Recommendations from SPNS/GEAM/SENBA/SENPE/AEDN/SEDCA/GEISIDA on nutrition in the HIV-infected patient


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Abstract

Objective: to make recommendations on the approach to nutritional problems (malnutrition, cachexia, micro-nutrient deficiency, obesity, lipodystrophy) affecting HIV-infected patients.

Methods: these recommendations have been agreed upon by a group of experts in the nutrition and care of HIV-infected patients, on behalf of the different groups involved in drafting them. Therefore, the latest advances in pathophysiology, epidemiology, and clinical care presented in studies published in medical journals or at scientific meetings were evaluated.

Results: there is no single method of evaluating nutrition, and different techniques —CT, MRI, and DXA— must be combined. The energy requirements of symptomatic patients increase by 20-30%. There is no evidence to support the increase in protein or fat intake. Micronutrient supplementation in only necessary in special circumstances (vitamin A in children and pregnant woman). Aerobic and resistance exercise is beneficial both for cardiovascular health and for improving lean mass and muscular strength. It is important to follow the rules of food safety at every stage in the chain. Therapeutic intervention in anorexia and cachexia must be tailored, by combining nutritional and pharmacological support (appetite stimulants, anabolic steroids, and, in some cases, testosterone). Artificial nutrition (oral supplementation, enteral or parenteral nutrition) is safe and efficacious, and improves nutritional status and response to therapy. In children, nutritional recommendations must be made early, and are a necessary component of therapy.

Conclusion: appropriate nutritional evaluation and relevant therapeutic action are an essential part of the care of HIV-infected patients.

Key words: Nutrition. HIV. Caquexia.

RECOMENDACIONES DE SPNS/GEAM/SENBA/SENPE/AEDN/SEDCA/GEISIDA SOBRE NUTRICIÓN EN EL PACIENTE CON INFECCIÓN POR VIH

Resumen

Objetivo: realizar recomendaciones sobre el abordaje de los problemas nutricionales (malnutrición, caquexia, déficit de micronutrientes, obesidad, lipodistrofia) presentes en la infección VIH.

Métodos: estas recomendaciones se han consensuado por un grupo de expertos en nutrición y en atención al enfermo VIH, en representación de las distintas sociedades firmantes. Para ello se han revisado los últimos avances fisiopatológicos, epidemiológicos y clínicos recogidos en estudios publicados en revistas médicas o presentados en congresos.

Resultados: no existe un único método de valoración nutricional, debiendo combinarse cuestionarios y técnicas como TAC, RNM y DEXA. Los requerimientos energéticos en enfermos sintomáticos aumentan en un 20-30%. No existe evidencia que respalde el incremento del aporte proteico o graso. La suplementación de micronutrientes sólo es necesaria en circunstancias especiales (Vitamina A en niños y embarazadas). El ejercicio aeróbico de resistencia es beneficioso tanto para la salud cardiovascular como para mejorar la masa magra y la fuerza muscular. Es importante seguir normas de seguridad en toda la cadena alimentaria. La intervención terapéutica en la anorexia y caquexia debe ser individualizada, combinando soporte nutricional y farmacológico (estimulantes del apetito, agentes anabolizantes y testosterona en algún caso). La nutrición artificial (suplementación oral, nutrición enteral o parenteral) es segura y eficaz, mejorando el estado nutricional y la respuesta al tratamiento. En niños, las recomendaciones nutricionales deben ser muy precoces, formando necesariamente parte del tratamiento.

Conclusión: La adecuada valoración nutricional y la pertinente actuación terapéutica son parte esencial de la asistencia del enfermo VIH.

Palabras clave: Nutrición. VIH. Caquexia.
Introduction

Knowledge of the nutritional needs of HIV/AIDS-infected patients remains an important issue due to the persistence of situations that require calculation or measurement. HIV/AIDS is still a pandemic and is one of the most important health problems in the world, particularly in Africa and Asia. This is compounded by the growing appearance of different profiles of metabolic or nutritional involvement in infected patients, specifically obesity and lipodystrophy.

This document has been structured according to the interest it may provide for different areas of healthcare. The authors are experts in their field, their contributions are based on the latest information available, and they follow strict and homogeneous norms in order to facilitate consultation and enable the recommendations to be applied in daily practice. This is followed by a review by all the authors to explain areas that may be less clear, to bring together the information presented in each chapter, and to avoid redundancy.

We have tried to provide a broad view of the nutritional problems of HIV-infected patients and guidelines on early diagnosis and treatment. Thanks to the multidisciplinary effort of the most prestigious experts in the fields of infectious diseases, endocrinology and nutrition, dietetics, pharmacology, and food safety, this text will be of help to Spanish healthcare professionals working directly or indirectly with HIV-infected patients. Thus, any advances in this field can be included in the following editions of this text.

