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A F N S ISSN 2575-0194 ARCHIVE OF FOOD AND NUTRITIONAL SCIENCE

Case Study

Beneficial effects of a ketogenic diet in a woman with Charcot-Marie-Tooth disease

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Abstract

Objective: To evaluate the effects on quality of life and body composition of a Ketogenic Diet (KD) in a woman with Charcot-Marie-Tooth (CMT) disease.

Methods: Physical (PCS) and mental (MCS) health conditions were evaluated with the SF-36 questionnaire; dual-energy x-ray absorptiometry was used to determine body composition; parameters were determined at baseline and after 12 weeks of KD.

Results: At baseline PCS and MCS were 20.6 and 20.7 respectively with 37.9% fat mass. After 12 weeks SF-36 values significantly improved: PCS 55 and MCS 66.1 with 33.9% fat mass.

Conclusion: KD improved the patient's quality of life and decreased fat mass. Further studies will be needed to better elucidate the beneficial effects of KD among people with CMT.

More Information

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Submitted: November 05, 2022
Approved: November 14, 2022
Published: November 15, 2022

How to cite this article: Rostanzo E, Aloisi AM. Beneficial effects of a ketogenic diet in a woman with Charcot-Marie-Tooth disease. Arch Food Nutr Sci. 2022; 6: 068-072.

DOI: 10.29328/journal.afns.1001040

Keywords: Ketogenic diet; Charcot-Marie-Tooth disease; Ketone bodies; KD; Neuropathy

Introduction

Academic interest in the potential of Ketogenic Diets (KD) has grown drastically in the last decade, with an increasing body of evidence regarding the therapeutical role of KD in a broad range of diseases.

Evidence suggests that a Ketogenic Diet, i.e. a "high-fat, low-carbohydrate, adequate-protein" dietary strategy, is effective against several diseases, including intractable epileptic seizures, metabolic disorders, tumors, autosomal dominant polycystic kidney disease, neurodegeneration, skeletal muscle atrophy, peripheral neuropathy [1] and recently also for eating disorders [2].

A study in mice suggested that features of neuropathy may be improved by a KD which positively impacted mechanosensation, reduced insulin elevations and promoted axonal growth. Moreover, an assessment of axonal growth revealed that ketone bodies increased neurite outgrowth, with the greatest growth occurring with a combination of glucose and ketone bodies as fuel sources [3].

Obesity, increased fat mass, insulin resistance, and metabolic disorders promote peripheral neuropathy with evident and intractable motor and sensory impairments [4]. In contrast, a KD may be beneficial to neurons by lowering fat oxidation and the associated ROS production which could improve peripheral nerve disease associated with poor mitochondrial function. These approaches may benefit peripheral axons and combat axonal degeneration, motor and sensory dysfunction, and pain experienced by millions of patients with neuropathies [5].

Charcot-Marie-Tooth (CMT) disease, a hereditary motor and sensory neuropathy that comprises a complex group of more than 50 diseases is the most common inherited neuropathy [6]. It encompasses a broad range of conditions characterized by motor and sensory polyneuropathy predominating in the distal lower limbs [7].

CMT is associated with a significant impairment of health-related quality of life [8]. The disparity between people with CMT and normal subjects was reported to be greater for physical dimensions than for mental health dimensions [9].

Heckett, et al. [10] examined body composition with a dual-energy X-ray absorptiometry (DXA) scanner and its association with physical performance, quality of life and clinical indicators in CMT disease. They found that greater lean body mass and lower fat mass of specific body regions are associated with better physical performance and higher quality of life [10].

An accurate analysis of body composition and an

appropriate dietary approach is essential for the quality of life in people with CMT and there is a lack of research reporting the effects of a tailored diet as a supporting strategy for the management of patients with CMT. Hence we hypothesized that KD may be a feasible approach for weight management and that ketone bodies should have a positive action against neurodegeneration.

The aim of the present case study was to evaluate the effects on the quality of life and body composition of a low-calorie KD in a woman with CMT.

Patient and methods

Patient description

The patient was a 39-year-old woman born in Italy. She was born at term and both her parents were healthy and were tested genetically with no case of the neuropathic disease in their families.

At 4 years old the pediatrician noted she had no patellar reflex and started to investigate for neuropathy. The patient showed pes cavus and hand atrophy, typical signs of CMT [11,12]. She underwent surgery to correct her hands and feet at 8 and 21 years old.

