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EFFECTS OF KETOGENIC DIET ON CARDIOVASCULAR RISK FACTORS: A CASE REPORT

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Abstract

Overweight and obesity are the major risk factors for cardiovascular diseases and their complications. They are associated with the onset of metabolic syndrome and adipose tissue dysfunction. Weight loss and dietary carbohydrate restriction have been reported to have a positive outcome on these disorders. Among various diets, the ketogenic diets, which are very low in carbohydrates, have become very popular.

We reported the case of a 40-year-old overweight man with abdominal fat accumulation, dyslipidemia and a family history of diabetes and hypertension, subjected to a weight loss program consisting of a 3-week very-low-carbohydrate ketogenic diet (VLCKD) to evaluate the effectiveness of this diet on cardiovascular risk factors.

Our case report showed that VLCKD led to an improvement in anthropometric, clinical and metabolic characteristics. We reported a significant reduction in body weight, blood lipid, glucose and insulin levels along with a halved HOMA-IR index after 3-week of VLCKD. Noteworthy was the marked reduction in the thickness of aorto-mesenteric fat compared to the baseline. Furthermore, we have not reported alterations in the main serum electrolytes and in the hepatic and renal function parameters.

Therefore, VLCKD appear to be a safe and effective program for weight loss and cardiovascular risk reduction in overweight and obese patients with visceral fat accumulation and metabolic syndrome.

Keywords: *Ketogenic diet, cardiovascular risk, metabolic syndrome, visceral fat.*

Introduction

Nowadays, cardiovascular diseases (CVDs) remain the leading cause of mortality worldwide (1). Therefore, controlling the CVD risk factors represents a major challenge.

CVD risk factors have evolved over the past decades. In fact, although on the one hand there is a lower influence of smoking and untreated hypertension and dyslipidemia, on the other hand there is an increase in overweight and obese patients with type 2 diabetes mellitus or metabolic syndrome (2,3). The latter is a cluster of metabolic abnormalities including insulin-resistance, high blood pressure, increased glucose and cholesterol levels, visceral fat accumulation (4).

Overweight and obese patients have excessive fat accumulation. However, recent studies have shown that not all fat depots have the same inflammatory and metabolic activities and that the accumulation of visceral fat, rather than subcutaneous fat, is associated with an increased cardiovascular risk (3).

Reliable methods for measuring body fat and its distribution are therefore of fundamental importance.

Anthropometric indices, such as body mass index (BMI), waist circumference (WC) and waist-to-hip circumference are simple and non-invasive methods to evaluate fat visceral accumulation but their reliability is still debated.

Although imaging techniques, including computed tomography (CT) and magnetic resonance imaging (MRI), have shown remarkable advances in ability to accurately and reliably quantify body fat distribution and to selectively distinguish subcutaneous adiposity from visceral abdominal adipose tissue (5), they remain expensive and, in the case of CT, expose subjects to ionizing radiation.

To overcome the limitations of these measurements, Monaco and colleagues (6) have developed an ultrasound protocol for the evaluation of visceral fat by measuring the thickness of fat between the abdominal aorta and the superior mesenteric artery (SMA), the aorto-mesenteric fat thickness (AMFT).

The "nutritional transition", characterized by increase in food supply, consumption of Western diets and reduced physical activity, has been one of the main factors of the considerable increase in the prevalence of overweight and obesity in recent decades (7). Therefore, there is a broad consensus that the most preventable drivers are modifiable factors associated with the environment and lifestyle, including dietary habits.

Weight loss is generally presented as a therapy to improve the conditions, including diabetes and metabolic syndrome, of such patients. In particular, dietary carbohydrate restriction has been reported to have a positive outcome on these disorders (8,9). Among various diets, the ketogenic diets, which are very low in carbohydrates (usually less than 50g/day), have become very popular.

We reported the case of an overweight man with abdominal fat accumulation, dyslipidemia and a family history of diabetes and hypertension, subjected to a weight loss program consisting of a 3-week ketogenic diet to assess the effects on cardiovascular risks.

Case Report

A 40-year-old overweight man with abdominal fat accumulation and high cholesterol levels underwent a 3-week very-low-carbohydrate ketogenic diet (VLCKD), integrated by an aminoacid supplement with whey protein, given their emerging role in maintaining muscle mass during weight loss (10). The energy intake of the VLCKD was about 800 kcal/day. The average daily distribution of macronutrients and micronutrients was 5-10% of carbohydrates (<50 g/day) derived mainly from vegetables, 60-70% of protein corresponding to 1.4 g/Kg of ideal body weight calculated by Lorentz's equations (11) and 25-30% of lipids. Multivitamin, proper integration of mineral salts, alkalizing product, herbal remedies with diuretic and hepatoprotective properties were indicated. A minimum intake of 2 L of mineral water was recommended during the day. Ketosis state was evaluated by urinary keto-stick.