As with any practical approach, we have applied the so-called levels of evidence based on the source of the data that support the suggestions, indications, and recommendations in this document (Level A: Comparative and randomized studies. Level B: Cohort studies or case studies. Level C: Descriptive studies or expert opinions). The fact that nutrition has only recently been perceived as important, and that nutritional follow-up is difficult in some centers accounts for the paucity of studies with definitive conclusions on HIV-infected patients. Nevertheless, and owing to the need for treatment to include nutrition, we feel that the time is right to prepare a clear and concise document in which the healthcare professional can identify what is certain and what is uncertain and worthy of further investigation in order to improve the care provided for patients infected by HIV.

Malnutrition

The term malnutrition includes conditions produced both by an excess of nutrients and by a lack of nutrients. However, it is generally used to refer to undernourishment, i.e. disorders stemming from a lack of macronutrients and micronutrients.

Table I
Criteria for a definition of wasting

- Unintentional weight loss of >10% in 12 months
- Unintentional weight loss of >7.5% in 6 months
- Loss of body cell mass of >5% in 6 months
- In men:
  - Body cell mass <35% of total body weight and BMI of < 27 kg/m²
- In women:
  - Body cell mass <23% of total body weight and BMI < 27 kg/m²
- BMI < 20 kg/m², regardless of sex

HIV infection and weight loss. Pathogenesis and importance of an early diagnosis. Differences between the pre-HAART and HAART eras

During the pre-HAART era, weight loss was usually accompanied by fever, diarrhea, and anorexia. Today, the situation has changed, but there are still many ways both the disease and treatment can contribute to an involuntary weight loss and reduction in energy production—changes in metabolism, increased energy needs, intestinal malabsorption, persistent diarrhea, and the reduced calorie-protein intake as a result of anxiety or depression accompanying HIV infection.

In patients taking HAART, weight loss produced by wasting due to metabolic alterations can be difficult to differentiate from lipodystrophy (especially lipaatrophy) or weight loss produced by low intake.2,10

It is essential to monitor patients’ weight, evaluate their nutritional status, and accurately assess the changes in body composition in order to act as early as possible and avoid more serious problems11.

Concepts

Undernourishment

This is defined as a disorder of body composition characterized by an increase in extracellular water, and a potassium and muscle mass deficit often associated with reduced fatty tissue and hypoproteinemia, which interferes with the normal host response to disease and its treatment.

Calorie-protein undernourishment occurs when daily requirements are not covered by diet. In many cases, it reverts when intake returns and the underlying problem is resolved.

Wasting

The 1987 CDC definition describes wasting as an involuntary weight loss of > 10% of baseline body weight plus chronic fever, weakness, or diarrhea.
According to the current definition of wasting, patients must fulfill at least one of the criteria shown in Table I. This definition stresses that most patients are asymptomatic, and that there are differences between the sexes with regard to fat distribution and muscle mass. It also includes a time profile.11,12

**Lipoatrophy**

This is the main differential diagnosis of wasting, and is defined as a loss of peripheral fat in the upper or lower limbs, buttocks, or face. The loss is asymmetrical, not necessarily associated with weight loss, and is not related to calorie-protein malnutrition. Wasting and lipoatrophy can be observed simultaneously in the same patient. This aspect is examined exhaustively in the GEAM/PNS recommendations on morphological and metabolic alterations in HIV-infected patients.13-15

**Pathogenesis of wasting**11,14,16

Many factors are involved in the pathogenesis of wasting and it is sometimes difficult to identify the main cause. It is characterized by a disproportionate loss of lean mass due to specific metabolic alterations as part of the body’s defense mechanism against a stressful situation. When this state is maintained, it leads to protein depletion, especially in skeletal muscle, and it does not recover with intake, since the whole process is caused by metabolic changes in cells (Algorithm 1). This is somewhat similar to the process in other diseases, including tumors; energy is obtained as an acute inflammatory response in which the tumor necrosis factor and interleukins 1 and 6 intervene.

Baseline energy expenditure increases in some AIDS patients from 20% to 60%. There have also been reports of hormonal alterations that exacerbate the situation. These include hypogonadism in men, reduced production of insulin-like growth factor I, the growth hormone messenger in men and women, which can lead to resistance and alteration of the energy balance.

**Recommendations**

- Alterations in weight and body composition are common in HIV-infected patients (Level B).
- It is important to suitably evaluate HIV-infected patients in order to make an early diagnosis of malabsorption (Level B).
- The incidence of wasting has fallen since the introduction of HAART, but it still exists (Level B).
- A differential diagnosis with lipoatrophy must be made (Level A).

**Nutritional needs of HIV-infected patients**

**Macronutrients**

Nutritional recommendations vary according to different factors that can act alone but that often combine in the same patient. Specific problems (diabetes, pancreatitis, renal insufficiency, obesity, lipodystrophy, and other metabolic alterations) require specific recommendations.

