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Clinical Condition, Nutritional Status and Food Consumption of Patients with Maple Syrup Urine Disease

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ABSTRACT

Maple syrup urine disease (MSUD) is an inborn error of metabolism caused by an enzyme deficiency and leads to the accumulation of branched-chain amino acids (BCAAs), which are toxic to the body in high concentrations. Part of the treatment is based on dietary control and a reduced intake of BCAAs. The objective of this study was to describe the clinical condition, nutritional status and food consumption of patients with MSUD. Two patients diagnosed with MSUD were selected. Interviews and nutritional, body composition, and food consumption assessments were carried out. Energy, macronutrients, micronutrients, BCCAs, and fiber contents were estimate. All clinical data were obtained from medical records. Both patients showed manifestations of neuropsychomotor development delay with intellectual disability. Regarding nutritional status, one patient was overweight, and the other was underweight, with low functional capacity in both of them. A monotonous dietary pattern and a low intake of energy, proteins, vitamins, and minerals were observed, but there was a high consumption of BCAAs by one of the patients. Developmental and intellectual disabilities were observed besides the changes in nutritional status (underweight and overweight), low functional capacity, dietary inadequacies in terms of energy, macronutrients, and micronutrients, besides a monotonous food consumption pattern.

Keywords: *Inborn Errors of Metabolism, Maple Syrup Urine Disease, Branched-Chain Amino Acids, Body Composition, Clinical Reports*

Introduction

The estimated global incidence of maple syrup urine disease (MSUD) is 1 in 185,000 newborns (Chuang, 2001). We do not know the number of people affected in Brazil. MSUD is also called leukinosis or branched-chain ketoaciduria. First described in 1954, it is a type of aminoacidopathy and consists of an inborn error of metabolism (IEM) of autosomal recessive inheritance. It is characterized by a marked

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increase in the serum concentration of branched-chain amino acids (BCAAs): leucine, isoleucine and valine (Menkes *et al*., 1954). The increase in BCAAs is caused by a deficiency in the branched-chain keto-acid dehydrogenase complex, that is necessary for the metabolization of these amino acids (Chuang, 2001; Martins *et al*., 2006).

MSUD can be classified into "classic" and "variant" forms. The classification depends on the age at the onset of symptoms and the severity and manifestations of the disease. The classic form is the most serious and manifests in the neonatal period. The variant forms are divided into four: 1) intermediate, where the symptoms and clinical manifestations do not appear in the neonatal period, instead occurring between the ages of 5 months and 7 years, and are the most serious manifestations of the variant form; 2) intermittent, where the patient's development is initially normal and metabolic decompensation occurs in the presence of an infectious condition or due to excessive protein consumption; 3) thiamine-responsive, which is similar to the intermediate form, but an improvement in the clinical picture is observed with the administration of thiamine; 4) lipoamide dehydrogenase deficiency E3, where manifestation in the neonatal period is uncommon, and which is differentiated by persistent lactic acidosis (Chuang, 2001).

The clinical manifestations of MSUD are diverse and depend on residual enzyme activity. Neurological manifestations are its main symptoms, such as neuropsychomotor developmental delay (NPMDD) and epileptic seizures, where the typical clinical feature of the disease is increased serum BCAAs. Patients also have a sugary odor similar to maple syrup, which is noticeable mainly in the urine. In addition to neurological impairment and the characteristic odor, impaired food intake is frequent among individuals with the disease due to restrictions related to amino acids. The age at diagnosis, neonatal condition and long-term metabolic control directly influences the development of individuals (Menkes *et al*., 1954; Rocha *et al*., 2007; Chuang, 2001).

Treatment is based mainly on the adoption of a BCAA-restricted diet, with minimal supplies of these nutrients throughout life, seeking to minimize neurological damage and maintain adequate plasma levels of amino acids. For this reason, dietary monitoring and follow-up are essential to promote satisfactory growth and development, avoid protein catabolism and maintain an adequate nutritional status (Chuang, 2001; Prasad *et al*., 1998; Schonberger *et al*., 2004; Strauss and Morton, 2003).

Few clinical reports have investigated nutritional status, body composition, or food consumption related to MSUD, instead only focusing on protein restriction and the use of a BCAA-free diet. However, food consumption and anthropometric assessments are essential. MSUD is a disease that limits the consumption of proteins, which are key macronutrients in the synthesis of muscle mass (Huang *et al*.,

2016) that affects the individual's weight and height development.