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Methods

Anthropometric parameters, blood pressure, blood sample analysis and AMFT were determined at baseline (day 0) and after 3 weeks of VLCKD (day 22). The anthropometric measurements were carried out according to standard procedures (12,13) by using calibrated instruments. The waist circumference was measured at the midpoint between the lowest rib bone and the iliac crest; the hip circumference was taken at the greatest posterior protuberance of the buttocks; the BMI was calculated as weight/height2, Kg/m^2.

Both at baseline and after 3week of VLCKD, a venous sample was taken after an overnight fast of 8-12 hours for the evaluation of the following parameters: glucose, insulin, total cholesterol, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol, triglycerides, aspartate aminotransferases (AST), alanine aminotransferases (ALT), creatinine, sodium and potassium.

Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) was calculated using fasting glucose and insulin values (14).

Systolic and diastolic blood pressure was recorded using a standard sphygmomanometer and reporting the average of three measurements obtained at 2-minute intervals (15).

Finally, AMFT was recorded by abdominal ultrasonography according to the procedure previously validated by Monaco et al. (6). Briefly, measurements were performed by compression of the abdominal cavity, 1 cm above the navel, with the subjects in the supine position and after a forced expiration. We reported the distance between the anterior wall of the abdominal aorta and the posterior wall of the SMA measured in a longitudinal scan at its maximum convexity; furthermore, we reported the distance between the abdominal aorta and the SMA measured in a transverse scan when they appear to be perfectly rounded.

Results and Discussion

In the present study, the dietary intervention was well tolerated, no side effects occurred and the patient compliance was high. Compared to baseline (day 0), 3-week dietary treatment has led to an improvement in anthropometric, clinical and metabolic characteristics, as indicated in Table 1.

The patient lost 11.22% of his initial body weight with an 11.15% reduction in BMI. The waist and hip circumferences were also decreased by 8.9% and 3.7%, respectively, after 3 weeks of VLCKD.

The effectiveness of the ketogenic diet in the treatment of weight loss has been widely reported (16) although the hypotheses on the underlying biological mechanisms are controversial. The various assumptions include reduction of caloric intake, satiating effect of proteins with reduced appetite, metabolic changes, effects on appetite control hormones, reduction in lipogenesis and increased lipolysis (17,18).

We also observed positive effects on cardiometabolic parameters. VLCKD was in fact associated with a significant improvement in most parameters of glucose and lipid metabolism. We reported a significant reduction in total cholesterol (-11.9%), LDL-cholesterol (-14.2%) and triglycerides (-24.6%) after 3 weeks of VLCKD compared to baseline.

In agreement with our results, the most recent studies show widely that the state of ketosis can really lead to significant benefits in blood lipid profiles, reporting a particularly marked effect on blood triglyceride levels along with positive effects on the reduction of total and LDL cholesterol (16,19). Volek et al. (20) also reported that very low carbohydrate diets increase the size of LDL particles by promoting a reduction in the risk of cardiovascular disease, since it is known that smaller LDL particles have greater atherogenicity.

Furthermore, there is a direct correlation between diet-related effects and endogenous cholesterol synthesis as the key enzyme involved in cholesterol biosynthesis is activated by insulin. Since the reduction of carbohydrates in the diet decreases glucose and insulin levels, this could be the mechanism by which ketosis can improve lipid profiles (16).

Remarkably, in this case report we found a significant reduction in blood glucose (-10.1%), as well as the insulin level and the HOMA-IR index had halved after the dietary treatment (-45.6% and -51.3%, respectively). Our results are supported by data in the literature reporting that ketogenic diets are often associated with decreased blood glucose levels and improved insulin sensitivity (18). We also evaluated some biochemical parameters to verify the safety of VLCKD on kidney and liver and we have not reported changes in liver enzymes (AST and ALT) and in parameters of renal function (creatinine).

This is in agreement with previous studies that report that VLCKD can be used safely for a limited 3-week period to stimulate ectopic and visceral fat loss, ensure weight loss and improve metabolism without compromising the kidneys, liver function and nutritional status including sarcopenia (19,20).

