Dietary intake and counseling, weight maintenance, and the course of HIV infection

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ABSTRACT

Objective To define relationships among dietary intake and counseling, weight maintenance, and the clinical course of patients infected with the human immunodeficiency virus (HIV).

Design A prospective cohort study in an HIV clinic in a county hospital.

Subjects HIV-infected patients (68 with and 40 without acquired immunodeficiency syndrome [AIDS]) who had a good performance status and no chronic diarrhea were assessed at entry to the study and after 6 months. The following assessments were made: energy and nutrient intake based on 7-day food records, anthropometric measurements, immunologic function as lymphocyte T-cell subpopulations (ratio of CD4 to CD8), and serum cholesterol level. Patients were monitored to determine clinical outcome.

Intervention All patients received standardized dietary counseling designed to address identified intake deficiencies and maintain body weight.

Main outcome measures Changes in energy and nutrient intake, body weight, and clinical outcome (ie, time to AIDS-defining illness and overall survival time).

Statistical analyses performed Group differences (HIV group vs AIDS group) were sought using χ^2 analyses and Student's t test. A multivariate regression model was used to determined the best predictors of clinical outcome.

Results At baseline, total energy intake (based on 30 kcal/kg usual body weight) was adequate in both HIV and AIDS patients (101±4% and 103±5% [mean±standard deviation] of need, respectively). Despite dietary counseling and continued maintenance of energy intake, body weight, serum cholesterol level, and CD4 level progressively decreased. Consequently, saturated fat intake was found to be *inversely* related ($P<.01$) to serum cholesterol level. Clinical outcome (after 3.5 years) was associated with baseline ratio of CD4 to CD8 ($P<.0001$), weight ($P<.01$), and serum cholesterol level ($P<.001$). Multivariate analysis related ratio of CD4 to CD8 ($P<.001$) and weight maintenance ($P<.001$) to favorable outcome in the final model.

Applications Weight loss in patients with HIV infection is independently prognostic of clinical outcome, and development of hypocholesterolemia is not favorable for clinical outcome. Because weight loss progresses despite conventional dietary counseling to identify energy need, interventions earlier in the disease course should be considered along with increased target levels for energy intake. *J Am Diet Assoc. 1995; 95:428-432, 435.*

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Progressive weight loss occurs in most patients infected with the human immunodeficiency virus (HIV) (1-4). Pilot studies have suggested that malnutrition is an indicator of adverse clinical outcome (5,6). Thus, an increasing number of HIV patients are candidates for dietary counseling and nutrition intervention (7-10). Reduced nutrient intake, malabsorption, systemic effects of infections, and hypermetabolism have been reported to influence development of malnutrition in such patients (2,5,8,9,11-13). Despite potential clinical importance, to our knowledge dietary intervention guidelines based on success-

ful clinical experience are not currently available for HIV-infected patients. In fact, relatively few studies have explored this area. Therefore, we conducted a prospective cohort study to assess the influence of dietary intake and weight maintenance, reinforced by concurrent standardized dietary counseling, on clinical outcome of patients infected with HIV.

METHODS

Patients with HIV infection, with or without an acquired immunodeficiency syndrome (AIDS)-defining illness, and a favorable performance status (asymptomatic or with minimal symptoms) were eligible for our study. Exclusion factors included chronic diarrhea (ie, persisting for more than 30 days and/or requiring medication), severe gastrointestinal symptoms, and infection of the central nervous system. Approximately 60% of the ambulatory population at an HIV clinic in a county hospital in a large metropolitan area met these criteria. Informed written consent in accord with federal and institutional requirements was obtained.

Study Design

All patients had baseline assessment of nutritional status (including anthropometric measurements); energy and nutrient intake based on 7-day food records; gastrointestinal symptoms (based on a standardized questionnaire developed previously to assess factors influencing weight loss as a result of cancer [14]); immunologic function, including measurements of lymphocyte T-cell subpopulations (ratio of CD4 to CD8); serum immunoglobulin levels; and serum cholesterol level. Assessments were repeated after 6 months. Patients were monitored to determine clinical outcome; clinical management was established by each patient's primary physician.