Therefore, this study aims to describe the clinical condition, nutritional status, and food consumption assessments of two patients with MSUD of the medical genetics outpatient clinic of a university hospital.

Methods

The medical genetics outpatient clinic of the university hospital has two patients (n = 2) with MSUD. This project was submitted to and approved by the Ethics Committee of the Federal University of Uberlandia through CAAE 83642017.4.0000.5152. The participants signed free and informed consent forms and were interviewed in July of 2018.

Data Collection

Demographic, clinical, biochemical and treatment data were collected from medical records. Weight history was also collected. All measures were performed by a trained registered dietitian.

Anthropometric Assessment and Nutritional Status

The anthropometric variables measured were weight, height, tricipital skinfold (TSF), subscapular skinfold (SSF) and arm circumference (AC), following the criteria in the literature (Lohman *et al*., 1988; Frisancho, 1990). Body fat was estimated and classified using the two-fold protocol according to Frisancho (1990).

In order to assess the body composition, bioelectrical impedance analysis (BIA) (Biodynamics 450, Seattle, WA) was performed, including data of fat free mass index (FFMI), body fat mass (BFM) and phase angle (PA). PA values above 8.02° for men and 6.98° for women, and a BFM percentage between 12.0% and 23.9% for women and between 8.0% and 19.99% for men. These values were considered adequate (Barbosa-Silva *et al*., 2005; Lohman, 1991).

Functional Capacity Assessment

The handgrip strength test was performed to evaluate functional capacity using a Jamar® dynamometer in the dominant hand and in the non-dominant hand (Hillman, 2005; Schlüssel *et al*., 2008). The values were classified according to Bohannon, *et al*. (2006). Values between 41.1 and 58.9 kgf for men and between 23.1 and 32.6 kgf for women for the non-dominant hand and values between 44.3 and 63.6 kgf for men and 26.7 and 34.4 kgf for women for the dominant hand were considered adequate.

Food Consumption Assessment

The frequency of consumption (dietary pattern) of different food groups was evaluated using a food frequency questionnaire (FFQ) and a 24-hour dietary recall (24HR), applied at the time of the interview and two more times in the following week through telephone contact, on non-consecutive days and including one day of the weekend (Casey *et al*., 1999). The household measures from the 24HR were converted into grams or milliliters using the Table for the Assessment of Food Consumption in Homemade Measures (Pinheiro *et al*., 2005). The macronutrient and micronutrient intake were evaluated using the Dietpro® software version 5.8. The mean of three 24HR was obtained for energy, carbohydrates, proteins, total lipids, branched-chain amino acids, total fibers, calcium, iron, zinc, phosphorus, potassium, magnesium, sodium, total cholesterol, thiamine, riboflavin, pyridoxine, niacin, vitamin C, and saturated, monounsaturated and polyunsaturated fatty acids. Macronutrient and micronutrient intake adequacy were obtained by comparing the consumption with the recommended Dietary Reference Intakes (DRIs) and the Brazilian Guideline for Dyslipidemia and Atherosclerosis Prevention (Frazier *et al*., 2014; Institute of Medicine, 2000), according to sex and age. The adequacy of micronutrient intake was evaluated according to the equation: $z = y - EAR / \sqrt{SDneed + (SDint / n)}$.

In the equation, z is the value in the Z-score table that corresponds to the probability of ingestion of a given nutrient being adequate for an individual; y is the average intake of a given nutrient obtained from applying the food survey on n days; EAR is the estimated average nutrient requirement; SDneed is the standard deviation of need, and SDint is the standard deviation of intrapersonal consumption. In clinical practice, it is usual to request a three-day food record (n = 3). Finally, we subtracted of the adequacy value from 100% to reach the prevalence of inadequacy values.

To check if the macronutrients and micronutrients were in accordance with the recommendations of the DRIs, EAR and adequate intake (AI) were used, following the evaluation recommendations (Institute of Medicine, 2000; 2011; 2019).

The amount of BCAAs consumed was estimated based on the protein content (in grams) in the foods and the conversion factors described in the literature (Table 1). They consider the concentration (%) of each of the BCAAs in the proteins according to the food group (da Cruz and Valadares, 2014).

Statistical Analysis

Descriptive statistics were performed to obtain absolute and relative frequencies. The medians, means and standard deviations of the data were also determined. The data were compiled and analyzed using the Statistical Package for Social Sciences software version x.25 (SPSS Inc., Chicago, Ill., USA).

