Assessment of the Nutrition Status of Patients With Huntington’s Disease

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OBJECTIVE: The purpose of the present study was to compare the nutrition status of patients with Huntington’s disease (HD) with that of control subjects by analyzing anthropometric and biochemical indicators, energy, and macronutrient intake and to determine which indicators are most altered in HD patients.

METHODS: We assessed the nutrition status of 25 HD patients and 25 age- and sex-matched controls by measuring anthropometric and biochemical indicators. Food intake data were obtained by the 3-d record method to assess mean daily energy and macronutrient intake. We studied variables reported by the patients such as increased or decreased appetite, mastication difficulties, and solid food and liquid food dysphagia. A neurologist assessed the clinical features of HD patients by using the Unified Huntington’s Disease Rating Scale.

RESULTS: HD patients showed significantly lower anthropometric variables but significantly higher kilocalorie intake. Among the subjective variables analyzed, patient-referred weight loss, increased appetite, mastication, and solid food dysphagia were significantly more frequent in HD patients than in controls. We also found relations between motor disability and some anthropometric parameters in HD patients. In particular, we found a significant correlation between total motor disability score and body mass index and arm muscle circumference ($r = -0.464$ and $-0.445$, respectively; $P < 0.05$) and with percentage of body fat ($r = -0.496, P = 0.012$).

CONCLUSIONS: It is of the utmost importance to identify nutritional alterations in HD patients and to find strategies to cover their kilocalorie and nutrient requirements to improve their quality of life. Nutrition 2004;20:192–196. ©Elsevier Inc. 2004

KEY WORDS: Huntington’s disease, nutrition status, anthropometric indicators, dietary assessment

INTRODUCTION

Huntington’s disease (HD) is a neurodegenerative, hereditary disorder characterized by a variety of clinical symptoms. Among the most frequent are movement disorders, especially chorea, emotional and behavioral disturbances manifested mainly as depression and irritability, cognitive impairment, and functional disability. Although initial symptoms are widely variable, psychomotor restlessness and minor motor anomalies are the most frequent early signs. The usual age of onset is during the fourth and fifth decades of life, but there are early- and late-onset cases. Juvenile HD is defined by an onset of symptoms before age 20 y, and childhood-onset (before age 10 y) HD occurs in 0.5% to 2% of all affected individuals.3

The neuropathologic changes include progressive neuronal degeneration and atrophy affecting the striatum and other areas such as the brain cortex, cerebellum, thalamus, and subthalamic nucleus. This autosomal dominant disease is caused by mutations of the huntingtin gene, located near the telomere of the short arm of chromosome 4 at locus 4p16.3. The mutated gene is characterized by a CAG trinucleotide expansion within the first exon.4 The clinical diagnosis of HD based on pedigree and neurologic examination is confirmed by the length of the CAG repeat.6,7

HD symptoms modify nutrition status, and weight loss is frequent among affected individuals.8 Djousse et al.9 suggested that the low body mass index presented by HD patients may be related to other components of the HD gene, which may be associated with a metabolic deficit leading to generalized body mass loss. Further, it has been postulated that an intrinsic defect in mitochondrial metabolism contributes to weight loss in patients with HD.10 Several studies have demonstrated mitochondrial electron transport chain dysfunction, especially in complex II and III, in brain biopsies of HD patients.11 Recent studies have not reported the presence of diabetes mellitus in these patients, but the abnormalities found at the level of energy metabolism in patients and transgenic mice may be related to direct adverse effects of the mutated huntingtin gene, as reported by Duan and collaborators.12 In one animal model of HD, transgenic mice R6/1, normal blood glucose levels were found, which indicates that the mutation does not induce a diabetes–like syndrome.13,14 In addition, animal models have suggested that the use of creatine and coenzyme Q10 may compensate for mitochondrial deficits and decreases in adenosine triphosphate.15,16 Also, the participation of this coenzyme has been proposed in neurologic patients, whereby mitochondrial function is deteriorated and oxidative stress occurs.17

