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Case report

Killing Three Birds with One Stone: VLCKD In a Female Patient with Obesity, Celiac Disease and Migraine

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Summary: Very Low-Calorie Ketogenic Diets (VLCKD) are indicated as a valid tool to treat morbid obesity. Growing evidence suggests an association between overweight/obesity and migraine symptoms and shows how weight reduction can improve pain and headache in these patients. This case report describes the clinical management of a patient affected by obesity, migraine, and celiac disease with a 6-month VLCKD supplemented with a probiotic. The nutritional intervention allowed a significant weight reduction and improvement of migraine symptoms, while being safe and suitable in the setting of a celiac disease.

Key words: VLCKD, celiac disease, migraine, obesity

Introduction

Very Low-Calorie Ketogenic Diets (VLCKD) contain a restricted quantity of energy (450-800 kcal per day) with a reduced content of carbohydrates (<50 g per day). VLCKDs are used as a therapeutic tool to treat morbid or complicated obesity (hypertension, type 2 Diabetes Mellitus, dyslipidemia, Obstructive Sleep Apnea Syndrome, Metabolic Syndrome, severe osteopathies or arthropathies); severe obesity with indication to bariatric surgery (during the pre-surgical period); and patients with indication to rapid weight-loss for severe comorbidities. Also, VLCKDs are indicated to treat other clinical conditions, such as: non-alcoholic fatty liver disease (NAFLD), drug-resistant epilepsy, Alzheimer disease, Parkinson disease, or cerebral neoplasms.

Migraine is a chronic neurological disorder characterized by attacks of moderate or severe headache and reversible neurological and systemic symptoms, and it is one of the most prevalent and disabling medical illnesses in the world (1,2). Growing evidence suggests a relationship between migraine severity and obesity. In particular, clinical features of migraine are associated to body mass index (BMI), and significant weight loss turned out to be associated to a clinical improvement of headache in patients with obesity featuring migraine (3–6).

Celiac disease (CD) is one of the most common food-related disorders worldwide, caused by an immune-mediated enteropathy against dietary gluten. The pathogenesis and diagnosis is well known and the only proven way to effectively treat CD is a gluten-free diet (GFD)(7,8). Strict adherence to the diet, in some

cases, is challenged by the presence of small amounts of gluten components in certain foods (9,10). Thus, a low-grade tissue inflammation and intraepithelial lymphocytosis can persist in celiac patients albeit following a GFD (11).

A gut-colonizing probiotic strain that is able to enforce tight junctions, to digest gliadin and up-modulate an anti-inflammatory gut response, could be a valid safeguard to guarantee a GFD (12). *Bifidobacterium longum* ES1 (CECT 7347) in an experimental model of gliadin-induced enteropathy, reduced inflammation halt enterotoxicity, as evaluated by histology tests (13). *Bifidobaterium longum* ES1, when administered along with a GFD to a cohort of children diagnosed with CD, significantly improved all signs and symptoms of the disease (14). Similarly, the findings of a small pilot study by ours carried out in a population with non-celiac gluten sensitivity (NCGS), suggested that a combined strategy of naturally gluten-free diet therapy with administration of the probiotic strain ES1, improve CD clinical symptoms and stabilized the intestinal microbiota (15).

The aim of this report is to describe the clinical case of a female patient affected by obesity, migraine and celiac disease, treated with VLCKD and ES1 strain for weight reduction.

Materials and Methods

We hereby describe the clinical case of a 50 year-old female who was followed for a diet therapy aimed at weight reduction at the "Obesità e Lavoro" Center in the Occupational Medicine Clinic L. Devoto, Fondazione Ca' Granda, Ospedale Maggiore Policlinico (Milan, Italy). A diet therapy was prescribed by a multidisciplinary team including a physician and a dietitian. Anthropometric variables were measured by impedance analysis, InBody230 Wunder, Biospace Co., Ltd. Blood parameters were collected along with several step of the diet therapy at the aforementioned center.

The patient voluntarily underwent a cycle ketogenic gluten-free diet for weight loss, for 24 weeks. During the dietary intervention, anthropometric and clinical variables were closely monitored and collected, as well as the plasmatic parameters regarding renal function, glycaemia, insulin, cholesterol (total, LDL and HDL), uric acid, and ketonuria and proteinuria. Collected data were analyzed retrospectively and reported in this work. The patient provided informed consent to the use of her data for further analysis and/or production of scientific reports.

Results

We present here a clinical report of a 50 year-old female celiac patient, who survived from kidney carcinoma. On February 2019 the patient's weight reached 92.5 kg (BMI 31.1), she started a new ketogenic diet cycle, following a VLCKD diet protocol (700 Kcal) based on products whose raw materials are gluten-free (Supplementary material TableS1) associated with *Bifidobacterium longum* ES1 probiobitc especially designed for celiac subjects. In the first phase she used 5 substitutive products per day; after one month of VLCKD, the patient lowered to 4 substitutive products per day, and introduced animal protein accompanied by vegetables during one of the main meals. From June she was allowed to consume animal proteins in both the main meals and from July carbohydrates were gradually reintroduced in the diet. Anthropometric analysis and blood analysis were carried out in January and June 2019 (Table 1). Data show that the diet did not affect kidney function.