Table 1: Amount (%) of BCAA present in the proteins (g) of the different foods.

Foods	Leucine	Isoleucine	Valine
Meats	10	6-7	7-8
Milk	9.8	6.4	6.9
Vegetables	4.6	3.5	4.1
Fruits	4.4	2.9	3.7
Cereals	8.1	3.8	5.1
Butter	8.3	5.8	6.7

Adapted from Herber, 2012 [24]

Results

Sample Description

The study was carried out on two patients: P01, a female patient who was 20 years old at the time of the study and diagnosed with MSUD at 12 years old; and P02, a male patient who was 25 years old and diagnosed at 14 years old. Both had NPMDD with intellectual disabilities.

The clinical condition of the patients is shown in Table 2. The patients were born at term, are children of non-consanguineous parents and do not have siblings with manifestations of the disease. In their first months of life, they presented manifestations such as inefficient breastfeeding, anorexia, lethargy and irritability, and used infant formula. P01 presented epileptic seizures at two years of age, while P02 presented epileptic seizures a few months after birth. They presented NPMDD and slower postural development in the first months of life.

P01 started monitoring with a neuropediatrician at ten years old, due to complaints of irritability and learning difficulties. She was hospitalized at eleven years old for urinary tract infection, showing elevated blood lactate and ammonia concentrations. After that, the diagnostic hypothesis of "mitochondrial disease" was considered. Under the supervision of a geneticist, she received diagnostic confirmation of MSUD at twelve years old. She also presented manifestations of other diseases: polycystic ovary syndrome, manifested at 15 years old, and biliary lithiasis, requiring a cholecystectomy in 2018.

Due to the NPMDD, P02 started monitoring at around two years old. At four years old, he was referred to a geneticist for follow-up, later leaving the clinic. He returned at 14 years old, when the diagnosis of MSUD was confirmed and the supplementation with thiamine (10mg / kg / day) began. The symptoms improved one year after starting treatment, but the patient complained of diffuse pain in his lower limbs and hyperkinetic behavior. He started using a BCAA-free formula at 16 years old, which maintained his clinical status, without any manifestation of symptoms. However, after seven years of use, he stopped using the formula due to poor flavor acceptance.

Both patients improved their symptoms when they started thiamine supplementation. Therefore, they may suffer from the thiamine-responsive variant form. In July of 2018, at the time of the evaluations for the present clinical reports, the patients presented no complaints and were clinically well, metabolically stable and asymptomatic. On physical examination, they had dry skin and hair. They maintained daily use of thiamine (P01 = 150mg / day; P02 = 100mg / day). In addition, P01 also used L-carnitine (200mg) + zinc gluconate (6mg), valproic acid (250mg / day) and baclofen (10mg / day).

Table 2: Characteristics of patients with MSUD.

Variable	Patient 1	Patient 2
Current age	20 years old	25 years old
Sex	Female	Male
Diagnostic age	12 years old	14 years old
Motor development milestones	Head control: 8 months Crawl: 1 year and 2 months Speak: 2 years and 6 months	Sit: 11 months Walk: 2 years and 8 months
Developmental complications	Inefficient breastfeeding, anorexia, lethargy and irritability	Inefficient breastfeeding
Epileptic seizures (age)	2 years old	First month of life
Form of the disease	Variant: Thiamine-responsive	Variant: Thiamine-responsive
Thiamine supplementation (mg / day)	150	100

Anthropometric Assessment

The body mass index (BMI) of the patients was assessed together with their weight and height history. The BMI of P01 (data from 2010 to 2018) ranged from 17.27 kg/m^2 to 25.9 kg/m^2, showing a large change in weight. The weight history shows that P01 increased in weight and changed classification range over the years. It shows that the onset of weight gain coincided with the diagnosis of polycystic ovary syndrome. P01 was classified as overweight at the time of the study, according to BMI. In addition, her total body fat percentage increased, as indicated in the BIA and subscapular skinfold (SSF). However, arm circumference (AC) and arm muscle circumference (AMC) percentiles were within the limits of normal weight. Her arm muscle area (AMB), arm fat area (AFA) and tricipital skinfold (TSF) percentiles indicated depletion risk. The patient's dynamometry indicated low functional capacity. The BMI of P02 (data from 2008 to 2018) increased from 15.03kg/m^2 in 2010 to 17.2kg/m^2. This history demonstrated the constancy of the low weight of P02. All of the anthropometric parameters of P02 were below the eutrophic limits, indicating malnutrition or depletion, with the exception of TSF and SSF. The FFMI, BFM and PA (by BIA) showed adequate body compartment percentages. The dynamometry of the patient also indicated low functional capacity.

