Energy balance in infants
born from HIV seropositive mothers

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Abstract

Objective: to carry out nutritional evaluation of infants born to HIV-seropositive women during outpatient follow-up and diagnostic evaluations; to compare energy balance of HIV infected and noninfected children.

Methods: energy balance (caloric intake, fecal energy excretion, and resting energy expenditure) was prospectively determined by indirect calorimetry of 13 infants (6 girls and 7 boys), ages 1 through 6 months and born to HIV-positive women, at two different examinations: before and after diagnosis of seropositive children. A complete nutritional evaluation, including physical examination and anthropometric measurements (weight, height, and skinfold thickness), was also carried out before and after diagnosis. After diagnosis, children were divided into two groups: infected (5/13) and noninfected (8/13). Throughout the study, children were submitted to monthly clinical evaluations; also, nutritional orientation was given to parents.

Results: in analyzing anthropometric measurements of both groups, malnutrition was observed in the infected group at both examinations. Average resting energy expenditure of infected children was significantly higher than that of noninfected children at both examinations: 64.5 ± 16.8 and 48.0 ± 5.7 (P<0.05), respectively, at first examination, and 68.0 ± 11.7 and 51.8 ± 3.1 (P<0.05), respectively, at second examination.

Conclusion: higher resting energy expenditure of infected children could be responsible for protein energy malnutrition in this group of children, and it can be identified even before final HIV-positive diagnosis. This is important for establishing an early nutritional plan for children born to HIV-seropositive women.


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Introduction

The increasing dissemination of acquired immunodeficiency syndrome (AIDS) represents one of the most significant current health problems.

Due to the increase in transmission among heterosexuals, the number of HIV-infected women has been increasing.
Consequently, the number of children infected by vertical transmission has also been increasing, with rates varying from 15 to 30% in different countries.1,2 In Brazil, from 1980 to 1996(2), 447 cases of HIV-positive children with less than 13 years of age were reported, out of which 1,097 resulted in death.3

Several studies have demonstrated that patients with AIDS have invariably presented weight loss to some degree during medical follow-up.4 Unintentional weight loss of over 10% (wasting) represents a frequent complication among HIV-infected patients, and it is similar to weight-loss in patients with consumptive infections and neoplastic status.5 Wasting is very common among AIDS patients, and it can be progressive and cause serious effects. Moreover, wasting has been found to affect patients before the final diagnosis of AIDS.6

A series of interrelated factors end up by affecting AIDS patients, and this situation leads to a status of malnutrition: reduction of food intake; nutrient malabsorption; and increase in nutritional needs.7-9

Mechanisms considered to be involved directly or indirectly in hypermetabolism due to HIV infection are hypothetical. Cytokines and their effect on resting energy expenditure (REE) and fever are some of the relevant factors that Grunfeld et al. have observed in trying to explain the increased nutritional needs of patients.4,10 In this sense, increase in REE also seems to be the primary cause for weight loss in adult asymptomatic patients.11 The referred mechanisms are contrary to findings of other authors, in which malnourished children infected with pathogens and who presented intestinal malabsorption indicated reduced REE. This reduction is most likely a metabolic response to loss of lean body mass.12-14

To be sure, nutritional status of HIV-infected patients is important and should be given more notice. Frequently, therapeutic and prophylactic medical approach to infected patients is carried out following strict procedures. However, patient’s nutrition is usually dismissed as being of lesser importance. Malnutrition is usually diagnosed only when the patient already presents a serious clinical status. Consequently, it is important to emphasize that patient’s nutrition should be taken into consideration in early overall examination of patients with AIDS.

Little is known about caloric needs of HIV-infected children. Considering that weight loss in AIDS patients involves reduction of caloric intake, nutrient malabsorption, infectious processes, and possible alterations in REE, it is clear why determining patient energy balance can help optimizing nutritional therapy.

The objective of our study was to evaluate the nutritional status of infants born to HIV-seropositive women during outpatient medical follow-up and diagnostic evaluation. We determined and compared energy balance of infants in order to understand which were the most important factors involved in nutritional problems presented by the children.

