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Case report

Very low-calorie ketogenic diet in the treatment of adaptive thermogenesis: A case report

Jônatas de Oliveira [a,*], Isis de Carvalho Stelmo [b], Leandro Silva Figueredo [c], Carolina Cristina de Freitas [d]

[a] School of Medicine, University of Sao Paulo, Sao Paulo, Brazil
[b] Department of Psychology, University of Roehampton, London, United Kingdom
[c] A Beneficência Portuguesa de São Paulo - R. Maestro Cardim, São Paulo - SP 01323-001, Brazil
[d] Parque Universitario, Franca, Brazil

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ABSTRACT

Objectives: The management of the phenomenon of adaptive thermogenesis poses a challenge to the successful treatment of overweight/obesity with a nutritional intervention that minimizes the loss of muscle mass, with little cognitive restraint use and disorganization of eating behavior. On the other hand, it creates a significant calorie deficit for the reduction of body fat. The aim of this case report was to discuss the effects of a very low-calorie ketogenic diet in a woman with obesity and low resting metabolic rate.
Case description: A 36-y-old white woman with a history of obesity and bulimia nervosa who has had difficulty losing and maintaining weight despite numerous dietary and pharmacologic treatments.
Results: There was a loss of 12 kg in 115 d, reaching 13.4 kg, with 11.4 kg of fat mass (FM). The resting metabolic rate showed an increase of 79% in relation to the initial rate, reaching normal levels for the predictive equations and maintaining this level in the first-year follow-up. Additionally, improvement of metabolic laboratory parameters and eating behavior traits were described.
Conclusions: In this specific case of bulimia nervosa resulting in hypometabolism (low resting metabolic rate/fat-free mass) and obesity, the very low-calorie ketogenic diet intervention has demonstrated a possibility of weight loss with little cognitive restraint use, thereby increasing resting metabolic rate in the short and medium terms, ultimately promoting a negative energy balance. In relation to the numeric results, it seems positive; however, more research is necessary to evaluate the effects on the overall relationship with food and its long-term repercussions.

Introduction

An adequate nutrition plan for weight loss is part of the treatment for individuals who are overweight or obese [1]. Attempts to lose weight based on diet culture, disordered behaviors, and cognition tend to be less successful [2]. Additionally, when a restriction is a consequence of an eating disorder history, from a psychological perspective, constantly going on diets that lead to the "yo-yo" effect could result in disorganized eating behavior and traumatic effects, such as a negative body image, a poor relationship with one's body, and restricting whole food groups without a strong motive [3,4].

Efforts required to achieve low calorie intake are a behavioral issue that challenges current treatments for eating disorders. Many individuals with eating disorders make changes that hamper their autonomy. These changes are often motivated by internalized thinness standards, fatphobia, and negative attitudes toward weight and body shape [5,6]. Adherence to eating plans and behavior modification typically necessitate cognitive effort. However, because of multiple factors, relying on cognitive restriction for controlling eating habits may lead to a lack of inhibition for future eating behavior. Moreover, bulimia nervosa presents altered components and is commonly associated with compulsive behaviors and heightened food cravings [7,8]

On the metabolic aspect, one of the negative consequences is the reduction of the resting metabolic rate (RMR) [7]. The history of weight cycling is associated with the development of a metabolic state below the RMR setting predicted with energy expenditure formulas. Obarzanek et al. [7] described RMR as significantly lower in women with bulimia nervosa than healthy volunteers

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*Corresponding author: School of Medicine, University of Sao Paulo, FMUSP, Av. Dr. Arnaldo, 455 - Cerqueira César, Sao Paulo (SP) 01246-903, Brazil.
E-mail address: oliveira.jonatas@usp.br (J. de Oliveira).

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(mean ± SE, 4201 ± 126 versus 4694 ± 172 kJ/d). Self-efficacy has been identified as a crucial element in weight loss and maintenance in various interventions [9,10]. How should one deal with hypometabolism in patients who have dedicated much of their lives to weight loss?