Table 3: Anthropometric profile of patients with MSUD.

Variables	Patient 1	Category	Patient 2	Category
Current age	20 years old	-	25 years old	-
Sex	Female	-	Male	-
Weight (kg)	62.4	-	59.0	-
Height (m)	1.5	-	1.8	-
BMI (kg/m^2)	25.9	Overweight	17.2	Underweight
AC (cm)	27.7	Normal	24.5	Malnutrition
Adequacy of AC (%)	103.3	Normal	77.0	Moderate Malnutrition
AMC (cm)	18.8	Normal	20.6	Malnutrition
Adequacy of AMC (%)	90.8	Normal	73.8	Moderate Malnutrition
AMA (cm^2)	21.6	Risk of depletion	23.8	Depletion
AFA (cm^2)	20.3	Risk of depletion	11.5	Depletion
TSF (mm. mean+_SD)	28.3 ± 0.4	Risk of depletion	12.3 ± 0.9	Normal
SSF (mm. mean+_SD)	26.6 ± 0.4	Overweigh	9.3 ± 0.4	Normal
FFMI (Kg/%)	42.6 / 68.5%	Low	51.7 / 87.6%	Normal
BFM (Kg/%)	19.8 / 31.6%	High	7.3 / 12.4%	Normal
PA (º)	8.7	Adequate	14.0	Adequate
BMR (kcal)	1413	-	1582	-
GS dh (Kgf)	4.0	Low functional capacity	8.0	Low functional capacity
GS ndh (Kgf)	6.0	Low functional capacity	18.0	Low functional capacity

Subtitle: BMI: Body Mass Index (kg/m^2); AC: Arm Circumference; AMC: Arm Muscle Circumference; AMA: Arm Muscle Area; AFA: Arm Fat Area; TSF: Triceps Skinfold – obtained from the average of three sequential measurements; SSF: Subscapular Skinfold – obtained from the average of three sequential measurements; FFMI: Fat Free Mass Index; BFM: Body Fat Mass; PA: Phase Angle; BMR: Basal Metabolic Rate; GS dh: Dominant hand grip strength; GS ndh: Non-Dominant hand grip strength. SD: Standard Deviation.

Assessment of Food Consumption

Both patients showed monotonous diets, with low frequency of fruits and vegetables consumption and a high frequency of processed foods. The intake of both was below the recommendations for energy, fiber, protein, vitamins and minerals, with a high prevalence of inadequacy of all micronutrients, except for the consumption of vitamin C by the P02. P01 presented an adequate intake of BCAAs, while P02's intake of these amino acids was above the recommendation for patients with MSUD.

In the 24HR and FFQ analysis, it was observed that P02 frequently consumed cereals, breads, beans, cakes, sweets, juice, meat, milk and derivatives. However, animal foods were eaten in small portions. His protein intake was below the recommendation, but he had a high intake of BCAAs. P01 rarely consumed animal products, only consuming eggs. This explains her low protein and BCAA intake. Her diet was based on the consumption of cereals, beans and vegetables.

Both patients showed adequate consumption of cholesterol, total lipids and saturated fatty acids, but inadequate portions of polyunsaturated and monounsaturated fatty acids, according to the

recommendations. In addition, they presented an adequate carbohydrate intake percentage according to the Acceptable Macronutrient Distribution Range (Institute of Medicine, 2000).

Table 4: Consumption of macronutrients and BCAA's of patients with MSUD.

Energy and nutrients (Recommendation)	Patient 1	Patient 2
	Mean ± SD	
Energy – kcal	1276.3 ± 567.5	1564.6 ± 130.7
Energy – (35 – 45 kcal/kg/day)	20.4 ± 9.1	26.5 ± 2.2
Carbohydrate – (45-65%)	60.9 ± 28.8	58.5 ± 12.3
Protein – (10-35%)	7.6 ± 3.5	11.2 ± 1.1
Protein – (1.1 – 1.7 g/kg/day)	0.4 ± 11.5	0.7 ± 4.1
Leucine – (15 – 50 mg/kg/day)	27.6 ± 4.6	69.9 ± 3.9
Isoleucine – (10 – 30 mg/kg/day)	13.2 ± 2.2	43.1 ± 2.6
Valine – (15– 30 mg/kg/day)	17.7 ± 2.9	51.2 ± 1.7
Lipids – (20-35%)	31.4 ± 11.9	30.2 ± 4.1
Monounsaturated fatty acids – (15%)	7.0 ± 2.5	7.8 ± 1.4
Polyunsaturated fatty acids – (5-10%)	15.2 ± 2.0	9.2 ± 2.2
Saturated fatty acids – (<10%)	7.2 ± 2.2	9.3 ± 0.6
Cholesterol - (<300 mg. mean ± SD)	0.0 ± 0.0	149.2 ± 21.6

SD: Standard Deviation.