**Energy and proteins**

There is no consensus on the baseline energy requirements of HIV-infected patients, although it is known...
that these are greater at all stages. There are few data on protein requirements, and an improvement in clinical patterns due to a greater intake of protein has not been proven.

The recommendations of the World Health Association (WHO) are shown in Table II.

**Micronutrients**

The general recommendations of the WHO on the need for micronutrients in HIV-infected patients are shown in Table III.

**Recommendations**

**Energy**

- During the asymptomatic phase, energy requirements probably increase by 10% in HIV-infected children, adolescents and adults (B). During the symptomatic phases, requirements increase by approximately 20-30% in children, with no weight loss, and in adults and adolescents (Level B).
- In symptomatic children with weight loss, requirements should be increased by 50-100% (Level B).
- HIV-infected pregnant and breastfeeding women should follow the recommendations for adolescents and adults. In addition to these requirements, they must consume the extra energy, proteins, and micronutrients necessary in their condition (Level B).

**Proteins**

- For all groups, protein requirements will be the same as in non-infected individuals of the same age, sex, and physical state and activity (Level B).

**Fat**

- There is no evidence that requirements are different due to HIV infection (Level B).

**Micronutrients**

- There is no evidence that micronutrient supplements reduce morbidity and mortality in infected adults, even in pregnant and breastfeeding women (Level A).
- There is evidence of the benefit of vitamin A supplement in children (Level A).
- During pregnancy and breastfeeding, the daily intake of vitamin A should not surpass RDI recommendations in infected women (Level A).

**Table III**

**WHO recommendations on micronutrient requirements in HIV/AIDS-infected patients**

<table>
<thead>
<tr>
<th>General</th>
</tr>
</thead>
<tbody>
<tr>
<td>In order to guarantee intake of micronutrients at RDI levels, a healthy diet is encouraged both in infected adults and in infected children.</td>
</tr>
<tr>
<td>Nevertheless, intake of micronutrients at RDI levels may be insufficient to correct nutritional deficiencies.</td>
</tr>
<tr>
<td>There is evidence that some supplements (vitamin A, zinc, and iron) can have adverse consequences in infected populations.</td>
</tr>
<tr>
<td>The safe upper limit of the daily intake of micronutrients in infected patients has yet to be defined.</td>
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</table>

<table>
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<tr>
<th>Children</th>
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<tbody>
<tr>
<td>Infected children aged 6 to 59 months who live in areas with limited resources should receive the same periodic supplements as non-infected children: vitamin A every 4-6 months (100,000 IU in children aged 6-12 months and 200,000 IU in children aged &gt; 12 months).</td>
</tr>
<tr>
<td>There are no data to guarantee the efficacy of a supplement with other micronutrients.</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Pregnant/breastfeeding women</th>
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<tbody>
<tr>
<td>Iron and folic acid. To prevent anemia in the general population, the WHO recommends daily supplements of folic acid and iron (400 μg of folate and 60 mg of iron) for 6 months of pregnancy, and twice-daily supplements to treat severe anemia. There are no data to recommend a different approach in infected women.</td>
</tr>
</tbody>
</table>

**Vitamin A.** Daily intake of vitamin A should not surpass RDI recommendations.

**Supplements with multiple micronutrients**

- The most suitable intake of micronutrients is through a correct diet.
- Nevertheless in areas where this is not possible, supplements with multiple micronutrients may be necessary during pregnancy and breastfeeding.

**Evaluation of nutritional status in HIV**

Very recent studies have observed that severe undernourishment, cachexia, continues to be a serious problem affecting more than 17% of infected patients, of whom more than 70% were receiving HAART. Cachexia is not only a problem of calorie-protein undernourishment; it also involves an alteration of body composition (BC) with a specific loss of body cell mass (BCM).

**Methods for evaluating nutritional status**

A good marker of nutritional status should bring together the following characteristics; it should not be
affected by non-nutritional factors, it should return to normal values with appropriate nutritional support, and it should be sensitive and specific. It should not be altered in patients who are not undernourished.

**Clinical history**

The following should be obtained: clinical data, dietary history, social factors (financial, work, etc.), and a physical examination with anthropometric data.

**Laboratory parameters**

These include the measurement of protein levels in plasma (albumin, transthyretine [prealbumin], and transferrin), calculation of nitrogen balance, creatinine-height balance, and measurement of trace elements, vitamins, and electrolytes. Immunological parameters to be measured include the lymphocyte count and delayed hypersensitivity skin tests.

**Functional tests**

These allow us to evaluate the repercussion of the loss of muscle mass by means of dynamometry, lunar nerve stimulation, and muscle biopsy.

