Nutritional aspects in patients with non-alcoholic steatohepatitis (NASH)

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Abstract. – Background and objectives: Metabolic alterations are a common feature in patients affected by non-alcoholic steato-hepatitis (NASH). A strong correlation exists between overweight, in particular visceral fat accumulation, and prevalence of NASH, especially in men. Thus, diet-induced weight loss represents a fundamental tool in disease management of these patients. The aim of the present study was to evaluate body composition and nutrient utilisation in patients with NASH, comparing them with patients affected by chronic hepatitis related to hepatitis C virus infection and with healthy subjects.

Materials and methods: Twenty male outpatients with NASH (age: 41 ± 11 yr; BMI: 26.2 ± 2.1 kg/m²) and 14 HCV male patients (age 44.6 ± 13 yr; BMI: 24.8 ± 2.8 kg/m²) were enrolled in the study. A group of 20 healthy male subjects (age: 39 ± 10 yr; BMI: 23.3 ± 1.1 kg/m²) were studied as controls. Body composition was assessed by anthropometry and dual-energy X-ray absorptiometry; resting metabolic rate and nutrient oxidation by indirect calorimetry. A 7-day food diary was collected. The main biochemical parameters were measured using standardised laboratory techniques.

Results: Body weight was higher in NASH patients with respect to HCV patients and control subjects (respectively 75.2 ± 8.9 vs 68.5 ± 9.4 and vs 67.0 ± 8.0 kg; P < 0.01) and this was essentially due to fat mass increase. Fat-free mass reduction was found in HCV patients with respect to both NASH and control subjects. Patients with NASH had a significantly higher waist circumference (P < 0.01) and a lower resting metabolic rate (RMR) with respect to HCV and control subjects. Energy intake was significantly higher in NASH patients (P < 0.01) compared to the other two groups.

Conclusions: NASH patients showed an increase in body weight, fat mass and visceral fat accumulation with respect to HCV and control subjects. The reduction in RMR, coupled with increase energy intake may explain the body composition alterations found in these patients.

Key Words:
Non-alcoholic steato-hepatitis, Nutritional aspects, Insulin, Leptin.
While these findings may have relevant implications in dietary recommendations in NASH, and in particular in order to optimise the nutrient composition of the diet, an evaluation of energy requirements should be strongly recommended in patients with NASH, to exactly estimate the calories' amount of the diet.

Recently, our research group investigated body composition, energy expenditure and substrate utilisation in patients with NASH comparing them with patients affected by chronic hepatitis related to HCV infection (HCV) and a group of healthy subjects.

In addition, there are ongoing studies on the relationship between several hormones and cytokines involved in body weight regulation, such as insulin and leptin, and the metabolic characteristics in these patients.

Materials and Methods

Twenty male outpatients with NASH (age: 41 ± 11 yr; BMI: 26.2 ± 2.1 kg/m²) and 14 HCV male patients (age 44.6 ± 13 yr; BMI: 24.8 ± 2.8 kg/m²) were enrolled in the study. A group of 20 healthy male subjects (age: 39 ± 10 yr; BMI: 23.3 ± 1.1 kg/m²) were studied as controls. Body composition was assessed by anthropometry and dual-energy X-ray absorptiometry (DEXA); resting metabolic rate and nutrient oxidation by indirect calorimetry. A 7-day food diary was collected.

Body Composition and Energy Requirements Measurement

All measurements were performed at 08:00 after an overnight fast. Body weight was measured to the nearest 0.1 kg with a beam scale, and height was measured to the nearest 0.5 cm with a wall-mounted stadiometer while the subjects were wearing light clothes and no shoes. Body mass index (BMI) was computed as the ratio between body weight (kg) and height (m²). Body composition was assessed by dual-energy X-ray absorptiometry (DEXA), using a whole body densitometer (Lunar DPX-L, Madison, WI; software version 3.65). Respiratory gas exchange measurements were performed over 60 min by continuous indirect calorimetry with an open-circuit ventilated-hood system (Deltatrac, Datex Instrumentarium Corp, Helsinki, Finland) under strictly standardized conditions, as previously described. Twenty-four-hour urine of the day before admission was collected in order to determine urinary nitrogen excretion by a BUN Analyzer II (Beckman Instruments, Fullertone, CA).

In another study recently performed by our group, 25 male outpatients with NASH (age: 43 ± 12 yr; BMI: 27.2 ± 3.5 kg/m²) were enrolled, and divided in two subgroups, according to body mass index (BMI: kg/m²) (BMI ≤ 26: N = 11; BMI > 26: N = 14). Twenty-height healthy male subjects (age: 39 ± 10 yr; BMI: 26.8 ± 2.8), divided into the same 2 subgroups (N = 13 and N = 15 respectively) were studied as controls. Body composition was assessed by dual-energy X-ray absorptiometry; nutrient oxidation by indirect calorimetry. Insulin resistance was measured using the homeostasis model assessment of insulin resistance (HOMA-IR) index, and correlation with leptin concentration was investigated.