The HD patients are typically leaner than unaffected individuals from the same family.18 Avitaminosis and other nutritional...
deficiencies have been reported as causes of death. 19 Despite these important observations, there have been few studies of the pathogenesis of weight loss in patients with HD. 20

Systemic disorders characterized by unintended weight loss and cachexia are typically associated with anorexia and decreased food intake. In contrast, patients with HD often report an increased appetite. Moreover, surveys have indicated that, on average, they consume more kilocalories than do unaffected individuals, suggesting that energy expenditure is increased in HD patients. 8, 18 Sanberg et al. 21 found that HD patients have weight loss despite consuming more kilocalories than control subjects. Because there is no evidence of malabsorption in HD patients, these data suggest that energy expenditure is increased at least in some HD patients. Pratley et al. 20 suggested that energy expenditure is elevated in patients with this degenerative disease, and that this might be caused by the choreic movement disorder. Some weight-loss-related factors in HD include choking on liquids and coughing on foods, which are observed frequently in these patients. 22

Dysphagia is a common complication that is frequently responsible for the potentially lethal respiratory events of aspiration or asphyxiation. HD patients demonstrate impaired control of many voluntary aspects of food intake that affect swallowing efficiency. In moderately advanced HD, observing water drinking is a simple bedside test to elicit dysphagic symptoms such as choking or coughing. However, less severely disabled patients may manifest only subtle dysphagia and/or respiratory events of aspiration or asphyxiation. 23

The mechanisms responsible for weight loss in patients with HD have not been extensively investigated. Kremer and Roos 24 hypothesized that weight loss may be attributed to the selective loss of neurons in the hypothalamic lateral tuberal nucleus, a region thought to be important in regulating food intake and energy expenditure.

Further, the nutrition status of HD patients in Mexico has never been assessed. At the Instituto Nacional de Neurología y Neurocirugía (INNN), we have observed that these patients experience important weight loss and are unable to feed themselves adequately. Thus, the purpose of the present study was to compare the nutrition status of HD patients with that of control subjects by analyzing anthropometric and biochemical indicators, energy, and macronutrient intake and to determine which indicators are most altered in HD patients.

MATERIALS AND METHODS

A comparative study of HD subjects and matched controls was designed. Patients diagnosed with HD were selected from families registered at the Department of Neurogenetics and Molecular Biology of the INNN. Those with an appointment during the following 6-mo-period were asked to enter the study. The inclusion criteria were adult-onset HD, at least 2 y of follow-up in our institution, diagnosis of HD confirmed by DNA analysis, and no nutrition support. Only those patients who did not present problems with intestinal absorption, diabetes mellitus, or hypertension and who were not confined to their beds were selected for this study.

The control group included 25 subjects matched by sex, age (± 2 y), and socioeconomic background who attended the INNN for non-degenerative neurologic diseases and without alteration of their nutrition status (those with ophthalmologic or neuro-otologic pathway difficulties and those with vascular headache under control). All had a file containing the clinical history, laboratory studies, and socioeconomic evaluation in a six-point scale. This protocol was approved by the Institutional Research and Bioethics Committee. Patients and control subjects provided written informed consent before their participation.

The anthropometric measurements carried out in the same standardized manner in each subject were weight, height, midarm circumference and triceps, biceps, and subcapular and suprailiac skinfold thicknesses. Skinfold thicknesses were measured with a Lange caliper (accuracy of ± 0.1 mm; Cambridge Biotech, Rockville, MD, USA). Weight was evaluated with a Seca 709 balance scale (accuracy of ± 0.01 kg). With these measurements, the following indicators were estimated: body mass index (BMI), 26 percentage of ideal body weight, 26 arm muscle circumference, 27 and percentage of body fat. 28 In addition, levels of albumin, hemoglobin, hematocrit, total lymphocyte count, glucose, cholesterol, and triacylglycerol were evaluated in blood samples.

