Applied nutritional investigation

Nutrient intake in neurofibromatosis type 1: A cross-sectional study


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A B S T R A C T

Objectives: To evaluate nutrient intake among adult neurofibromatosis type 1 (NF1) patients.

Methods: A cross-sectional study of 60 NF1 patients (29 men, 31 women) who were ≥18 y old and were evaluated from September 2012 to September 2013 in a neurofibromatosis outpatient reference center. Patients underwent nutritional assessment, including anthropometric and dietary data collection. Food intake was evaluated using three, non-consecutive, self-reported 24-h dietary recall surveys, and nutrient intake was analyzed according to the recommendations of the dietary reference intake document.

Results: Forty-three patients (72%) recorded energy consumption lower than the estimated daily energy requirement (EER). Men (25/29, 86.2%) were more likely to fail to meet their target EER, compared to women (18/31, 58.1%) (P = 0.016). Inadequate intake of vitamin D, magnesium, calcium, and pyridoxine was noted between men and women, and all patients consumed excess sodium. NF1 patients did not consume adequate amounts of fiber or vitamins A and C. Excessive consumption of saturated fatty acids and lipids was also observed in both male and female patients.

Conclusions: In this study, NF1 patients consumed an unhealthy diet that was rich in fats and sodium and lacking in fiber, vitamins, and minerals. Further studies are needed to investigate the role of these dietary and nutritional patterns in the severity of the clinical manifestations of NF1.

Introduction

Neurofibromatoses are a group of genetic diseases that are characterized by multiple neural tumors, as well as cutaneous symptoms [1]. Neurofibromatosis type 1 (NF1) is the most prevalent form, and is caused by inherited or de novo mutations on chromosome 17, resulting in reduced neurofibromin synthesis, which subsequently reduces tumor suppression [1]. The diagnostic criteria for NF1 are almost exclusively clinical, and were established by the National Institute of Health (NIH) Consensus [2]. The most common clinical features of NF1 are café au lait spots, dermal neurofibromas, plexiform neurofibromas, axillary and/or inguinal freckling, Lisch nodules, and bone dysplasia. NF1 can also exhibit multisystemic involvement, including ophthalmic, cardiovascular, endocrine, musculoskeletal, central and peripheral neurologic, learning, and speech disorders [3–5].
Although the clinical manifestations of NF1 are well established in the literature, the nutritional aspects are not well documented. A recent search of the MEDLINE, SCOPUS, Lilacs, and SciELO databases did not identify any clinical studies regarding the eating habits, dietary patterns, or nutrient intake of NF1 patients. Therefore, investigations regarding the nutritional habits of NF1 patients may be relevant, as several features of this disease may be related to nutritional status or food intake. NF1 may also be affected by conditions that are linked to inadequate eating habits, such as underweight [6], short height [6], changes in bone metabolism [6,7], low levels of vitamin D [8], reduced muscle strength [9], and constipation [10]. Considering the influence that nutritional status can have on NF1 patients’ health and quality of life, the present study aimed to assess the nutrient intake of NF1 patients, thereby providing novel clinical information.

Methods

Sample

This cross-sectional study included all consecutive NF1 patients >18 y old who were evaluated in a Brazilian Neurofibromatosis Outpatient Reference Center from September 2012 to September 2013. The study was approved by the Ethics Committee of the Federal University of Minas Gerais, and all patients provided their written informed consent. Patients were excluded based on musculoskeletal limitations, the use of medications that might compromise the nutritional status assessment, or the presence of diseases that required a specific diet or food consumption.