Dietary Assessment and Counseling

Seven-day food records were used to estimate energy and macronutrient and micronutrient intake (15,16). Instructions in record keeping provided by registered dietitians incorporated food scales and models to enhance accuracy in regard to portion size. The food records were reviewed by a registered dietitian who used a standardized protocol to clarify portion size and food preparation questions. Records were analyzed using a computerized nutrient database developed by the Harbor-UCLA General Clinical Research Center and based on Handbook No. 8 of the US Department of Agriculture (17). The database was supplemented from published sources or manufacturer's data as needed.

The goals of dietary counseling, which were based on nutritional intake and status at baseline, were to address identified energy and nutrient deficiencies and maintain body weight. An energy intake deficiency was considered to be less than 30 kcal daily per kilogram actual or pre-illness usual weight; deficiencies in micronutrients were considered as less than 66% of Recommended Dietary Allowances (RDAs) (18). Patients with deficiencies were counseled by registered dietitians in accord with standard nutrition clinical practice. In this context, dietary counseling was used in conjunction with enteral supplements, if needed, to address deficiencies. Enteral tube feedings or parenteral nutrition were not given to any patient in the study.

Anthropometric Assessment

Assessments included current weight, height, triceps skinfold thickness, and midarm circumference. Patients were weighed clothed, without shoes, on the same printing beam scale according to a standardized protocol.

Laboratory Assessment

Blood for determining cholesterol level was drawn from patients who had fasted at least 10 hours (no food or liquid except water).

Table 1
Characteristics of HIV patient population

Characteristic	Patient population	
	HIV only	AIDS
Patients (No.)	65	43
Age (years)	35 ± 3[a]	37 ± 3
Sex (% male)	96	88
Intravenous drug use history (% used)	5	6
CD4 cell count	376 ± 39	114 ± 19[b]
Azidothymidine use (%)	40	81[b]
Body weight (% usual)	101 ± 1	98 ± 2
Serum albumin level (g/L)[c]	42 ± 1	40 ± 1
Serum cholesterol level (mmol/L)[d]	4.29 ± .18	3.72 ± .23[b]

[a]Mean ± standard error.
[b]HIV vs AIDS patient groups; $P < .01$.
[c]To convert g/L albumin to g/dL, multiply g/L by 0.1. To convert g/dL albumin to g/L, multiply g/dL by 10.
[d]To convert mmol/L cholesterol to mg/dL, multiply mmol/L by 38.7. To convert mg/dL cholesterol to mmol/L, multiply mg/dL by 0.026. Cholesterol of 5.00 mmol/L = 193 mg/dL.

Table 2
Gastrointestinal symptoms influencing energy and nutrient intake and/or assimilation in patients with HIV infection by degree of weight loss at entry to study

Symptom	Weight loss[a]	
	Yes (n = 28)	No (n = 80)
	%	
Sore mouth	24	20
Diarrhea (sporadic)[b]	21	17
Nausea	23	13
Abdominal fullness	18	17
Vomiting	9	5

[a]Loss of ≥5% of usual body weight.
[b]Patients with chronic diarrhea (≥3 stools per day × 30 days) or diarrhea requiring medication were not eligible for entry to this study.

The blood was immediately centrifuged, and stored at –20°C until analysis according to an enzymatic method (19). Flow cytometry and monoclonal antibodies were used to quantitate circulatory helper/suppressor lymphocyte T-cell subsets (CD4,CD8).

Clinical End-point Assessment

Criteria of the Centers for Disease Control and Prevention were used to define progression from HIV infection to AIDS (22). Overall survival time was calculated from the date of entry to the study to date of death. Event-free survival time was calculated from the date of entry to the study to date of either an AIDS-defining illness or death from any cause. The median follow-up period was 3.5 years.

Statistical Analysis

Baseline data from 108 patients were used for clinical outcome analyses. Differences between groups (HIV vs AIDS, HIV baseline vs 6-month follow-up, AIDS baseline vs 6-month follow-up) were determined by means of χ^2 analysis and Student's t test. Survival curves were constructed using life-table analysis, and differences were tested for event-free survival and overall survival (20,21). A multivariate Cox proportional hazards regression model was used to determine the best predictors of clinical outcome. All calculations were performed according to the survival analysis in BMDP (BDMP Statistical Software, vol 2, version 1990, University of California).

