean mass loss **[10]** which is equivalent to one decade of senescence. Percentual of lean mass loss from the total weight reduction seen with Tirzepatide, Retatrutide, and Semaglutide were 25%, 33%, and 39% respectively **[11]**. It is worth noting that these numbers were extracted from different studies and not from head trials. Thus, comparisons between these agents should be taken with caution. This scenario is relatively new in the field and points out the need for mitigation strategies to be started in conjunction with aGLP-1 when treating people with obesity. At this moment the scientific literature is still scarce regarding randomized controlled trials that address this issue. Thus, this case report helps to shed light on the utility of ready-to-consume nutritional supplements in the management of drug-induced lean mass loss.

In this case report the use of a ready to drink, metabolic friendly specific nutritional supplement associated with resistance training and diet were able to reduce the lean mass loss associated with the use of Semaglutide 2,4 mg. Independent of the body composition method used (DXA, electrical bioimpedance or plicometry) we could demonstrate a mitigation in the impact on muscle mass loss. Our patient lost 2,8 kg of lean mass (according to DXA) - which represented 2.5% of the total weight loss. In the pivotal study - STEP1 - with Semaglutide **[1]** this percentual was 39%. As such our preventive strategy was deemed as effective.

It is important to emphasize that this study is a case report and, therefore, its conclusions should not be considered definitive. Additional investigations are needed to support more robust findings. The approaches used in this case reflect practical, real-world interventions that can be applied in other diverse clinical scenarios. This case highlights the importance of evidence-based yet adaptable strategies that align with patient-centered care in real-life settings.

Final Considerations

In conclusion, it is of utmost importance to initiate a mitigation strategy against lean mass loss at the same time an aGLP-1 is started for an obese patient. The more practical and cost-effective the tools used are the better the compliance. Therefore, this case report is an example for the clinician of the meaningful impact that a metabolic-friendly ready to drink nutritional supplement can have - a non-pharmacological strategy frequently forgotten by endocrinologists.

Patient Perspective

Throughout my 39 years of life, I have faced recurring challenges related to obesity and overweight, undergoing several pharmacological treatments. When analyzing past photographs, I notice a cyclical pattern of weight loss and regain, alternating between phases of being thin, overweight, and obese.

Regarding pharmacological treatment, I have tried various approaches, including amfepramone, sibutramine, and lorcaserin. While using these medications, my diet remained relatively controlled, and I engaged in physical activities such as capoeira, jiu-jitsu, and road running. However, I never exercised with the consistency required to establish a truly healthy lifestyle. As a result, I repeatedly experienced the so-called "yo-yo effect," characterized by periodic weight loss and regain.

Although my youth and metabolism helped mitigate the impact of these fluctuations over the years, by the

end of last year, my condition had significantly worsened. Weighing 116.3 kg, I was diagnosed with hypertension, dyslipidemia, and joint pain, which made even simple daily tasks difficult.

Faced with this scenario, a radical lifestyle change became essential. I started treatment with "Wegovy", reaching the full dosage without experiencing the common side effects. Although the medication partially reduced my appetite, I was still able to eat normally. For the first time, I sought professional nutritional guidance, and my nutritionist developed a tailored meal plan. As part of this strategy, "Nutren Control" was included twice a day to enhance satiety during work hours, when my hunger was most intense.

Additionally, I introduced, for the first time, a weight training routine under the supervision of a personal trainer. Although I did not fully meet the recommended frequency, I maintained an average of two sessions per week for six months. During the study, I noticed that consuming "Nutren Control" at critical times (10 AM and 4 PM) helped control my appetite, possibly due to a mild nausea effect, which was likely intensified by the simultaneous use of 2.4 mg of semaglutide weekly. This effect facilitated adherence to my meal plan, helping me maintain regular mealtimes and make healthier food choices.

Currently, without medication, I have noticed the return of my appetite, but I have developed a greater awareness of my eating habits. Now, I can clearly distinguish between physiological hunger and the mere desire to eat. Although I have yet to achieve the ideal consistency in weight training, I continue to follow my meal plan, and my nutritional reeducation has positively influenced my entire household. Today, the diet that was once "mine" has become "ours." Undoubtedly, this has been the greatest legacy of this journey.
Patient: E.B.

CRediT

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Nestle Health Science provided the medications and supplements.

Ethical Approval

This case report was approved by the Research Ethics Committee (approval number: 7.353.838), in accordance with current ethical guidelines.

Informed Consent

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Data Sharing Statement

No additional data are available.

Conflict of Interest

The authors declare no conflict of interest.

Disclosure

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Similarity Check

It was applied by Ithenticate®.

Application of Artificial Intelligence (AI)

Not applicable.

Peer Review Process

It was performed.

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