Methods

We carried out a 22-month follow-up of 13 infants (6 girls and 7 boys) born to HIV-infected women, admitted to the Infectology Unit at the Instituto da Criança, Hospital das Clínicas, Universidade de São Paulo. Prior to carrying out any procedure, informed consent was obtained from parents or person legally responsible for the children. This study was approved by the Ethics and Research Committee of the School of Medicine at Universidade de São Paulo.

After carrying out anamnesis and clinical examinations, we performed nutritional evaluation, anthropometric measurements (weight, height, arm-muscle circumference, skinfold thickness), timed 24-hour nitrogen balance (ingestion minus excretion), and determined REE through indirect calorimetry technique. All children were submitted to these procedures at the beginning of follow-up and after determining the result of HIV diagnosis. Interval between the examinations of children varied from 2 to 6 months.

At both examinations, all children were clinically stable and asymptomatic. Adults responsible for the children were given nutritional orientation throughout the study during outpatient follow-ups.

After determining energy balance, children were submitted to monthly examinations. Until final diagnosis was obtained, children were also submitted to laboratory exams for the detection of antibodies (ELISA, Western Blot, and VIHA) and of antigen (P24). These exams were useful in confirming HIV infection, since 5 out of the 13 children in our study were confirmed HIV positive. Consequently, we divided patients into two groups: infected and noninfected infants.

In order to determine metabolic balance, all children were administered the same diet for 1 week prior to hospital admission. Infants were clinically stable at admission into the hospital.

Within a 24-hour period, all food intake and all eliminated urine and feces were rigorously accounted for. Food and feces samples taken from patients were homogenized, aliquoted, and stored in a freezer. This procedure was also carried out at the second full examination. Caloric values of foods (milk and soup) and feces were determined using bomb calorimetry (Parr, model 1271, USA). Nitrogen balance results were assessed for food, urine, and feces. These results were obtained using the Kjeldahl method.15 REE was determined using indirect calorimetry with a whole-body calorimeter assembled in our environment.16 REE was calculated using the modified Weir formula17:

\[
REE = \frac{3.9 \times V_{O2} + 1.106 \times V_{CO2}}{1.44} - [2.17 \times UN],
\]

where \( V_{O2} \) and \( V_{CO2} \) = consumption of oxygen and production of carbon dioxide (ml/min), respectively; \( UN \) = urinary nitrogen excretion (g/day); and REE = resting energy expenditure (kcal/kg/day).

Energy balance was calculated by the difference between energy intake and energy loss. The latter is the sum of
Excretion of energy in feces and in urine, and the former is the energy measured by the calorimeter; this results in REE. Assessment of components that determine energy balance allowed to establish a more adequate nutritional therapy for the children studied.

Energy balance (kcal/kg/day) was calculated using the formula: \[ SE = (EI - FE) - REE, \] where EI = energy intake; FE = fecal energy; and SE = stored energy, or final balance.

Statistical analysis included calculating median, average, and standard deviation. For comparison of averages, we employed Student’s t test with significance level of 5%.18

Results

Table 1 presents the main clinical and anthropometric characteristics, as well as the body fat percentage of both groups of infants at both examinations.

In analyzing Table 1, it is possible to observe that infected children presented lower weight and height gain than noninfected children. Among infected infants, for an average period of 6 months, median weight gain was around 1,310 g; whereas among noninfected infants, for an average period of 2 months, weight gain was around 1,000 g. As for height gain, during a 6-month interval, infected patients grew 9 cm (median), whereas during a 2.5-month interval, noninfected patients grew 7 cm (median).

Average Z scores for weight/age and height/age and average body fat of both groups indicate that nutrition of infected children was seriously compromised already at first examination. Nutritional orientation provided during outpatient follow-up was not sufficient for the improvement of these values before the second examination.

Differences between average values of energy balance components at first and at second full examination of infected patients were not significant. Likewise, differences between average values of energy balance components at first and at second full examination of noninfected patients were also not significant.

Table 2 presents a comparison of average values of energy balance components of infected and noninfected patients at both examinations. It is possible to observe that REE is significantly higher among infected patients at both examinations.