Data collection

Data regarding each individual’s food intake were obtained using three self-reported 24-h dietary recall surveys (24 HR) on non-consecutive days, 2 d during the week and 1 d during the weekend (a non-typical day), in accordance with the recommendations of the Institute of Medicine (IOM) [11], which proposes at least two 24 HR be used for similar studies. This method has been successfully used in previous studies [12,13], as well as in large population-based surveys, such as the National Health and Nutrition Examination Survey [14] or the Brazilian “Pesquisa de Orçamento Familiar” [15]. The 24 HR can be used for the accurate analysis of both macronutrients and micronutrients, and imposes a relatively minimal burden on the respondents [12,13,16]. The interviewer was trained regarding how to record portion sizes, and the subjects provided detailed descriptions of all food and drink they consumed, as well as the cooking methods, ingredients, and the use of oil and salt during food preparation. After collecting the 24 HR, potential confounding variables were evaluated by questioning the subjects regarding food quantities, added ingredients, and the brands they consumed.

The amount of each nutrient that was consumed was converted into grams using a table of measurements [17], and the mean value for the 3 d was used in our analysis. Any related dietary supplements were also considered in the survey and were included in the data analysis. The following dietary constituents were evaluated: energy, protein, lipids, cholesterol, carbohydrates, dietary fiber, calcium, magnesium, manganese, phosphorus, iron, sodium, potassium, copper, zinc, thiamine, riboflavin, pyridoxine, niacin, vitamin C, vitamin A, and vitamin D. Saturated fatty acids, monounsaturated fatty acids (MUFA), polyunsaturated fatty acids, and linoleic acids were also evaluated. The Brazilian Table of Food Composition was used for the analysis [18], and if a food or nutrient was not found in the Table of Food Composition, other tables were used [19,20]. For the analysis of micronutrients, the ingested amounts were compared to the daily estimated average requirement (EAR). When EAR values were not available, the adequate intake (AI) value for that nutrient was used. For participants who consumed more than the EAR or AI, their intake was compared to the tolerable upper intake level (UL) [11].

For the analysis of nutrient intake, the probability of adequacy (Z-score) corresponds to the probability that nutrient intake is normally distributed. Therefore, we used the Z-score to determine the corresponding P value, which was multiplied by 100 to obtain the probability of adequate intake. To calculate the prevalence of inadequate nutrient intake, the probability of adequate intake was subtracted from 100, as proposed by the IOM [11].

EARs have been established for calcium, copper, iron, magnesium, phosphorus, zinc, pyridoxine, thiamine, riboflavin, niacin, vitamin A, and vitamin D, therefore Z-score analysis was used for these nutrients. Vitamin A and C have established EARs, although the Z-scores cannot be analyzed, as these nutrients have intrapatient variability of >60%. Therefore, qualitative analysis is more appropriate for vitamins A and C, as it uses the EAR and recommended dietary allowances (RDA) values to classify the intake as adequate or inadequate, by comparing the average ingested value directly to the EAR and RDA values. For nutrients that use Al reference values, if the mean intake is less than the AI, the adequacy of the intake cannot be determined, and qualitative analysis was considered more appropriate, which was conducted by classifying the intake as under or over the Al values [11].

The total energy consumed by each NF1 patient was compared to their estimated energy requirements (EER) proposed by the IOM, taking into consideration their sex, weight, age, height, and physical activity. The energy consumed was then classified as under or over the EER values [11,21]. Macronutrients distributions, as a percentage of the total energy intake (TEI), were compared to the acceptable macronutrients distribution range for adults [11,21]. The World Health Organization (WHO) recommendations for fatty acids [22] and cholesterol [23] were also used.

As it is difficult to accurately estimate the amount of salt added during cooking, many studies only consider the sodium that is contained in the reported foods, resulting in an underestimated daily sodium intake. To address this limitation, the average daily salt intake for the Brazilian population (8.13 g) [15] was added to the patients’ reported sodium intake values, and it was the only source of salt used in the analysis. All foods and cooked dishes were analyzed in the absence of salt.