In this case, the main issue for an individual with decreased RMR during treatment could be their metabolic response would not be as effective as expected because of caloric restriction [7,11]. This may occur because of the difficulty in adjusting one's behavior and thinking to comply with a low-calorie plan [10]. Furthermore, there is a risk for an increase in binge eating and food cravings due to the imposed restrictions, which may be compounded by a history of unsuccessful diet attempts and disordered eating behaviors [12,13].

It has been suggested that a treatment plan should aim at increasing RMR with a limited and controlled use of cognitive restriction, particularly related to carbohydrate intake [14]. This is important as restricting this macronutrient is common in low-carbohydrate and keto diets. It is common to identify individuals with low RMR during the preintervention period due to previous treatments or lack of adequate diets [1,4]. Therefore, the beneficiary with overweight/obesity associated with a low RMR may benefit from a very low-calorie nutritional intervention capable of modifying the state of adapted thermogenesis. This study investigates the effects of a very low-calorie ketogenic diet (VLCKD) in a woman with obesity and low RMR.

Case report

The patient to be discussed here was a 36-y-old single white woman, born and residing in Brazil, with a history of obesity and difficulty losing and maintaining weight after multiple nutritional and pharmacologic treatments. During the nutritional therapy with the behavioral approach treatment, the patient disclosed that she would eat bread while on the treadmill. Physical activity has always been a compensatory practice to cope with her food intake.

She has always sought validation for her self-image and relationships through her body shape and numerous restrictive diets. Consistent with the phenomena of RMR and weight cycling that are commonly observed in individuals with bulimia nervosa [7], the patient exhibited a pattern of repeatedly losing and regaining weight, often through cycling. As a result, she frequently turned to restrictive diets, which progressively became less effective over time. In Brazil, these diets are ordinarily shared in magazines and, sometimes, prescribed by professionals who might not be up to date with evidence-based practice. But it is important to say that usually, these restrictive diets are practiced without professional supervision [14]. Throughout the nutritional treatment, after the remission of binge eating, it was noticed that the patient's weight had not changed. Cognitions and behaviors of the eating disorder were not present, and the patient presented with less diet mentality and more freedom to eat, according to the concepts proposed by intuitive eating. After the complaint about the weight, food intake was observed, as well as behavioral patterns. Then we suspected RMR.

During the pretreatment assessment with VLCKD, the diagnoses considered were a personal history of bulimia nervosa in remission, generalized anxiety disorder, going on therapy, using trazodone 75 mg/d, topiramate 100 mg/d, and fluoxetine 80 mg/d. On anthropometric examination, the patient had a body weight of 74.3 kg and a body mass index (BMI) of 28.7 kg/m^2 (reference value 25– 29.9 kg/m^2, classification: overweight). She also had data from multifrequency bioelectrical impedance analysis (BIA; 5, 50, and 500 kHz) tracking tetrapolar (InBody370), body fat percentage (BF%) of 42%, configuring obesity (reference value >35%) [15].

Evaluation of emotional and eating behaviors

Before and after the dietary protocol, a dietitian conducted a behavioral assessment using an online form that included the Binge Eating Scale (BES), the Food Cravings Trait Questionnaire (FCQ-T) and the Food Cravings State Questionnaire (FCQ-S), and the Depression and Anxiety Scale (DASS-21).

To determine the pretreatment level of binge eating, the dietitian filled out the BES. This scale has been widely used to determine the presence and severity of binge eating [16]. The version used in this study was translated into Brazilian Portuguese and validated in Brazil. Scores are interpreted based on the cutoff points, which classify individuals according to the presence and severity of binge eating, as follows: absence of binge eating (≤17 points); moderate binge (18–26 points); severe binge (≥27 points). In a study to verify the sensitivity of the BES to the presence of binge eating, the cutoff point of 17 was compared with the Structured Clinical Interview (SCID), demonstrating a sensitivity of 97.9% [16].