Furthermore, although ketogenic regimens are known to cause electrolyte imbalances, we have not reported alterations in the main serum electrolytes (sodium and potassium) probably thanks to the correct integration of mineral salts during the dietary treatment. Indeed, as proposed by Castaldo et al. (19), these complications can be avoided by using appropriate supplements.

In our case report, the blood pressure was considerably stabilized after 3 weeks of VLCKD. Ketogenic diets are known to regulate blood pressure, although studies on this topic are scarce. However, recent studies suggest a potential role of dietary proteins in regulating blood pressure. In particular, the different source of proteins, animal or vegetable, and their amino acid composition seem to interfere with the mechanisms of regulation of blood pressure promoting an increase or reduction (22).

Teymoori and colleagues (23) reported that the dietary amino acid pattern rich in branched chain, aromatic and alcoholic amino acids and proline increased the risk of hypertension while the sulphuric and small amino acid pattern tended to reduce the risk of hypertension. Since amino acids are consumed in combination and not separately they interact and show synergistic effects, therefore further studies are needed to evaluate and understand the beneficial and harmful effects of the amino acid associations on chronic diseases.

Finally, a significant reduction in the thickness of aorto-mesenteric fat compared to the baseline was noteworthy. A decrease of about 20% and 30% was recorded in the AMFT measurements performed on the transverse and longitudinal ultrasound scanning, respectively, after the dietary treatment (Figures 1 and 2).

The AMFT measurement represents a valid tool to assessing the accumulation of visceral fat. It is indeed an economic, non-invasive and independent-operator, therefore reproducible and reliable method (6).

Visceral fat accumulation plays a crucial role in the onset of cardiometabolic diseases,therefore its reduction can be very effective in reducing risk factors.

In fact, numerous evidences show that visceral fat can be considered a real endocrine organ that produces biologically active molecules such as pro- and anti-inflammatory cytokines and adipokines (3). As described by Matsuzawa (24), the dysregulation of adipokines, especially of adiponectin, seems to be the key mechanism for the development of type 2 diabetes, metabolic syndrome and cardiovascular disease. In fact, adiponectin has antidiabetic, antiatherogenic and anti-inflammatory functions and its plasma levels decrease in subjects with visceral fat accumulation.

Conclusion

Some markers such as the AMFT measure, indicative of visceral fat, together with the calculation of the HOMA-IR index, indicative of insulin resistance, and circulating lipid levels can be a useful tool to identify subgroups of patients characterized by an increased cardiovascular risk.

The use of "food as medicine" is an ancient concept based on a healthy lifestyle including eating habits and physical activity aimed at preventing and treating metabolic imbalances.

VLCKD appear to be a safe and effective program for weight loss and cardiovascular risk reduction in overweight and obese patients with visceral fat accumulation and metabolic syndrome.

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Table 1. Anthropometric, clinical and metabolic parameters before and after the dietary treatment.

Characteristic	Baseline (day 0)	After VLCKD (day 22)
Body weight, Kg	98	87
BMI, Kg/m^2	29.6	26.3
Waist circumference, cm	112	102
Hip circumference, cm	109	105
Glucose, mg/dl	89	80
Insulin, µU/ml	9.05	4.92
HOMA-IR	1.99	0.97
Total cholesterol, mg/dl	201	177
HDL cholesterol, mg/dl	46.3	45.8
LDL cholesterol, mg/dl	141	121
Triglycerides, mg/dl	114	86
AST, UI/dl	25	25
ALT, UI/dl	28	27
Creatinine, mg/dl	1.15	1.10
Sodium, mEq/L	146.3	144.5
Potassium, mEq/L	3.90	4.07
SBP, mmHg	95	113
DBP, mmHg	61	72
Heart rate, bpm	60	63

**Abbreviation: BMI, body mass index; HOMA-IR, homeostasis model assessment of insulin resistance; SBP, systolic blood pressure; DBP, diastolic blood pressure.*
*** The reported values are provided by the patient*