At 24 years old she received a diagnosis of hereditary motor and sensory neuropathy by the University Hospital "San Martino" of Genoa, with an indication for physiotherapy and rehabilitation programs to ameliorate ambulation.

The following genetic mutations were recorded:

Polymorphism (c.102G>C) in the *GDPA1* gene in which a silent variant in the first exon converts a codon specifying serine, Ser34Ser; it was also found in a five-generation Turkish family with autosomal recessive CMT2 in 2009 [13].

These types of mutations lead to recessively or dominantly inherited peripheral neuropathies indicating that *GDAP1* is essential for the viability of cells in the peripheral nervous system [14]. Such types of gene mutation have been observed particularly in patients from Mediterranean countries, but also in those from other European regions [15-18].

Quality of life assessment

The patient's general health conditions were assessed with the Short Form 36 (SF-36) questionnaire [19]. It includes one multi-item scale that assesses eight health concepts: 1) limitations in physical activities because of health problems; 2) limitations in social activities because of physical or emotional problems; 3) limitations in usual role activities because of physical health problems; 4) bodily pain; 5) general mental health (psychological distress and well-being); 6) limitations in usual role activities; 7) vitality (energy and fatigue); 8) general health perceptions. The first four scales are included in the Physical Component Summary (PCS) and the other four in the Mental Component Summary (MCS). Each one of the eight scales is assigned a score from 0 to 100, where a higher score means better health in that area [20].

The study was conducted in full agreement with national and international regulations and the Declaration of Helsinki (2013). Verbal and written consent was obtained from the patient.

The patient was taking part in a study on mental well-being and nutrition approved by the Ethics Committee for Research in the Human and Social Sciences (CAREUS) of the University of Siena with protocol number 2742.

Anthropometric measurements and body composition

The patient's body weight was measured to the nearest 0.1 kg on electronic devices (SECA®) in underwear and without shoes. The height was calculated with a stadiometer (SECA®) to the nearest 0.1 cm; Body Mass Index (BMI) was calculated as weight (kg)/ height (m^2).

Waist and hip circumferences were taken with a measuring tape in meters.

To evaluate body composition a whole-body dual-energy X-ray absorptiometry (DXA) scanner was used (Osteosys-Primus, Meditech, Italy). The scan was performed under standardized conditions and following the standardized positioning on the scanning bed.

After the scan, the sub-region analysis tool was used to draw customized regions of interest (ROI).

Dietary treatment

The patient's body composition was taken into account to prescribe a suitable KD with an energy intake of around 1000 kcal/die (≤ 50 g/die of carbohydrates).

Dietary adherence was tested through urinary ketone excretion, as measured with keto-sticks, until the end of the KD.

The KD provided 55% of energy from fat and < 10% of calories from saturated fat. Dietary lipid intake derived from extra virgin olive oil, fresh fish, and nuts.

The patient followed the KD and was tested with the same instruments and under the same conditions at 5 weeks (T1) and at 12 weeks (T2) to test for any changes.

Results

Short Form-36 (SF-36)

SF-36 results at baseline and after 12 weeks are reported in Table 1.

All the SF-36 items, and thus both PCS and MCS, were improved after 12 weeks. The main improvements recorded were in Role- physical and Role-emotional items.

Table 1: SF-36 outcomes at baseline and after 12 weeks. Each one of the eight scales is assigned a score from 0 to 100, where a higher score means better health in that area.

ITEM	Baseline	After 12 weeks
Physical functioning	15	35
Role-physical	25	100
Bodily pain	22.5	45
General Health	20	40
Vitality	5	45
Social functioning	12.5	62.5
Role-emotional	33.3	100
Mental health	32	52
Physical Component Summary (PCS)	20.6	55
Mental Component Summary (MCS)	20.7	66.1

Body composition

At baseline, the patient's BMI was 23.1 and, according to BMI categorization, she was classified as normal weight (BMI < 24.9) [21]. However, according to the DXA evaluation, she was classified as Normal Weight Obese (NWO). The NWO syndrome is characterized by normal body weight and BMI but high-fat mass (> 30%) [22]. The patient's fat mass was 37.9% at baseline with a Visceral Adipose Tissue (VAT) of 114.4 cm^2. Cross-sectional studies have proposed that a threshold level of VAT exceeding 110 cm^2 in women induces deleterious changes in the metabolic profile [23].