Anthropometrics and laboratory blood tests were included to characterize our patient population. The anthropometric measurements followed the protocol proposed by WHO [24]. Blood tests included complete blood count, fractional and total cholesterol, tricylglycerol, albumin, and fasting blood glucose levels. Weight and height were measured and used to calculate the patient’s body mass index (BMI) [24]. The BMI categories used in this study were normal weight (BMI 18.5–25 kg/m²), underweight (BMI < 18.5 kg/m²), and overweight (BMI ≥ 25.0 kg/m²) [24]. To complement the BMI analysis, waist circumference (WC) and body fat percentage (BF) were evaluated. According to WHO [25], the minimum normal cut-off points for WC are 94 cm (men) and 80 cm (women). To calculate the BF, body density was calculated using the linear regression equations for men and women that were proposed by Durnin and Womersley [26]. These equations do not use a plenty of skinfold thickness, which may be of interest in NF1 patients, as the presence of a neurofibroma at the measurement site was an exclusion criterion in this study. The BF was then calculated using the Siri’s equation [27], and classified according to Lohman’s criteria [28].

Statistical analyses

All statistical analyses were conducted using the Statistical Package for Social Sciences version 19.0 for Windows (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was used to evaluate normality and determine the appropriate statistical test. Quantitative variables were described using absolute and relative (percentage) frequencies. Grouped comparisons of qualitative variables were performed using chi-square tests. Quantitative variables with normal distribution were expressed as mean and standard deviation, and compared using the two-tailed Student’s t test for independent samples. Quantitative variables that were not normally distributed were presented as median and interquartile range (IQR), or minimum and maximum, and compared using the nonparametric Mann-Whitney U test. P values < 0.05 were considered statistically significant.

Results

Sixty patients who were 18–64-y-old were included in this study, and no patients were excluded based on the exclusion criteria. Twenty-nine patients (48.3%) were men and 31 (51.7%) were women. Ten of the 60 patients (16.7%) had a low level of education (<8 full y) and 29 of the 60 patients (48.3%) had low income (per capita family income up to 1 minimum wage). Using the BMI categories, 6 of the 60 patients (10%) were classified as underweight, 35 (58.3%) were normal weight, and 19 (31.7%) were overweight. There was no significant difference in BMI between the sexes. After analyzing the WC categories, 17 of the 60 (28.3%) participants had measurements greater than the WHO minimum normal cut-off points. After analyzing the BF categories, 10 of the 60 (30%) patients were classified as high BF. There were no significant differences in the categorization of WC and BF between the sexes. Demographic, anthropometric, and laboratory data for the NF1 patients are listed in Table 1.

The average number of meals was 4.37 ± 0.86 per d. Table 2 shows the average intake of energy, macronutrients, fiber,
Energy intake was significantly greater among men (P = 0.016). The difference between EER and energy intake was significantly greater among men (P = 0.019). The mean daily consumption of protein per kilogram of body weight was 1.24 ± 0.49 g/kg/d, and no significant difference was observed between men and women (P = 0.627).

Table 3 shows the prevalence of inadequate nutrient intake for vitamins and minerals, as compared to their EAR. Women with NF1 had a higher prevalence of inadequate intake for iron, copper, pyridoxine, vitamin D, and calcium. For vitamin C, 39 of the 60 patients (65%) consumed less than the EAR, 5 (8.3%) consumed between the EAR and RDA, and 16 (26.7%) consumed more than the RDA and UL.

Discussion

In our study, NF1 patients were found to have an unhealthy diet that was rich in fats and sodium, as well as an inadequate estimated dietary intake of fiber, vitamins, and minerals. More than 50% of men and women had inadequate intake for various nutrients, which has also been reported in the adult Brazilian population [15], where inadequate intake of magnesium (men 74.8%, women 74.6%), vitamin D (men 99.6%, women 99.8%), calcium (men 83.5%, women 90.3%), and pyridoxine (men 15.5%, women 29.3%) is common. Therefore, detailed analysis of micronutrient deficiency is necessary, as inadequate intake is not the only cause of deficiency, although it may contribute if the intake is inadequate and occurs over an extended period.