Food cravings were evaluated using the FCQ-T and the FCQ-E. These questionnaires assess different aspects of the intense desire for food: one assesses the intense desire as a constitutional element (FCQ-T), and the other evaluates the intense desire for food as a transitory element (FCQ-E) [17,18].

To monitor the emotional state during treatment, the DASS-21 was used. This is a shortened form of the initial version of 42 items that measure negative emotional states of stress, anxiety, and depression [19]. The scale was adapted to Brazilian Portuguese and presented satisfactory results with a Cronbach's α of 0.92 for the Depression subscale (DASS-D), 0.90 for Stress (DASS-S), and 0.86 for Anxiety (DASS-A), indicating good internal consistency [19].

Treatment

RMR was investigated by the standard method of the calibrated TMR (Comed-Fit) method, tested as per the developer's test. The preintervention value of 798 kcal/d was repeated, resulting in a hypometabolic state (46.5% lower than that confirmed by the Harris–Benedict predictive and 43% lower by the Mifflin-St prediction Mifflin-St expected value) [20].

Because of the hypometabolic state, a modified VLCKD nutritional intervention from a commercial diet (DietKal) was indicated to achieve an adequate calorie deficit. The nutritional program had carbohydrate restriction (<50 g/d), lipids (only 10 g/d of olive oil), and high biological value protein meal replacement. Each meal replacement contained an average of 15 g of protein, 4 g of carbohydrates, 3 g of fat, and 90 to 100 kcal/unit.

A total weight loss of 14 kg was predicted, divided into two phases, 80% in the VLCKD phase and 20% in the "adaptation" phase. The VLCKD phase was a three-step calorie deficit with a progressive increase of calories. The source of protein was introduced at each new step by introducing low-fat animal protein (e.g., beef or fish) at lunch or dinner. The initial protocol of 800 kcal/d was modified to 550 kcal/d at step 1; 2700 kcal/d in step 2, and 800 kcal/d in step 3 to promote a calorie deficit. The amount of protein offered varied between 0.8 and 1.2 g/kg according to the patient's ideal body weight, calculated using BMI to avoid loss of lean mass.

During the VLCKD phase, the patient maintained ketone body levels >0.3 mmol/L, configuring a state of ketosis (ranging from 0.3 to 1.0 mmol/L). β-hydroxy-β-methylbutyrate (β-HMB) concentration was measured weekly with the reference method to be used domestically: a portable ketone monitor (FreeStyle Optium, Abbott) with ketone test strips [21].

Table 1
Body composition and resting metabolic rate measurements monitored during the protocol

Phases	Weight (kg)	BMI (kg/m^2)	BF% (%)	FM (kg)	FFM (kg)	RMR (kcal/d)	RMR/FFM (kcal/d/kg)	Adequation with Harris–Benedict (%)	Metabolic classification
Preintervention	74.3	28.7	41.6	30.9	43.4	798	18.38	53	Slow
End of VLCKD (78 d)	62.1	24.1	36.8	22.9	39.2	1425	36.35	103	Normal
End of protocol (193 d)	60.9	23.6	32	19.5	41.4	1624	39.22	119	Fast
After 1 y	62.2	24.9	31.3	19.4	42.8	1683	39.32	122	Fast

VLCKD, very low-calorie ketogenic diet; BMI, body mass index; BF%, body fat percentage; FM, fat mass; FFM, fat-free mass; RMR, resting metabolic rate
Classification of RMR according to the Harris–Benedict predictive equation: Slow (90% less than predictive); Normal (measured value is predictive is within 90% to 110% of predictive); Fast (110% higher than predictive). Method: Resting metabolic rate: indirect calorimetry. (Cosmed calorimetry, Fitmate model). Body composition: bioelectrical impedance analysis, Multifrequency (5, 50, and 500kHz), tetrapolar (InBody370).