Body circumferences and DXA were repeated after 5 weeks and after 12 weeks. The outcomes are shown in Table 2.

The patient showed a fat mass accumulation, particularly in the lower limbs; 49.9% of the total body fat was in the lower limb region, probably due to difficulty walking. Moreover, the patient had a lower lean body mass. In this regard, healthy females compared with women with CMT had lower % body fat, less android fat and lower limbs fat mass [10].

Table 2: Anthropometric measurements and DXA outcomes at baseline, after 5 weeks, and after 12 weeks of KD.

	Baseline	5 weeks	12 weeks
Weight (kg)	52	51	49
BMI	23.1	22.7	21.8
Waist (cm)	80	78	74
Hip (cm)	92	92	88
Total Body			
% Fat Mass	37.9	37	33.9
Lean Body Mass (kg)	31.3	30.8	30.7
Fat Mass (kg)	20.1	19.1	16.6
Trunk			
Lean Body Mass (kg)	15.2	15.1	15.3
Fat Mass (kg)	7.9	7.7	6.4
Upper Limbs			
Lean Body Mass (kg)	2.8	2.9	3.1
Fat Mass (kg)	1.9	1.9	1.7
Lower Limbs			
Lean Body Mass (kg)	8.7	8.2	8.2
Fat Mass (kg)	9.9	9.2	8.3
Visceral Adipose Tissue (cm^2)	114.4	103.1	79.6
Visceral Adipose Tissue (g)	550	495	382
Skeletal Muscle Mass Index (SMI)	5.1	4.9	5.0

Furthermore, we evaluated the presence of sarcopenia expressed as Skeletal Muscle mass Index (SMI) (appendicular skeletal muscle mass/height^2); the cutoffs by gender are men: 7.26 kg/m^2, women: 5.5 kg/m^2 [24]. Strength and physical performance were not evaluated due to the patient's grip impairment and difficulty in walking.

After 12 weeks of the KD, the patient showed a decrease in both body weight and total body fat percentage with the maintenance of total lean body mass. VAT returned to the threshold levels (< 110 cm^2). Lower limb fat mass decreased from 9.9 kg at baseline to 8.3 kg after 12 weeks, while total body fat percentage remained above 30%.

Discussion

The aim of the case study was to evaluate the effects of a KD on a woman with CMT.

The potential of KD has been shown in several neurological diseases. In our patient the beneficial effects of the KD were associated with an improvement in the quality of life and a decrease in fat mass (diet and surgically induced) is known to improve the inflammatory state in obese subjects [25]. Moreover, the anti-inflammatory and neuroprotective roles of ketone bodies are known [26].

The major ketone bodies β-hydroxybutyrate and acetoacetate have potential neuroprotective properties and are known to have direct effects on specific inflammatory proteins, transcription factors, reactive oxygen species, mitochondria, epigenetic modifications and gut microbiome composition [27].

Moreover, a neutral lipid-enriched high-fat diet promoted the maintenance of myelinated axons in neuropathic mice after the 6-week-long dietary intervention [28].

Hachett, et al. [10] reported that optimizing favorable body composition profiles (higher lean body mass and lower fat mass) in people with CMT disease may be clinically important for their quality of life.

Tools such as body impedance analysis (BIA), which is widely used among the general population, may be inadequate in patients with neurological disorders [29]. For this reason, DXA is considered one of the most versatile imaging techniques for the evaluation of metabolic bone disorders, such as osteoporosis, sarcopenia and obesity [30] and for the evaluation of body composition.

To our knowledge, this is the first study to evaluate the feasibility of a KD and its effects on health and body composition in a patient with CMT. Currently, the treatment of patients with CMT is focused on physiotherapy, rehabilitation, and pain management; there is no cure or effective drug treatment for CMT and surgical treatment includes correction of skeletal and soft-tissue abnormalities [11,31,32].

Our aim was to highlight the importance of nutritional support for these patients. An adequate diet should prevent or delay the onset of several diseases related to an excess of fat mass and low physical activity. In addition, for people with CMT, KD could be a valid approach against neuronal degeneration [5]. Further research with a larger number of subjects is needed to confirm our conclusion.

Acknowledgment

We thank the patient for her consent and the University of Siena for financial support.

Author contributions

All authors have contributed equally. All authors have read and agreed to the publication of the manuscript.

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