Table 3 presents a comparison of average values of nitrogen balance (g/kg/day) of infected and noninfected patients at both examinations. Difference between nitrogen balance of infected and noninfected patients at both examinations was not significant.

Discussion

A comparative analysis of average Z scores for weight/age, height/age, and weight/height indicates that nutrition of infected patients, already at the first examination, was significantly and seriously compromised. This was also observed at the second examination.

Table 1 - Clinical and anthropometric characteristics of infected and noninfected patients

<table>
<thead>
<tr>
<th></th>
<th>Noninfected</th>
<th></th>
<th>P*</th>
<th>Infected</th>
<th></th>
<th>P*</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>1st examination</td>
<td>2nd examination</td>
<td></td>
<td>1st examination</td>
<td>2nd examination</td>
<td></td>
</tr>
<tr>
<td>Patients (n)</td>
<td>8</td>
<td>8</td>
<td></td>
<td>5</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>5M, 3F</td>
<td>5M, 3F</td>
<td></td>
<td>2M, 3F</td>
<td>2M, 3F</td>
<td></td>
</tr>
<tr>
<td>Age (m)</td>
<td>4 (1-6)</td>
<td>6 (6-10)</td>
<td>ns**</td>
<td>5 (1-6)</td>
<td>11 (3-12)</td>
<td>ns</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>6.05 (2.92-7.64)</td>
<td>7.01 (5.94-8.75)</td>
<td>ns</td>
<td>3.67 (2.50-5.81)</td>
<td>4.98 (3.42-8.70)</td>
<td>ns</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>59 (47-70)</td>
<td>67 (64-71)</td>
<td>ns</td>
<td>56 (50-60)</td>
<td>65 (57-73)</td>
<td>ns</td>
</tr>
<tr>
<td>Z score W/A</td>
<td>-0.7±0.8</td>
<td>-0.9±0.6</td>
<td>ns</td>
<td>-3.1±1.5</td>
<td>-2.8±1.5</td>
<td>ns</td>
</tr>
<tr>
<td>Z score H/A</td>
<td>-0.7±1.4</td>
<td>-0.9±1.2</td>
<td>ns</td>
<td>-3.3±1.8</td>
<td>-2.9±1.8</td>
<td>ns</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>18 (7.0-20.0)</td>
<td>18 (12.0-25.0)</td>
<td>ns</td>
<td>3.7 (2.9-18.3)</td>
<td>8.0 (4.8-21.0)</td>
<td>ns</td>
</tr>
</tbody>
</table>

* P<0.05
** ns = nonsignificant

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Results indicating that weight and height were more seriously compromised before final diagnosis are similar to those of Miller et al., in 1993, in a study involving 86 children born to HIV-infected women. In that study, nutrition was more seriously compromised among 52 children whose diagnosis of HIV infection was confirmed. These findings are also similar to those of Winter & Chang, in 1996.

In our study, average values of caloric intake of infected and noninfected patients, at both examinations, were similar. This finding is in agreement with that of Grunfeld et al., in 1992, in which there was no difference between food intake of HIV-positive adults and of controls. Grunfeld et al. did not confirm their initial hypothesis that lower caloric intake would be the main cause of weight loss in patients with AIDS.

As for excretion of energy, our study shows that it was similar in both groups at both examinations. In turn, excretion of energy is highly variable and can be influenced by various factors, such as type and amount of food intake, concomitant infection, and malabsorption. The composition of the intestinal flora itself, in addition to endocrine abnormalities or dysfunction of cells of the epithelium of the intestinal villi and crypts, caused by HIV, may also affect the amount of energy excretion.

REE was the only component of energy balance which presented a significant difference between the two groups. In comparing average REE values of both groups at both examinations, it is possible to observe that, at first examination, the group of infected children presented a significant increase in REE in relation to the noninfected group (64.5 versus 48.0 kcal/kg/day, respectively). This REE increase was also observed at second examination (68.0 versus 51.8 kcal/kg/day).

Many studies have carried out assessment of REE in adults infected with HIV. Hommes et al., in 1991, observed an increase of 8% in REE in relation to a control group. In comparing separate results of different authors, the average increase in REE is around 12%.