Table 5: Consumption of micronutrients and fibers of patients with MSUD.

Micronutrients and Fibers	DRI (EAR)	Patient 1 Mean values ± SD	Prevalence of inadequacy (%)	DRI (EAR)	Patient 2 Mean values ± SD	Prevalence of inadequacy (%)
Calcium (mg)	800.0	86.7 ± 29.9	85	800.0	299.9 ± 29.2	85
Iron (mg)	8.1	3.6 ± 1.7	85	6.0	3.9 ± 0.8	70
Phosphorus (mg)	580.0	302.0 ± 134.2	85	580.0	566.7 ± 51.6	70
Magnesium (mg)	255.0	112.6 ± 42.4	98	330.0	163.2 ± 31.5	98
Niacin (mg)	11.0	3.8 ± 3.2	85	12.0	6.3 ± 4.0	70
Riboflavin (mg)	0.9	1.8 ± 0.1	70	1.1	0.2 ± 0.0	93
Thiamine (mg)	0.9	0.6 ± 0.2	70	1.0	0.4 ± 0.1	85
Pyridoxine (mg)	1.1	0.5 ± 0.1	85	1.1	0.2 ± 0.1	93
Vitamin C (mg)	60.0	53.6 ± 22.6	70	75.0	599.8 ± 250.5	2
Zinc (mg)	6.8	3.0 ± 1.0	85	9.4	6.1 ± 1.2	70
AI comparison						
	AI			AI		
Fibers (g)	25.0	20.0 ± 5.6	Bellow	38.0	11.7 ± 3.8	Bellow
Potassium (mg)	2600.0	1953.2 ± 825.3	Bellow	3400.0	3000.2 ± 1198.6	Bellow
Sodium (mg)	1500.0	1848.3 ± 840.9	Above	1500.0	1765.4 ± 235.3	Above

Subtitle: DRI: Dietary Reference Intakes; EAR: Estimated Average Requerement; AI: Adequate intake

Discussion

This clinical report involved two adult patients with MSUD, neuropsychomotor developmental delay (NPMDD), and intellectual disability. Regarding nutritional status, P01 was overweight and showed a high amount of body fat, and P02 was underweight. Both presented anthropometric parameters indicating the depletion of fat-free mass and low functional capacity. Regarding food consumption, they showed a monotonous diet, with low energy, macronutrient and micronutrient consumption. Finally, P02 showed high consumption of BCAAs.

Many studies describe the pathophysiology of MSUD, focusing on several aspects of clinical manifestations (Huang *et al*., 2016; Schonberger *et al*., 2004; Sgaravatti *et al*., 2003; Morton *et al*., 2002; Kimball and Jefferson, 2006; Zinnanti and Lazovic, 2012; Chuang *et al*., 2004). To the best of our knowledge, no studies have investigated the nutritional status, body composition and food consumption. These topics are especially important, considering that the treatment focus is based on dietary control, essentially reducing the BCAAs intake. BCAA reduction has the potential to reduce or limit the intake of protein sources. This could cause deficits in the development of fat-free mass, changes in body composition and in the functional capacity.

The first symptoms presented by the patients occurred in the initial six months of life, manifesting primarily through epileptic seizures and later by NPMDD. When P01 was 12 years old and P02 was 14 years old, both were treated with thiamine and showed an improvement in their health condition. Because of the improvement they are diagnosed with the thiamine-responsive variant form of MSUD.

Considering that the patients seem to have a thiamine-responsive form, the use of this vitamin results in a decrease in the accumulation of BCAAs (leucine, isoleucine and valine). Therefore, the low consumption of BCAAs associated with the use of thiamine may explain the absence of clinical manifestations in the patients at the time of the study.