Outcomes

The VLCKD phase was completed based on the weight loss result: 12.2 kg, equivalent to 87.14% of the predicted weight in 78 d. The patient started a hypocaloric diet, referred to as the "adaptation" phase, with a progressive supply of 800 to 1200 kcal/d. The final three steps of the treatment were aimed to encompass a progressive incorporation of different food groups and dietary interventions focused on eating behavior to support weight maintenance. There was a loss of 1.2 kg in 115 d, reaching 13.4 kg, a value close to the expected, being 11.4 kg of fat mass (FM; Table 1).

According to BES, initial data is an indicator of the presence of binge eating (18 points) according to the established cutoff point (>17 points presence of compulsion at a moderate level). After the treatment, it resulted in the absence of binge eating (11 points). Regarding food cravings, in the FCQ-T, the outcome was 119 points, decreasing to 77 points. On the food cravings scale (state), from 7 points pretreatment, the patient had a final score of zero. In the pretreatment, the DAS scores resulted in 18 points (7 stress, 7 anxiety, and 4 for depression), with an increase to 26 points in the post-treatment (15 stress, 5 anxiety, and 6 for depression).

There was 94.2% weight loss at the end of the nutritional intervention protocol, resulting in a eutrophic BMI of 23.6 kg/m^2 (18.5–24.9 kg/m^2) and FM of 32% (reference value: >35% obesity), changing from obesity to overweight (reference value: 32–35%) [15]. At the end of the VLCKD, the RMR showed an increase of 78.5% from the initial one, reaching normal levels for the Harris–Benedict and Mifflin–St Jeor predictive equations (reference value: 90–110%) [20,22], maintaining this level in the 1-y follow-up (Table 1). The patient engaged in home weighing once a week, face-to-face consultations, and frequent telemedicine with medical staff. She underwent vitamin and mineral supplementation. Biochemical data were performed before the start of ketosis, after ketosis, and after the end of treatment (Table 2). The patient was encouraged to engage in light physical activity (e.g., walking).

Discussion

Obesity is a condition affected by factors such as genetics, environment, and psychosocial factors that may result in an imbalance between energy intake and expenditure. It is an excess fat storage that arises from an imbalance between energy intake and expenditure. Disordered eating and eating disorders can also cause obesity and increased fat accumulation [1–3,5]. Reduction in RMR is commonly seen after weight reduction therapy for the treatment of obesity and in individuals with a history of weight cycling [23], common in eating disorders such as bulimia nervosa [7]. This case was challenging because of the cognitive-behavioral changes that occur when a cognitive restriction is used alongside the internalization of ideals of thinness and fatphobia, which are part of the psychopathology of bulimia nervosa. Additionally, the history of unsuccessful diets impaired the patient's RMR. Therefore, examining the efficacy of the VLCKD intervention, in this case, appears more arduous compared with a case of obesity without an eating disorder. This phenomenon of adaptive thermogenesis is a disproportionate decrease in RMR in relation to body mass [4,11], which makes negative energy balance difficult [24].

Some individuals decrease the ability to lose FM because of adaptive thermogenesis [24]. A hypometabolic state is a determinant for short-term weight regain, regardless of the association between lifestyle change and medication. However, in the VLCKD approaches, no changes were observed in the RMR in the medium and short term [11,25,26]. However, these studies did not present individuals with a low RMR/fat-free mass (FFM).

A recent study looked at the correlation between a low-carbohydrate diet and RMR in adults. An association was observed between low carbohydrate consumption, higher fat, and protein with higher RMR. In this study, there were individuals with an RMR/FFM <19 kcal/kg [27]. Therefore, it is possible to suspect that individuals with a low RMR-to-FFM ratio could benefit from a low-carbohydrate diet to increase RMR. The patient in the present report, in addition to having a low RMR/FFM, evolved with an

Table. 2
Laboratory assessment monitored during the protocol

Biochemical tests	Reference values	Preintervention	End of VLCKD (78 d)	End of protocol (193 d)
Fasting plasma glucose (mg/dL)	70–99	94	87	84
Fasting plasma insulin (mU/L)	2–13	17	8	7
HbA1c (%)	<5.7	5.5	5.1	5.4
LDL-C (mg/dL)	<110	78	80	77
HDL-C (mg/dL)	>50	48	43	66
Triacylglycerides (mg/dL)	<150	67	80	80
Homocysteine (mmol/L)	5–14	10.1	9.3	5.4

HbA1c, hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol

increase in RMR/FFM during VLCKD, maintaining it after the protocol (Table 1).