The dietary assessment was conducted with a 3-d record: 29 all individuals (or caregivers) were asked to register all foods consumed on 2 weekdays and 1 weekend day. Precise indications were provided about how to keep the records, and all individuals were interviewed and asked direct questions to improve the reliability of the data. Real-size plate, glass, cup, and spoon of common food servings were used to estimate the weight and/or volume of the food ingested. The weight and/or volume of foods and liquids, the description of foods ingested, and preparation methods were requested in pre-coded questionnaires, and the mean food intake for 3 d was estimated. The 3-d record in seven HD patients was obtained from relatives or caregivers in charge of feeding them because of dementia. The remaining cases and the control subjects were able to keep the records themselves; however, to guarantee consistency of the records, each HD patient was supervised by a family member. The information was processed with computer software 30 providing the compositions of Mexican food and industrialized products consumed in this country. In this manner, we estimated the intake of total energy (total kilocalories), carbohydrates (g), proteins (g), and lipids (g).

Neurologic assessments were performed by a single neurologist, a specialist in movement disorders, according to the Unified Huntington’s Disease Rating Scale. 31 The scale analyzes four domains of clinical performance and capacity in HD: motor function, cognitive function, behavioral abnormalities, and functional ability.

By filling out a questionnaire about subjective nutritional awareness, patients and controls reported whether they experienced weight loss, increased appetite, decreased appetite, mastication difficulties, solid food dysphagia, and liquid food dysphagia within 6 mo before the study.

The database was analyzed with Epi-info 6.0 and SPSS 10.0 statistical software for Windows. After evaluation of central tendency parameters of the quantitative variables, differences between groups were analyzed with independent-samples t test. Associations between dichotomy or nominal variables were analyzed by the chi-square test. Correlations between numerical variables were expressed as Pearson’s coefficient. P ≤ 0.05 was considered statistically significant.

RESULTS

Twenty-five HD patients were evaluated, 13 (52%) male and 12 (48%) female. The clinical characteristics of HD patients and controls and the results of the molecular analysis are summarized in Table I. Socioeconomic status was intermediate (levels 2 and 3) in all patients. The following anthropometric indicators were significantly lower in the HD group than in the control group: mean weight, BMI, percentage of ideal body weight, midarm circumference, arm muscle circumference, and percentage of body fat (Table II).

Body biochemical indicators were decreased in the HD group but did not reach significant differences when compared with the control group (Table III). The dietary assessment showed that mean energy intake was significantly higher in the HD patients than in the controls due to a significantly higher carbohydrate consumption (Table IV).
TABLE I.
CLINICAL CHARACTERISTICS OF HD PATIENTS AND CONTROL SUBJECTS

<table>
<thead>
<tr>
<th></th>
<th>HD patients (n = 25)</th>
<th>Controls (n = 25)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td></td>
</tr>
<tr>
<td>Male (%)</td>
<td>46 ± 12</td>
<td>46 ± 8</td>
<td>0.047</td>
</tr>
<tr>
<td>HD onset age (y)</td>
<td>40 ± 12</td>
<td>19 ± 6</td>
<td>0.012</td>
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<tr>
<td>CAG repeat length (%)</td>
<td>45 ± 8</td>
<td>36–62</td>
<td></td>
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<tr>
<td>UHDRS score</td>
<td>28 ± 0</td>
<td>0 ± 0</td>
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</table>

TABLE II.
ANTHROPOMETRIC INDICATORS IN HD PATIENTS AND CONTROL SUBJECTS

<table>
<thead>
<tr>
<th>Anthropometric indicators</th>
<th>HD patients (n = 25)</th>
<th>Controls (n = 25)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>58.2 ± SD</td>
<td>66.7 ± 10.1</td>
<td>0.0047</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.60 ± 0.09</td>
<td>1.63 ± 0.09</td>
<td>0.229</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>22.2 ± 2.4</td>
<td>24.6 ± 1.5</td>
<td>0.0001</td>
</tr>
<tr>
<td>Ideal body weight (%)</td>
<td>98.4 ± 13.9</td>
<td>109.6 ± 8.0</td>
<td>0.011</td>
</tr>
<tr>
<td>Midarm circumference (cm)</td>
<td>27.9 ± 4.0</td>
<td>30.9 ± 3.2</td>
<td>0.005</td>
</tr>
<tr>
<td>Arm muscle circumference (mm)</td>
<td>274.8 ± 39.4</td>
<td>302.7 ± 30.3</td>
<td>0.007</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>27.6 ± 8.9</td>
<td>37.9 ± 7.1</td>
<td>0.0004</td>
</tr>
</tbody>
</table>