Analytic Measurements

A blood sample was collected after an overnight fast in an ice bath, immediately centrifuged at 1500 × g for 15 min at 25° C, and stored at -20° C until analyzed. Total protein, albumin, glucose, hemoglobin, iron, ferritin, transferrin, iron binding capacity, vitamin B-12, folic acid, haematocrit, white and red blood cell counts were measured by using standard laboratory techniques. Plasma insulin concentration was measured by microparticle enzyme immunoassay (Abbott Imx, Pasadena, CA). Leptin was assessed by commercial radio-immuno assay (Linco, St. Charles, MO); the intra and inter-assay coefficient of variation was less than 9% and 7% respectively and the sensitivity was 0.5 ng/ml.

Statistical Analysis

Data are given as means ± SD. Comparison between groups was made by Bonferroni adjusted t-test. The coefficient of determination (R²) was used as a measure of goodness of fit of the generated equation. A two-tailed p value < 0.05 was considered statistically significant.
Results

Body weight was higher in NASH patients with respect to HCV patients and control subjects (respectively 75.2 ± 8.9 vs 68.5 ± 9.4 and vs 67.0 ± 8.0 kg; \( P < 0.01 \)) and this was essentially due to fat mass (FM) increase (29.8 ± 4.8 vs 26.8 ± 5.0%; \( P < 0.05 \)). A reduction in fat-free mass (FFM) was found in HCV patients with respect to both NASH and control subjects. Patients with NASH had a significantly higher waist circumference (104 ± 6 cm; \( P < 0.01 \)) with respect to HCV (95 ± 6 cm) and control subjects (92 ± 5 cm). After adjustment for age and body composition, resting metabolic rate (RMR) was lower in NASH compared to HCV and control subjects, while HCV patients showed an increase in RMR and in lipid utilisation with respect to the other 2 groups (\( P < 0.01 \) both). Energy intake was significantly higher in NASH patients (2210 ± 840 kcal/die; \( P < 0.01 \)) compared to both HCV (1980 ± 760 kcal/die) and control subjects (1880 ± 570 kcal/die). The body composition characteristics and circulating leptin level in the 3 groups examined are reported in Table I.

NASH patients had higher insulin (17.6 ± 8.4 vs 8.2 ± 2.3 µIU/ml; \( P < 0.01 \)) and leptin level (10.4 ± 5.3 vs 7.1 ± 2.2 ng/ml; \( P < 0.01 \)) than controls. HOMA-IR index (units) was significantly higher in overweight than in normal weight NASH patients (4.23 ± 0.72 vs 2.95 ± 1.34; \( P < 0.01 \)), and higher in NASH patients compared to BMI-matched controls. A positive correlation was found between body fat and leptin and HOMA-IR in NASH patients (respectively \( R^2 = 0.76; P < 0.001 \) and \( R^2 = 0.62; P < 0.001 \)), while a negative correlation was reported between ghrelin and HOMA-IR (\( R^2 = 0.58; P < 0.001 \)) (unpublished data).

Discussion

The evaluation of metabolic features and nutritional requirements represents a fundamental tool in the management and therapy of NASH. The use of sophisticated techniques for energy expenditure and body composition assessment, such as indirect calorimetry and DEXA, coupled with the measurement of the main hormones involved in body weight homeostasis, is able to provide relevant information for diagnosing metabolic disorders and for planning a correct nutritional support. Recent evidences suggest that these patients have an increase in body weight, fat mass and visceral fat accumulation with respect to HCV and control subjects. The reduction in RMR, coupled with increase energy intake may explain the body composition alterations found in these patients.

In addition, recent evidences show that NASH patients had increased body fat, blood leptin and insulin concentration, while lower ghrelin level than healthy subjects (unpublished data). Insulin resistance was higher in NASH patients compared to BMI-matched controls and positively correlated with body fat, indicating that maintenance of a normal body weight could reduce the risk of developing metabolic alterations in NASH.

Table I. Body composition characteristics and blood leptin concentration in the 3 groups examined.

<table>
<thead>
<tr>
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<th>NASH (n = 20)</th>
<th>HCV (n = 14)</th>
<th>Controls (n = 20)</th>
</tr>
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<tbody>
<tr>
<td>Age (yr)</td>
<td>41 ± 11</td>
<td>44 ± 13</td>
<td>39 ± 10</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>174 ± 6</td>
<td>173 ± 4</td>
<td>174 ± 5</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.2 ± 2.1***</td>
<td>24.8 ± 2.8*</td>
<td>23.3 ± 1.1</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>104 ± 6***</td>
<td>95 ± 6*</td>
<td>92 ± 5</td>
</tr>
<tr>
<td>FM (%)</td>
<td>29.8 ± 4.8***</td>
<td>26.8 ± 5.0*</td>
<td>23.0 ± 4.2</td>
</tr>
<tr>
<td>FFM (kg)</td>
<td>52.7 ± 5.4*</td>
<td>50.1 ± 6.4*</td>
<td>51.6 ± 6.1</td>
</tr>
<tr>
<td>Leptin (ng/ml)</td>
<td>12.2 ± 4.3***</td>
<td>4.9 ± 1.6*</td>
<td>7.5 ± 2.1</td>
</tr>
</tbody>
</table>

BMI: Body mass index; FFM: free-fat mass; FM: fat mass. * and ***: \( P < 0.05 \) and \( P < 0.01 \) vs controls; * and ***: \( P < 0.05 \) and \( P < 0.01 \) vs HCV.
An accurate nutritional and metabolic evaluation of these patients may allow to optimize their dietary treatment and to identify those patients at higher risk of metabolic complications, such as diabetes, dyslipidaemia and cardio-vascular diseases.

References