According to Schonberger, *et al*. (2004), even with continuous treatment, NPMDD is more common in children with MSUD. Sgaravatti, *et al*. (2003) and Morton, *et al*. (2002) show that neurological damage occurs due to the low density of white matter, changes in myelination, in addition to atrophy and cerebral edema. Schonberger, *et al*. (2004) show that these brain changes can be explained by the deficit of BCAAs in the brain, in contrast to the high concentrations of these amino acids in the blood. This reduction is approximately one third of that found at the serum level and enough to disrupt the synthesis of some proteins and neurotransmitters.

In terms of anthropometry, the AMA measure suggests muscle mass inadequacy for P01. In this

patient, muscle mass depletion is corroborated by the BIA and the low FFMI. P02 received a classification of depletion and malnutrition for most anthropometric parameters. The below normal weight values of both patients may be related to the low consumption of energy and foods of animal origin. These foods are composed by proteins with a high biological value (rich in BCAAS) and indicated in less quantity for patients with MSUD. Leucine is an important regulator of protein synthesis. This effect is mediated through the mammalian target of rapamycin-dependent (mTOR) and mTOR-independent pathways (Kimball and Jefferson, 2006). In addition, low energy consumption when associated with low protein intake may indicate protein-calorie malnutrition.

The patients' PA values seem to indicate good cell balance (Eickemberg *et al*., 2011). PA is associated with cell quality, size and integrity and a healthy individual tends to have values between 5 and 15 degrees (Barbosa-Silva *et al*., 2005; Eickemberg *et al*., 2011). PA reflects the state of hydration and the amount and types of tissues, such as muscles and fat mass, so some studies indicate that PA can reflect nutritional status and be a predictor of malnutrition. However, these authors point out that PA may be able to detect malnutrition at an early stage (Rinaldi *et al*., 2019). The adequate PA value may not predict good nutritional status because it refers to two patients with chronic nutritional impairment. There may be an impairment resulting from the disease, or the patients may not have applied their maximum strength because they did not understand the activity.

Regarding the food consumption analysis, protein intake is below the recommended range: 1.1g/kg to 1.7g/kg of proteins with a low BCAA content (Frazier *et al*., 2014). Even with a low total protein intake, one of the patients engaged in excessive consumption of BCAAs. Therefore, the consumption of BCAA-free proteins could be optimized. In addition, other protein consumption strategies could be used on these patients because thiamine supplementation seems to increase tolerance to BCAAs in patients with the thiamine-responsive form of MSUD (Zinnanti and Lazovic, 2012).

The values of energy intake per kilogram of weight are below the recommendation (35 to 45 kcal / kg) and this may explain the low weight of P02 (Frazier *et al*., 2014). In contrast, P01 is overweight despite the evidence of low energy consumption, and her clinical profile suggests that being overweight may be associated with polycystic ovary syndrome. There is an association between polycystic ovary syndrome the disease and excess weight, abdominal adiposity and insulin resistance (Escobar-Morreale, 2018).

Frazier, *et al*. (2014) suggest the adoption of a high-calorie and high-protein diet with low BCAA content. According to these recommendations, the patients' diet showed to be inadequate. These authors also recommend that patients receive vitamin and mineral supplementation. Such supplementation could

be recommended for the patients in the present study, considering that their micronutrient intake was below the recommendations (Institute of Medicine, 2000).

It is important to carry out an individualized and constant nutritional intervention. Increased energy supply is recommended for P02 and BCAA-free proteins are recommended for both patients. These changes are essential for adequate food intake and metabolism, minimizing the loss of muscle mass. In addition, it is necessary to improve the diet quality to increase the vitamins and minerals supply.

P02 received supplementation of a specialized diet for MSUD for seven years, but interrupted the treatment because he did not like the taste of the specific nutritional supplement. Therefore, alternative ways of offering adequate amounts of proteins and their amino acids should be considered.

Conclusion

The patients with maple syrup urine disease showed a neuropsychomotor developmental delay and an intellectual deficit. Regarding their nutritional status, one was overweight, and the other was underweight, with a high fat percentage, low functional capacity, and showed fat-free mass depletion in both patients. A low intake of energy, macronutrients, micronutrients, and a monotonous diet were observed. Therefore, these patients need individualized, continuous and specialized nutritional intervention, in order to correct their dietary deficiencies and unhealthy dietary pattern. Besides, we also recommended evaluate the anthropometric and functional capacity assessment in the clinical routine.

Consent to Participate: Written informed consent was obtained from the parents.

Consent to Publish: The parents has consented to the submission of the case report to the journal.

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