TABLE III.
BIOCHEMICAL INDICATORS IN HD PATIENTS AND CONTROL SUBJECTS

<table>
<thead>
<tr>
<th>Biochemical indicators</th>
<th>HD patients (mean ± SD)</th>
<th>Controls (mean ± SD)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin (g/dL)</td>
<td>3.98 ± 0.37</td>
<td>4.04 ± 0.41</td>
<td>0.637</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>15.10 ± 1.63</td>
<td>15.49 ± 2.44</td>
<td>0.526</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>45.36 ± 4.07</td>
<td>47.79 ± 7.85</td>
<td>0.186</td>
</tr>
<tr>
<td>Total lymphocyte count (cells/mm³)</td>
<td>1907.68 ± 523.27</td>
<td>1971.75 ± 456.10</td>
<td>0.668</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>90.00 ± 11.90</td>
<td>91.05 ± 10.60</td>
<td>0.759</td>
</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
<td>194 ± 44.70</td>
<td>215.35 ± 42.98</td>
<td>0.116</td>
</tr>
<tr>
<td>Triacylglycerol (mg/dL)</td>
<td>193.20 ± 101.94</td>
<td>208.45 ± 92.19</td>
<td>0.605</td>
</tr>
</tbody>
</table>

TABLE IV.
DIETARY ASSESSMENT IN HD PATIENTS AND CONTROL SUBJECTS

<table>
<thead>
<tr>
<th>Diet indicators</th>
<th>HD patients (mean ± SD)</th>
<th>Controls (mean ± SD)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy intake (kcal)</td>
<td>2325.1 ± 551.4</td>
<td>1948.4 ± 270.2</td>
<td>0.003</td>
</tr>
<tr>
<td>Carbohydrate intake (g)</td>
<td>330.1 ± 98.4</td>
<td>252.1 ± 72.6</td>
<td>0.003</td>
</tr>
<tr>
<td>Protein intake (g)</td>
<td>92.3 ± 36.0</td>
<td>80.2 ± 18.1</td>
<td>0.14</td>
</tr>
<tr>
<td>Fat intake (g)</td>
<td>71.7 ± 20.2</td>
<td>68.3 ± 18.0</td>
<td>0.5</td>
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DISCUSSION

Among the subjective variables, reported weight loss, increased appetite, mastication difficulties, and solid food dysphagia were significantly more frequent in the HD group (Table V). The presence of mastication difficulties was significantly associated with weight loss in the HD group (P = 0.012). Although solid food dysphagia was related to weight loss (P = 0.049), liquid food dysphagia did not reach statistical significance (P > 0.7).

We analyzed the relation between the scores on different subscales of the Unified Huntington’s Disease Rating Scale and the nutritional aspects by means of Pearson’s correlation analysis. We found a significant association between the total motor disability score and the following variables: BMI (r = −0.464, P = 0.019), arm muscle circumference (r = −0.445, P = 0.019), and percentage of body fat (r = −0.496, P = 0.012). When comparing chorea (its extension and magnitude in a 0–22-point scale) and anthropometric values, we obtained significant relations with BMI (r = −0.548, P = 0.001) and percentage of body fat (r = −0.468, P = 0.001).