The overall weight reduction during the VLCKD cycle was 12.2 kg, with a mean weight reduction of 3 kg per month (in June 2019 her BMI was 26.1). During the diet therapy she reported mild headache for the first 2 weeks, which ameliorated and then disappeared after the first month, together with an improvement of the articular pain (no more need of NSAIDs). VLCKD ended in August 2019, followed by a balanced hypocaloric-hypoglycemic diet according to the indication of the new pyramid of the Mediterranean Diet (16).

Discussion

The prevalence of obesity shows an increasing trend worldwide and is related to important personal

Table 1. Anthropometrics and lab routine at baseline and after 6-month diet therapy

	Reference values	Baseline	After 6-months
Height	cm	173	173
Weigh	kg	92.5	80.3
BMI	Kg/m2	31.1	26.7
FM	kg (%)	39.9 (42.1%)	28.8 kg (34.4%)
FFM	kg (%)	55.3 (58.9%)	53.3 kg (65.6%)
Glycaemia	mg/dl 60-100	98	99
Triglycerides	mg/dl <150	101	81
Total Chol.	mg/dl <200	198	201
HDL Chol.	mg/dl >40	58	57
LDL Chol.	mg/dl <100	124	142
Insulinemia	mU/ml 2.0-25.0	13.9	10.9
HOMA index	0.23-2.50	3.36	2.66
Creatininemia	mg/dl 0.66-1.09	0.75	0.80
Urinary ketonic bodies	Up to 2	0.0	0.0
Albuminuria	Up to 15	15.0	0.0

BMI: Body Mass Index; FM: Fat Mass; FFM: Fat-Free Mass; HDL: high-density lipoprotein; LDL: low-density lipoprotein; HOMA: Homeostasis Model Assessment.

and social burden. It is well known that obesity is associated with other medical conditions and complications (e.g. cardiovascular, metabolic, depressive), but growing evidence suggests an association between obesity and pain disorders including headache and migraine (4,6).

VLCKDs are indicated as a therapeutic tool to treat morbid or complicated obesity, severe obesity with indication to bariatric surgery, patients with indication to rapid weight-loss for severe comorbidities(17–20). Also, VLCKDs are used to treat other clinical conditions, such as: non-alcoholic fatty liver disease (NAFLD), drug-resistant epilepsy, Alzheimer disease, Parkinson disease, or cerebral neoplasms. Scientific evidences show that after 6 months, overweight patients who followed diets low in carbohydrates lost more weight than patients who followed low-fat diets, with improvements also in systolic and diastolic pressure, fasting blood glucose, triglycerides, total cholesterol and high-density lipoprotein (HDL) cholesterol (21). According to a recent meta-analysis conducted to study whether the VLCKDs (providing < 50g of carbohydrates per day) can reduce weight and cardiovascular risk factors more effectively than conventional low-calorie diets (LCDs) (limited energy diets, in which less than 30% of energy is provided by fat), it was observed that VLCKDs lead to greater reduction of weight, triglycerides and diastolic blood pressure. Conversely, it was associated with increased HDL and low-density lipoprotein (LDL) cholesterol levels. In addition, the subjects assigned to a VLCDs had a greater weight reduction over the long term than those who followed a LCD (22). Thus, VLCKD could be considered an alternative tool for the management of obesity.

Nevertheless, despite the promising results of VLCKD in weight reduction, the maintenance of such a reduction should be considered as a main issue. In fact, the problem concerning obesity is not only represented by weight loss, but by maintaining the weight achieved. Therefore, a detailed follow-up of the patients who underwent a VLCKD diet would be of interest.

Migraine is one of the many pathological conditions that has been reported to benefit from ketogenic diet (23–28). The underlying mechanisms of KD efficacy could be related to the enhancement of mitochondrial metabolism which might

counteract neural inflammation (29). The improvement of migraine symptoms in our case report are in accordance with these findings.

Our reported results are in accordance with the evidence provided by literature, describing a positive role of ketogenesis on weight reduction but also on migraine symptoms. Therefore, VLCKD represent a valid, safe, and useful therapeutic tool for the management of complex patients such as the one hereby described. Limited literature is available on VLCKD and celiac patients, but this case represents an example of how, under strict medical supervision, a ketogenic gluten-free diet plus a probiotic well-documented for its anti-gliadin role (*B. longum* ES1), as well as being effective for weight reduction (30), is safe and suitable for celiac subjects.

Conflict of interests: No potential conflict of interest relevant to this article was reported by the authors

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