Table 2 - Comparison of average values of energy balance components (kcal/kg/day) of infected and noninfected patients at both examinations

<table>
<thead>
<tr>
<th>1st examination</th>
<th>Infected</th>
<th>Noninfected</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intake of energy</td>
<td>147.6±45.0</td>
<td>154.3±77.7</td>
<td>ns**</td>
</tr>
<tr>
<td>Fecal energy</td>
<td>15.8±16.1</td>
<td>4.1±4.3</td>
<td>ns</td>
</tr>
<tr>
<td>REE</td>
<td>64.5±16.8</td>
<td>48.0±5.7</td>
<td>*</td>
</tr>
<tr>
<td>Energy balance</td>
<td>67.1±41.1</td>
<td>102.2±82.0</td>
<td>ns</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2nd examination</th>
<th>Infected</th>
<th>Noninfected</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intake of energy</td>
<td>135.1±60.4</td>
<td>112.5±73.9</td>
<td>ns</td>
</tr>
<tr>
<td>Fecal energy</td>
<td>15.4±24.1</td>
<td>4.4±3.3</td>
<td>ns</td>
</tr>
<tr>
<td>REE</td>
<td>68.0±11.7</td>
<td>51.8±3.1</td>
<td>*</td>
</tr>
<tr>
<td>Energy balance</td>
<td>51.7±52.2</td>
<td>65.3±88.2</td>
<td>ns</td>
</tr>
</tbody>
</table>

* P<0.05    ** ns = nonsignificant

Table 3 - Comparison of average values of nitrogen balance (g/kg/day) of infected and noninfected patients at both examinations

<table>
<thead>
<tr>
<th></th>
<th>Noninfected</th>
<th>Infected</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st examination</td>
<td>0.5±0.3</td>
<td>0.3±0.2</td>
<td>ns</td>
</tr>
<tr>
<td>2nd examination</td>
<td>0.2±0.3</td>
<td>0.2±0.1</td>
<td>ns</td>
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<tr>
<td>P</td>
<td>ns**</td>
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</tbody>
</table>

* P<0.05    ** ns = nonsignificant
In our study, comparative analysis of average values of REE in both groups indicated that, at first examination, REE of infected patients was 34.4% higher than that of noninfected patients. Likewise, at second examination, REE was also higher among infected patients (31.3%). Up to this date, there are no data regarding REE measurements in HIV-infected children.

There are many hypotheses regarding causes of REE increase in children with AIDS. It is believed that cytokines, tumor necrosis factor alpha, and interleukin-1 and 6, analogously to a situation of sepsis, may be involved in this process, since AIDS patients have presented increased plasmatic concentration of cytokines. In situations of short-term weight loss with increased REE, it is also necessary to investigate the possibility of concomitant secondary infection. It seems that this was not the case of the patients in our study.

Despite the difference in REE of infected and noninfected patients at both examinations, the resulting daily energy balance was similar for both groups at both examinations. These results may seem contradictory. However, severe nutritional involvement in infected children is a result of the significant increase in REE of these patients. Since there was a great variability in energy balance components, and the difference in REE was significant, we consider REE as the most important energy balance component; it should be determined as soon as possible in infected patients.

Similarly to what occurs with adult HIV-positive patients, apparently, the increase in REE of HIV-seropositive children also occurs early, during the asymptomatic phase of the disease, when there are no clinical manifestations of infection. In our study, prior to the diagnosis of AIDS, average values of REE of infected infants were already 34.4% higher than those of noninfected infants. Likewise, at the second examination, average values of REE of infected infants were 31.3% higher than those of noninfected infants. These results are fundamental for recommending early increase in caloric intake and nutritional therapy for children born to HIV-seropositive women.

In conclusion, it is possible to observe that REE is a helpful indicator of HIV infection even during the asymptomatic phase. Determining REE values with noninvasive procedures, such as indirect calorimetry, can be helpful in investigating suspected diseases and in developing strategies for early nutritional therapies. Our final objective was to contribute to the preservation of the patients’ immunology balance and lean body mass, and also to the improvement of the patients’ quality of life.

References