Shifting dramatically, the energy metabolism to ketogenesis and fatty acid oxidation has a profound effect on mitochondrial function and content. There is an increase in the expression and activity of mitochondrial proteins involved in oxidative phosphorylation and fat oxidation. These findings provide more conclusive support for an increase in oxidative capacity in response to nutritional ketosis [28]. In addition to serving as energy substrates, the ketone body can also exert favorable metabolic effects, serving as metabolic regulators and signaling molecules. β-HMB exerts antioxidant and anti-inflammatory effects, may affect epigenetics by inhibiting histone deacetylation, suppresses sympathetic nervous system activity and reduces lipolysis, and, through unknown mechanisms, plays a role in appetite suppression. It is tempting to speculate that exposure to ketosis leads to metabolic adaptation with improved mitochondrial bioenergetics [25,29].

β-HMB increases mitochondrial respiration. These findings could provide a partial explanation of the observed rise in metabolic rate in elevated ketone states and could aid in the development of novel interventions for obesity [30].

Considering behavioral aspects involved in the traumatic history of weight changes and reinforcement of cognitions of bulimia psychopathology [23] and increased food cravings and binge eating [8], in the present results, we were able to note that these two parameters improved with treatment time. In the case of food cravings, initial data (119 points) decreased to 77 points. The patient showed no binge eating according to BES (11 points). We highlight the previous work with individualization of nutritional treatment, psychotherapy, and medication that, over time, prepared the patient to be able to differentiate self-imposed restriction from the effects of VLCKD.

In addition to the remarkable increase in RMR presented over the months by the patient in this study, there was sustained loss of FM and recovery of FFM over the 1-y follow-up. There is a greater predisposition to body weight regain, especially after weight loss in individuals with decreased thermogenesis [4,31]. However, published research demonstrates that VLCKD can induce significant weight loss and maintain its effectiveness for 2 y. This is attributed to VLCKD for causing FM loss and little FFM loss, preserving more metabolically active tissue (skeletal muscle and bone) [11,24].

According to the results of the patient's biochemical tests, blood glucose, high- and low-density lipoprotein cholesterol (HDL-C and LDL-C, respectively) values improved during the treatment period, in line with a study that evaluated the effect of VLCKD weight loss. The results of this other investigation demonstrated that individuals who received the VLCKD diet had a greater decrease in body weight, triacylglycerides, LDL-C, and an increase in HDL-C [32]. Another study showed that patients in nutritional ketosis had significantly lower baseline blood glucose and triacylglycerides than those without ketonuria, in addition to exhibiting a reduction in LDL-C [13]. Thus, it could be suggested that calorie restriction associated with the ketogenic state is more successful in improving body composition and metabolic control in individuals with obesity compared with isocaloric or high-carbohydrate and low-fat diets [17,32].

Conclusion

In this study, the patient with obesity associated with hypometabolism (low RMR/FFM) benefited from the use of a VLCKD to increase RMR in the short term, favoring a negative energy balance. This suggests that VLCKD could be an effective and safe nutritional intervention for weight loss in a short period of time, as long as it is supervised by a dietitian or other specialized health professional throughout the whole treatment. In relation to the numeric results, it seems positive, as well as the possible associated benefits, such as reduction of cardiovascular risk factors and discrete loss of FFM levels; however, further research is necessary to evaluate the effects on the overall relationship with food and its long-term repercussions in a larger number of individuals.

Declaration of Competing Interest

None.

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