**Methods of global evaluation and screening in patients at risk of undernourishment**

a) Global subjective evaluation adapted to HIV (GSE). This can be used in hospitalized patients or ambulatory patients and divides patients into three groups:
   A. Well nourished.
   B. Moderately nourished or at risk of becoming undernourished.
   C. Severely undernourished.

b) Other methods to be taken into account:

   MUST: this is a method used to screen for the risk of malnutrition, and is currently recommended by the European Society of Parenteral and Enteral Nutrition (ESPEN) as a method of population screening.

c) Analysis of body composition.

The most widely used methods in habitual clinical practice, due to their application in BC studies, are bioelectric impedance (BIA), dual X-ray absorptiometry (DXA) and techniques for measuring regional fat (CT and MRI).

**Recommendations**

- HIV-infected patients should have their nutritional status evaluated (Level A).

**General recommendations**

Nutritional intervention and education should form part of the HIV-infected patient’s care package from...
diagnosis and throughout follow-up. There is firm scientific evidence that advice on nutrition, in addition to offering suitable dietary habits, is efficacious in improving the state of health of these patients. Training for healthcare professionals, the development of behavioral skills, and the use of protocols and guidelines adapted to these patients can improve the quality of care. The following nutrition strategies should be applied to all HIV-infected patients: 1) integration of nutritional therapy in the patient’s care package; 2) early nutritional intervention; 3) systematic nutritional evaluation from diagnosis and at each of the periodic check-ups; 4) tailored diet and adaptation of the diet to the different stages and chronic complications (glucose intolerance, dyslipidemia, hepatic or renal insufficiency, etc.).

It is particularly important to determine the risk of malnutrition in order to set priorities for evaluation and nutritional therapy. The American Dietetic Association (ADA) classifies this risk into three levels: high, medium, and low, and recommends that these interventions take place before one week in high-risk patients, and before one month in medium-risk patients. Furthermore, the ADA recommends adapting the visit schedule to the patient’s CDC category (at least three visits per year in stage I, three to six visits in stages II and III), and carrying out more frequent monitoring in children.

Lifestyles and psychological variables: nutritional advice

Prolonged use of drugs leads to toxicity, which has a proven impact on quality of life, with the result that a multidisciplinary approach is essential. Therefore, patients must participate actively in decision-making and in the management and care of their illness.

Therapeutic scenarios and the most frequent clinical situations

In the case of nutritional problems, the main challenge for the clinician is often to differentiate between whether the disorder is organic in nature, or psychological. The key lies in a wide view by the clinician, and visits should include, first, an evaluation of nutritional and emotional aspects and, second, the use of suitably communicative language.

There are two types of situation associated with nutrition in the HIV-infected patient:

1. Physical symptoms that can have an organic, toxic, or psychological origin: Tiredness, loss of appetite, dry mouth and throat, nausea, diarrhea/constipation, problems swallowing—if neither an organic nor iatrogenic cause can be determined, the patient should be asked:
   1. if there have been any noticeable changes in his/her daily routine.
   2. if any events in particular are worrying him/her.
   3. about his/her state of mind.

Approach: if emotional problems are present or suspected as the origin of these symptoms, the patient must be referred to a psychologist or other qualified professional.

2. Eating disorders based on a mental disorder: These are very difficult to detect during a consultation, since the patient has no complaints and tends to hide any problems. Therefore, the clinician should use the physical signs of the disorder as clues. Advantage should be taken of any information on eating habits and health provided by those accompanying the patient.

General clinical approach: the interview is a basic tool given the possibility it offers to collect information and boost the physician-patient relationship. Feedback received during the interview is extremely important,
since it allows teamwork to be continually redirected. Specialized questionnaires make it possible to obtain data on the patient’s eating disorder. The ACTA questionnaire is valid for this purpose.

**Communication strategies**

The basic aspects of the communication process are as follows:

**Priorities.** When patients inform their physician. These situations are of particular interest, since they represent the manifestation of what is most worrying for the patient.

**Personality variables.** A patient’s personality characteristics make him/her more or less receptive to advice on nutrition, as well as to adherence and cooperation with their therapy provider.

**Lifestyles.** When approaching therapy, it is always necessary to consider the patient’s lifestyle and concerns, as these can condition his/her behavior.

**Recommendations**

- It is important to have support material during consultations in order to provide specific information and resources (Level C).
- Non-profit-making organizations (NGO) are yet another element to extend these recommendations (Level C).
- If emotional alterations are observed, the patient must be referred to a clinical psychologist and/or psychiatrist for evaluation and therapy (Level C).

**Nutrition and physical exercise in HIV-infected patients**

In recent years, different studies have been published on the effect of exercise on the status and progress of HIV-infected patients. Moderate exercise also helps to maintain the metabolic capacity for synthesizing proteins, by increasing muscle mass, even in patients suffering from the wasting syndrome.

**Therapeutic approach to the HIV-infected patient**

Table V shows a series of simple norms to be followed.