**DISCUSSION**

Analysis of anthropometric indicators showed that HD patients had significantly lower body weight, BMI, percentage of ideal body weight, midarm circumference, arm muscle circumference, and percentage of body fat than did the control group. The BMI found in the HD patients of this survey is in accordance with that reported by Farrer and Yu. The reason for this may be constant involuntary movements, rigidity, or other characteristics of the disease. Interestingly, a correlation was found between anthropometric indicators (BMI and percentage of body fat) and maximal chorea (evaluation only of the main symptoms in the mouth, face, trunk, and limbs) in the HD group, and the total motor score also showed an important relation with these nutrition variables. These results indicated that HD affects nutrition status through the complexity of concomitant movement disorders such as the main hyperkinetic one, rigidity, balance, and coordination impairment. Cigarette smoking in most of our HD patients (8 versus 1 control in the control group) also may have contributed to the weight loss in these subjects, although tobacco has not been related to the progression of the disease.

Biochemical indicators were decreased in the HD group but were not statistically significant from those of the control group. Thus, whereas certain anthropometric indicators were altered in HD patients, biochemical measurements were not. We have not
found previous reports on alterations of biochemical indicators in HD patients. The analysis of 3-d records showed that our HD patients had higher kilocalorie intake than did the controls ($P = 0.003$). These results are not in accordance with those reported by Morales et al.$^6$ who found no significant difference in kilocalorie intake between HD patients and control subjects. In addition, despite a higher kilocalorie intake in HD patients, none of them were overweight, suggesting an increase of energy expenditure among these patients. Moreover, two HD patients (8%) had a lower percentage of ideal body weight.

Carbohydrate intake was higher in the HD group. This result is similar to that of Farrer and Yu$^{18}$ who reported that carbohydrate consumption is higher in HD patients than in controls, but that the quantities of protein and fat were similar. Mastication difficulties, which occurred in 32% of HD patients, were significantly associated with weight loss. Kremer et al.$^{24}$ reported that severe weight loss is a typical characteristic of advanced disease. Further, Myers et al.,$^{32}$ in a 36- to 72-mo follow-up period, stated that body weight is a strong predictor of disease progression, as individuals with greater body weight at diagnosis show slower decline and also because weight decreases after several months.

Maintenance of normal body weight depends on the long-term balance between energy intake and energy expenditure. Weight loss can result from decreases in intake or increases in expenditure, or a combination of both. Some weight loss–related factors in HD frequently observed in these patients are inadequate caloric intake due to choking on liquids, coughing on foods, inadequate access to food for financial or social reasons, poor dietary planning, and food-preparation difficulties.$^{22,23,33}$ In this study we found a significant association between weight loss, mastication difficulties, and solid food dysphagia. However, it is not clear from these results whether weight loss is due to involuntary movements, decreased intestinal absorption, or metabolic dysfunction.$^{21}$ Nevertheless, our patients presented a high caloric intake despite their mastication difficulties.

Another important factor was the prevalence of symptoms that characterize HD patients such as choreic movements. Some researchers have stated that, to prevent weight loss due to these movements, it is necessary for a caregiver to feed these patients.$^{33}$ Patrley et al.$^{30}$ reported that the mean of 24 h of sedentary energy expenditure is 14% higher in HD patients than in controls. As a consequence, HD subjects tended to be in a negative energy balance, with an average of $-184$ kcal/24 h. Thus, it is crucial to find strategies to improve the nutrition status of HD patients, to monitor nutrition risk indicators, and to cover their particular caloric requirements that are higher than those of control individuals, estimated at approximately 3000 to 4000 kcal to maintain adequate body weight. In addition, to improve their quality of life, it is necessary to fulfill nutrient and water requirements, modify the texture of foods, fraction eating times, or use hypercaloric nutritional supplements$^{34}$ to maintain an acceptable nutrition status.

The methods used to assess the nutrition status of HD patients were easily available and inexpensive. Our results suggest that the treatment and surveillance of HD patients should involve closer interaction between nutritionists and physicians. Nutritional evaluation and dietary management should be integral parts of the treatment of HD patients to ensure better overall assistance.

**ACKNOWLEDGMENTS**

The authors thank Pérez-Severiano Francisca and Macías Nayeli for their very helpful comments on this report.

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