Insufficient dietary intake of MUFAs was also detected, which might be caused by the low consumption of MUFAs-rich foods, such as olive oil, avocado, or oilseeds, which has been reported in the general Brazilian population [15]. In the present study, mean LDL levels for men and women were greater than the reference values, which have been reported to be associated with a high intake of saturated fat and an increased risk of coronary heart disease [29]. Adequate consumption of MUFAs is also directly related to healthier lipid profiles [29], and might be suggested for NF1 patients.

In this study, the mean intake of linoleic acid (n-6) was approximately 10 times greater than the mean intake of linoleic acid (n-3). According to recent studies, there is a consensus that the n-6:n-3 ratio should be approximately 1:5 to 1:1 [30]. An increased
linoleic acid may play an important role in NF1. Mashour et al. [31] in this study might be caused by the patients commonly observed in NF1. Arachidonic acid, potentially regulate the development of a malignant peripheral nerve sheath in vitro, which is a feature that is commonly observed in NF1.

The prevalence of insufficient fiber intake (less than AI values) in this study might be caused by the patients’ low consumption of fruits, vegetables, and whole grains. Adequate dietary fiber consumption can lower patients’ risk of cardiovascular diseases, diabetes, hypertension, obesity, and gastrointestinal disorders [32]. In contrast, lower dietary fiber intake can lead to constipation, which was reported by several subjects in the present study. Pedersen et al. have also recently investigated constipation in children with NF1 [10]. Therefore, further studies should attempt to determine the causal factors for constipation in NF1 patients.

Understanding the prevalence of inadequate nutrient intake is an important part of nutritional epidemiology, as a healthy diet and nutritional status can influence the patient’s quality of life [33,34]. Previous studies have shown that the clinical severity, visibility, and social representations of NF1 are correlated with quality of life, as reported by NF1 patients and their families [35, 36]. Although similar results are observed in the non-NF1 Brazilian population, the unhealthy diet that we observed in NF1 patients highlights the importance of nutritional care, and must be investigated further in future studies.

Regarding anthropometrics characteristics, the prevalence of underweight adults in the Brazilian population is 2.7% (1.8% for men and 3.6% for women) [37]. In this study, 6 of the 60 NF1 patients (10%) were underweight, which is greater than the 5% mark that WHO uses to identify malnourishment in a population [37]. In addition, 13 of the 29 men (44.8%) and 6 of the 31 women (19.4%) were overweight, compared to 49% of the Brazilian adult population (50.1% for men and 48% for women) [37]. These discrepancies might be explained by the fact that 43 of the 60 patients reported daily energy consumption less than their EER, which would indicate a trend toward being underweight in the NF1 population. After analyzing their body composition, 28.3% of patients were found to have a WC less than the WHO minimum cut-off points, and 30% were classified as having high BF, which were similar to the percentage of patients who were overweight (31.7%) or had an energy intake < EER (28.3%).

NF1 patients may also have a lower basal metabolic rate, as they have a reduced muscle mass [9], which could lead to an overestimation of their daily energy expenditure when using the predictive equations. Although the basal metabolic rate was not previously been treated in the outpatient center were invited to participate in this study. Other potential limitations include changes in dietary habits, errors in dietary reporting, and interpersonal variation in daily consumption. The external validity of this study must be viewed with caution, as the socioeconomic
characteristics and place of residence must be considered when extrapolating results to other nutritional studies. Randomization and the inclusion of a control group (with unaffected patients) would be useful in improving the external validity of similar studies. As this is the first study of nutrient intake in NF1 patients, further controlled studies should be conducted to address these limitations and validate our results.

Conclusions

NF1 patients in this study consumed an unhealthy diet that was rich in fats and sodium, and lacking in fiber and micro-nutrients, especially magnesium, calcium, vitamin D, and pyridoxine. Further studies should investigate the possible correlation and effect of diet and nutrition on the clinical features of NF1.

References