<table>
<thead>
<tr>
<th>Dietary orientation for exercise in HIV-infected patients</th>
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<tbody>
<tr>
<td>- Calculate the individual calorie intake</td>
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<tr>
<td>- Divide the diet into 5 or 6 meals per day</td>
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<tr>
<td>- At least 60% should be in the form of carbohydrates with a high glycemic index</td>
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<tr>
<td>- Limit carbohydrates with a low glycemic index to &lt;10% of the total</td>
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<tr>
<td>- Proteins must have a high biological value and represent 10-15% of the total calorie intake</td>
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<tr>
<td>- Fats must be limited to a maximum of 30% - vegetable fats are preferred</td>
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<tr>
<td>- Evaluate the addition of enteral nutritional supplements to cover the calorie-protein requirements</td>
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<tr>
<td>- If necessary, supplement with vitamins from groups B, A, and E</td>
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<tr>
<td>- If necessary, supplement with minerals, especially Fe, Zn, and Se</td>
</tr>
<tr>
<td>- Strict control of the hydro-electrolytic mechanism</td>
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<tr>
<td>- Strict clinical control</td>
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**Ergogenic aids**

Ergogenic aids are any type of compound, substance, or external aid used to enhance sports performance. Athletes, particularly in strength sports, use creatine as a means of increasing muscle mass and strength, and although its effects on healthy athletes are controversial, they continue to be used. In a recent study involving patients on HAART, creatine was administered to a group of 17 patients, and placebo to a group of 16; creatine was observed to significantly improve lean muscle mass compared with placebo. However, in both groups, a similar increase in strength was observed (40%), with no significant differences. Overloads of branched amino acids and proteins have also been used to increase lean mass. No improvement has been observed after use in comparisons with control groups.

**Recommendations**

- Aerobic and resistance exercise is beneficial for the cardiovascular health of patients with HIV infection (Level A).
- Aerobic and resistance exercise can improve lean mass and muscular strength in HIV-infected patients on antiretrovirals (Level A).
- There is not sufficient evidence to show the benefit of using ergogenic aids such as creatine in HIV-infected patients on antiretrovirals (Level C).
- In any case, we must recommend moderate and regular aerobic sports, as this can also improve the mental health and quality of life of these patients, and become an important concomitant therapy (Level A).
Dietary recommendations in special situations

Dietary recommendations in special situations should aim to tailor food and meals to individual patient needs, improve and counter the effects brought about by special situations that could lead to malnutrition, optimize nutritional status, and prevent and/or treat possible nutritional deficiencies. We should include these recommendations during pregnancy, vegetarian diets, and recommendations for gastrointestinal alterations—these can be consulted in the complete document at www.msc.es and www.gesida.es

Recommendations

• During pregnancy and breastfeeding, the risk of malnutrition increases due to the increase in energy expenditure. Therefore, specific nutritional recommendations may not be sufficient, and it is necessary to evaluate the indication of nutritional support (Level B).

• Advice on diet should be on an individual basis and adapted to the needs of each patient (Level C).

Norms for food safety

Quality of food and drinks is very important for HIV-infected individuals, especially when they have been inappropriately handled or when water is not suitable for drinking.78,79

Precautions to be taken with food and drinks

The following recommendations should be observed for the handling, preparation, and consumption of food and drinks:

Safety. Only foods that have been hygienically handled and have undergone the necessary checks by the corresponding health authorities should be eaten.

Raw products. Raw or lightly cooked eggs, meats, poultry, fish, or shellfish (including marinated products, anchovies in vinegar, etc.) should not be consumed. The same applies to milk or dairy products that have not been treated industrially.

Eggs and sauces. Patients should not consume unpasteurized sauces or other products made with eggs. Only packed sauces that have undergone heat treatment (mayonnaise, salsa rosa, béarnaise, hollandaise, etc.) should be consumed. The same applies to milk or dairy products that have not been treated industrially.

Shopping. When shopping for food, patients should pay particular attention to quality, both in the case of fresh products (vegetables, fruit, meat, etc.) and in the case of preserves (tinned food, frozen food, etc.). The characteristics of all foods should be verified.

Storage. Recently purchased foods should be conserved in suitable conditions. Thus, perishables (meat, poultry, and fish) must be stored in the refrigerator at temperatures below 3 °C, and fruit, vegetables, eggs, and dairy produce at between 5 °C and 7 °C. Frozen foods should be kept at no more than -18 °C.

Thawing. Frozen products (potatoes, croquettes, vegetables, etc.) can be consumed by heating them directly where possible. When this is not possible, they should be thawed for the necessary time by keeping them in the refrigerator until they have thawed.

Preparation. When food is being prepared for cooking or made ready for eating, special attention must be paid to handling. Avoid speaking, sneezing, coughing, or touching the face, nose or hair.