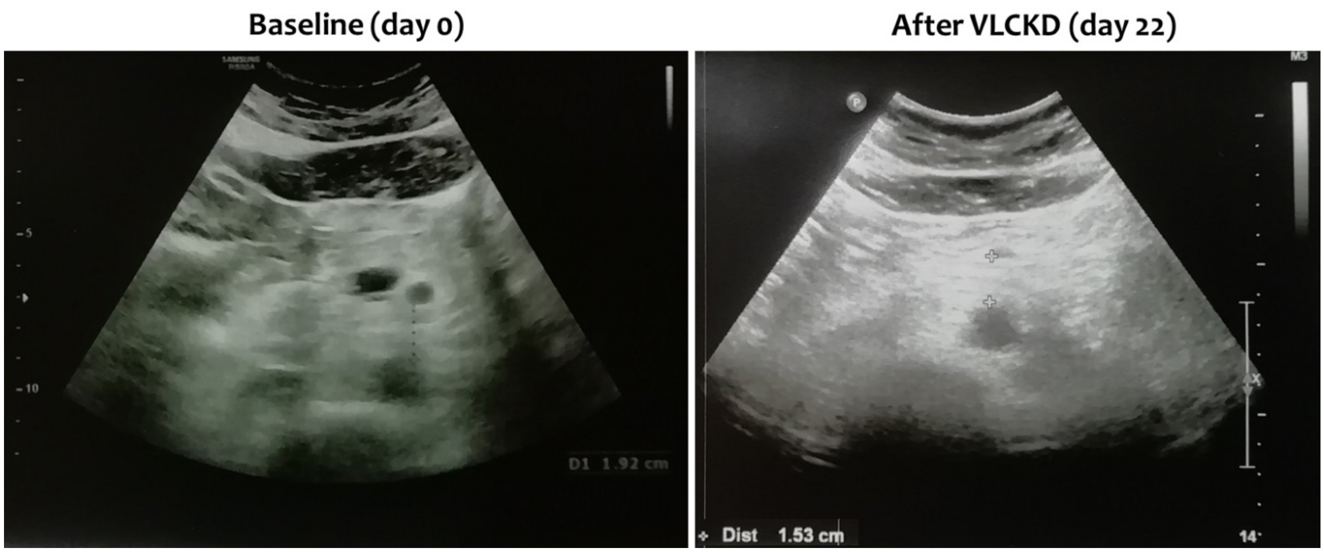

Figure 1. Measurements of the aorto-mesenteric fat thickness (AMFT) performed on the transverse ultrasound scanning in the patient before and after dietary treatment.

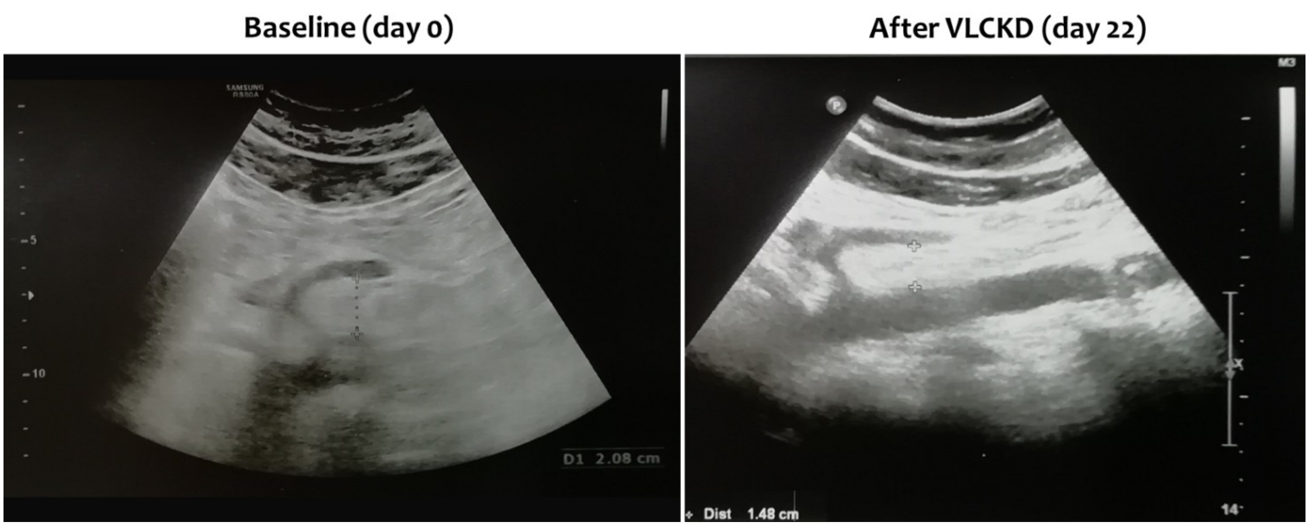

Figure 2. Measurements of the aorto-mesenteric fat thickness (AMFT) performed on the longitudinal ultrasound scanning in the patient before and after dietary treatment.