Hand-washing.

Conservation. Those foods to be consumed after cooking and appropriate storage (e.g. in the refrigerator) should be reheated to boiling point in the case of soups and other liquid products, and to 70 °C at the center of other products.

Recommendations

• Immunodepressed patients who receive suitable training and education in food hygiene and handling can benefit from improved health, with reduced incidence of diarrhea and the subsequent improvement in global nutritional status (Level C).

• Training programs in food hygiene and manipulation should include a study of the food chain, from acquisition to preparation and consumption. Special attention should be paid to foods consumed outside the home (Level C).

Pharmacological interactions

HIV and drugs interact in 2 ways. On the one hand, HIV can affect the absorption of some active ingredients and reduce their bioavailability. On the other, some drugs can affect the patient’s nutritional status by producing gastrointestinal side effects.87 Any approach to this topic should also take into account food interactions, the consumption of drugs of abuse, and the increasingly extended use of the so-called “medicinal plants”.88,89

There are four types of interaction:

1. Effect of nutrients on pharmacokinetics. These effects are grouped according to how they affect the processes of release, absorption, distribution, metabolism, and elimination of drugs).

2. Effect of drugs on nutrient kinetics

a) Effects on the metabolism91

b) Effects on excretion92

3. Effects of nutritional status on availability

a) Gastrointestinal alterations

b) Liver alterations93,94

4. Effect of drugs on nutritional status

a) Action on gastrointestinal motility
Recommendations

• The only antiretroviral whose pharmacokinetics is affected by food is didanosine (Level A).
• Knowledge and efficacious management of drug-food interactions can influence the success of treatment and slow down the progress of the disease (Level C).
• The consumption of some herbal preparations can compromise the efficacy of antiretrovirals that are metabolized by CYP450 3A4 (Level A).
• Calcium and phosphorus determinations should be made in patients being treated with tenofovir due to the possibility of developing hypophosphatemia (Level B).

Pharmacological therapy

Several pharmacological treatments have been tried to improve the clinical signs of cachexia, i.e., anorexia and extreme weight loss.

The drugs studied can be classified according to their mechanism of action as orexins or appetite stimulants, anabolic steroids, and cytokine production modulators (see Table VI).

| Table VI |

| Drugs assayed in the treatment of AIDS as wasting disease |

1. Orexins or appetite stimulants
   – Megestrol acetate; Dronabinol.

2. Anabolic steroids
   – Testosterone enanthate; Oxandrolone; Nandrolone; Oxymetholone; Recombinant GH; rGH + IGF-1.

3. Cytokine production modulators
   – Thalidomide; Pentoxyphylline; Omega 3 fatty acids; NSAIDs (Ketotifen).

Recommendations

• The only antiretroviral whose pharmacokinetics is affected by food is didanosine (Level A).
• Knowledge and efficacious management of drug-food interactions can influence the success of treatment and slow down the progress of the disease (Level C).
• The consumption of some herbal preparations can compromise the efficacy of antiretrovirals that are metabolized by CYP450 3A4 (Level A).
• Calcium and phosphorus determinations should be made in patients being treated with tenofovir due to the possibility of developing hypophosphatemia (Level B).

Appetite stimulants

The best-known and used drugs in HIV patients are megestrol acetate and dronabinol. Both have CNS, gastrointestinal and cardiovascular side effects. Despite this, the results obtained in patients suffering from anorexia have been satisfactory.

Anabolic steroids

Testosterone has been shown to increase body lean mass and improve quality of life. Consequently, an improvement in insulin sensitivity has been observed. The use of other synthetic anabolic agents such as oxandrolone, nandrolone, and oxymetholone has also been associated with an increase in weight and lean mass in patients with HIV-associated cachexia in placebo-controlled studies both in isolation and associated with resistance exercise. Nevertheless, despite being associated with increases in lean mass, testosterone or its derivatives at supraphysiological doses in eugonadal males can reduce HDL levels and cause liver dysfunction and hypogonadism; therefore, it should be used with caution.

More recent studies do not show any advantage with nandrolone in patients with moderate or severe weight loss compared with growth hormone (GH). Recombinant GH in isolation has improved nitrogen balance and increased lean mass and body weight in HIV-infected patients with cachexia. Furthermore, it seems to provide certain advantages with regard to improved functional capacity and quality of life compared with testosterone and other anabolic steroids.

Multivitamins

The administration of vitamin and oligoelement supplements continues to be controversial, there being no accurate definition of ideal recommendations for this type of patient. If a micronutrient deficiency is detected, we recommend replacing the drug following the same lines as in any other situation of deficiency.

Recommendations

• HIV-infected patients with anorexia-cachexia syndrome must be treated. Therapy should be tailored and should include therapy specific to HIV infection and opportunistic infections, identification and treatment of the causes of malnutrition, and provision of appropriate pharmacological and nutritional support (Level A).
• If AIDS-related cachexia is accompanied by anorexia, appetite stimulants should be used. Hypogonadism in males should be treated with testosterone (Level A).
• Anabolic agents and resistance training can be used to improve weight and body composition on an individual basis (B).

Artificial nutrition

Artificial nutrition is indicated in all undernourished patients or in patients at risk of undernourishment who cannot, or do not want to eat by mouth.

The following patients are eligible for oral supplementation (OS) and enteral nutrition (EN):

– patients who maintain a sufficient digestive functional capacity with scarce oral intake (< 1000 kcal and 30 g of proteins).
– patients who present processes such as dysphagia (motor or functional) and who have a risk of malnutrition or already present frank malnutrition.
– patients who present malabsorption-maldigestion and who have a risk of malnutrition or already present frank malnutrition.
– patients with poor adherence to antiretroviral therapy.
– patients with opportunistic infections or tumors.

Patients for whom EN is contraindicated or for whom it does not cover 100% of their needs are eligible for parenteral nutrition (PN).

Oral supplementation is indicated when natural food is sufficient to cover the body’s needs and the patient has a functioning intestine. The different formulas of OS can prove effective to increase the total supply of energy and micronutrients in these patients. Enteral
nutrition. The indications would be insurmountable anorexia, severe malnutrition, motor or functional odynophagia and/or dysphagia, tumors, neurological alterations, enteropathy, pancreatitis, side effects of radiotherapy and chemotherapy, and low-flow fistulas. The access route depends on the patient’s clinical situation and the expected duration of the intervention. The oral route is indicated in patients who adhere to therapy, do not have dysphagia, and who accept the product. The nasogastric route is for patients with motor or functional dysphagia, or undernourished patients who require extra amounts and cannot ingest them orally. In some cases, it may be necessary to use a nasoenteric tube or an ostomy.

There is no consensus on the best enteral formula for HIV-infected patients. The most important factor is that the choice of enteral formula in this group caters for the patient’s clinical situation at all times, taking into account the degree of catabolism, requirements, digestive function, concomitant digestive disorders, etc., as with the healthy population. Enteral nutrition can be administered in boluses, with gravity systems, or with infusion pumps (this system is obligatory in patients with jejunostomy).

Parenteral nutrition is indicated in patients for whom EN is contraindicated, but who need nutritional support; or in patients with opportunistic infections which lead to severe diarrhea and malabsorption; and in patients who cover at least 75% of their requirements with EN. Patients with HIV infection have a high degree of catabolism with very high calorie-protein needs. Furthermore, special care must be taken with some elements such as zinc and selenium. Therefore, for the PN formula, the following are recommended:

- Calorie intake: 35 kcal/kg/day; 1.
- Nitrogen intake: between 1.2 – 1.75 g/kg/day of protein.
- 60%-70% of the non-protein calorie intake must be carbohydrates (glucose). No more than 5 mg/kg/min of glucose.
- 30%-40% of the non-protein calorie intake must be lipids. No more than 0.11 g/kg/h.
- Iron, mineral, vitamins, oligoelements and water supplements will be administered on an individual basis.

Home artificial nutrition. This allows patients the benefits of AN at home with the aim of optimizing their quality of life. It requires the collaboration and training of patients and their families in home artificial nutrition techniques and a minimum availability of human and material resources.

**Recommendations**

- OS with artificial formulas optimizes the response to therapy and improves patients’ nutritional status (B).

**Table VII**

<table>
<thead>
<tr>
<th>Dietary recommendations in HIV-infected-children</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Limit total fat intake: 1-3 years, 30-40% of calorie intake; 4-18 years, 20-35%.</td>
</tr>
<tr>
<td>- Saturated fat intake should be as low as possible and must not exceed 10% of calorie intake.</td>
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<tr>
<td>- Cholesterol must be present in as small a quantity as possible and must not exceed 300 mg/day.</td>
</tr>
<tr>
<td>- Reduce the consumption of sodium and trans-fatty acids.</td>
</tr>
<tr>
<td>- Reinforce the intake of fruit and vegetables, calcium, potassium, fiber, magnesium, and vitamins D and E.</td>
</tr>
<tr>
<td>- Fiber intake should be 14 g per 1,000 calories, which means 19-38 g per day depending on age and sex.</td>
</tr>
<tr>
<td>- During puberty, the intake of iron, calcium, and folic acid should be closely monitored.</td>
</tr>
<tr>
<td>- Added sugars should not exceed 10% of total calories.</td>
</tr>
<tr>
<td>- Daily potassium intake is 3,000 mg for children aged 1-3 years up to 4,700 mg in children aged 14-18 years.</td>
</tr>
<tr>
<td>- The recommended intake of sodium should be below 2,300 mg: 1,000 mg for children aged 1-3 years, 1,500 mg for children aged 4-13 years, and 2,300 mg for children aged 14-18 years.</td>
</tr>
<tr>
<td>- Recommended calcium intake: 3 daily portions of dairy produce throughout childhood (1-3 years: 600 mg/day, 4-8 years: 800 mg/day) and 4 portions during adolescence (9-13 years: 1,300 mg/day, 14-18 years: 1,500 mg/days).</td>
</tr>
<tr>
<td>- Avoid excess “competing drinks”, i.e. sweet fizzy drinks, and snacks.</td>
</tr>
<tr>
<td>- Administration of multivitamin supplements may be indicated, especially vitamin A.</td>
</tr>
</tbody>
</table>

- Oral EN via tube or ostomy is safe and efficient since it improves nutritional status with a gain in weight, lean mass and fatty mass, provides functional benefits (immune system and quality of life), and the different formulas are well tolerated. There is no evidence that immunomodulatory formulas offer additional advantages (B).
- The choice of enteral formula in HIV-infected patients must take into account the patient’s clinical situation at all times, given the degree of catabolism, requirements, digestive function, concomitant metabolic disorders, etc., as with the healthy population (C).
- Nutritional support with PN in HIV-infected patients must take into account the same factors as for other groups (C).

**Nutrition in HIV-infected children**

**Nutritional risk situations in HIV-infected children**

The introduction of HAART during the early months of life means that it is unusual to find under-
nourished children. Children with a stable disease may suffer from subclinical undernourishment (suboptimal intake of essential nutrients), especially during puberty. The coexistence of lipodystrophy, dyslipidaemia, insulin resistance, and inadequate bone mineralization complicates diet planning. Paradoxically, overweight is increasingly common, due to the excessive intake of calories and fats, which mirrors the situation in healthy children of the same age.

**Nutritional evaluation**

This should include a clinical history, dietary history, physical examination, anthropometry, body composition markers, and complementary examinations (bone age, DXA of the spinal column).

**Consequences of a change in habits and diet among children in our area**

Our objective is to promote from an early age a healthy lifestyle with physical activity and a healthy diet. In developed countries there has been a change in the consumption of food in the population aged < 18 years. This involves sweet fizzy drinks, non-citric fruit nectars, pizzas, salted snacks, semi-skimmed milk, and a reduction of as much as 36% in whole milk, bread, fruit and vegetables. The current situation of children is further complicated by sedentary habits, and the danger of obesity and osteoporosis.121,122

**Nutritional intervention**

This is the set of measures necessary to achieve an optimal nutritional situation, by avoiding metabolic and cardiovascular risks.

1. **Efficacious HAART.** Associated with an improved nutritional status. The first intervention should be an efficacious therapeutic regimen.123
2. **Carefully selected HAART.** There is no ideal regimen; therapy should be initiated when strictly necessary and less toxic NRTIs should be combined with NNRTIs or PIIs with a better metabolic profile.124
3. **Diet.** Recommendations on energy requirements should take age into account and will be modified according to physical activity (sedentary, active, or sporting)121,123 (table VII). The most important nutritional problem for infected children today is the increase in lipids and the risk of osteopenia.123,126
4. **Dietary supplements.** Vitamins are indicated in children with a stable disease may suffer from subclinical undernourishment (suboptimal intake of essential nutrients), especially during puberty. The coexistence of lipodystrophy, dyslipidaemia, insulin resistance, and inadequate bone mineralization complicates diet planning. Paradoxically, overweight is increasingly common, due to the excessive intake of calories and fats, which mirrors the situation in healthy children of the same age.

5. **Lifestyle changes.** Physical exercise reduces blood lipid levels, even heart rate, reduces the frequency of AHT, and improves bone mineralization. These benefits are more obvious in pre-adolescence.
6. **Other treatments.** At present, statins and fibrates are only indicated in selected adolescent cases.

**Recommendations**

- Nutritional recommendations in HIV-infected children should be early and form part of integral therapy (Level A).
- Recommendations on energy intake in infected children should be made taking into account age and sex, although a dynamic calculation will also be made and modified according to the degree of physical activity (Level B).
- Supplementation with multivitamins and minerals can be occasionally recommended, especially if diet is deficient and during periods of risk: first year of life, convalescence, and adolescence (Level B).
- Vitamin D and calcium supplements have not been shown to be efficacious in children with osteopenia; the best approach is to ensure that the recommendations for intake of dairy products are being observed (Level B and C).
- Physical exercise in children reduces blood lipid levels, even heart rate, reduces the frequency of AHT, and improves bone mineralization. These benefits are very obvious in pre-adolescence (Level B).
- At present, there are no indications for pediatric administration of drugs that modify blood lipids and insulin resistance, such as the statins and fibrates used in adults. These are only authorized in selected adolescent cases (Level B).

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