Table 3
Serial changes in clinical and nutritional parameters in patients with HIV infection

Clinical parameter	Patients with HIV infection only		Patients with AIDS	
	Baseline	6 mo	Baseline	6 mo
CD4 cell count	398 ± 46[a]	340 ± 45	103 ± 23	72 ± 23[b]
Body weight (% usual)	101 ± 1	100 ± 1	98 ± 2	96 ± 2[b]
Serum albumin level (g/L)[c]	42 ± 1	42 ± 1	40 ± 1	40 ± 1
Serum cholesterol level (mmol/L)[d]	4.32 ± 18	4.26 ± 16	3.98 ± .16	3.69 ± .26[b]
Total dietary intake (kcal/d)	2,175 ± 87	2,185 ± 87	2,275 ± 91	2,287 ± 205
Cholesterol intake (mg/d)	328 ± 22	356 ± 32	414 ± 50	447 ± 54

[a]Mean ± standard error from patients with determinations at both baseline and 6 months.
[b]HIV vs AIDS patient groups; $P<.05$.
[c]To convert g/L albumin to g/dL, multiply g/L by 0.1. To convert g/dL albumin to g/L, multiply g/dL by 10.
[d]To convert mmol/L cholesterol to mg/dL, multiply mmol/L by 38.7. To convert mg/dL cholesterol to mmol/L, multiply mg/dL by 0.026. Cholesterol of 5.00 mmol/L = 193 mg/dL.

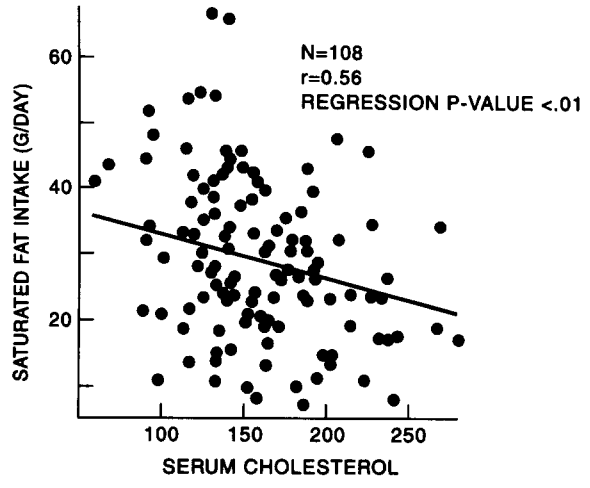

FIG 1. Total saturated fat intake (g/day) vs serum cholesterol level (mg/dL) in patients infected with human immunodeficiency virus.

RESULTS

The characteristics of the 108 HIV patient cohort are outlined in Table 1. At baseline, serum albumin level and percentage usual body weight were somewhat lower in the AIDS group compared with the HIV group, but not significantly so. Serum cholesterol level was significantly lower ($P<.01$) in the AIDS group. Although eligibility criteria excluded patients who had chronic diarrhea or severe gastrointestinal symptoms, other gastrointestinal symptoms that could have influenced intake and/or alimentation were not uncommon (Table 2). However, the frequency of these symptoms was similar in patients who experienced weight loss and those who did not, and the symptoms did not explain the weight loss in this population.

Daily energy and nutrient intakes at the time of entry to the study were determined from 442 food-record days in HIV patients and 301 food-record days in AIDS patients. Daily energy intake was similar in HIV and AIDS patients and was calculated to be adequate for weight maintenance based on 30 kcal/kg usual body weight (101±4% vs 103±5% [mean±standard error of the mean] for HIV and AIDS patients, respectively) or 30 kcal/kg ideal body weight. Intakes of macronutrients also appeared sufficient to meet identified needs. Of vitamins and micronutrients, only vitamin B-6, zinc, and folic acid were less than the RDA (74%, 65%, and 57% of need, respectively) in both HIV and AIDS groups; differences between groups were not significant.

Serial changes in study parameters for patients with baseline and follow-up determinations, based on a total of 1,124 food record days, are outlined in Table 3. As immunologic function decreased (as manifest by decreased CD4 levels), modest but progressive decreases in body weight occurred. The body weight change occurred despite relatively constant energy intakes (calculated to be adequate for weight maintenance by conventional criteria) and in the absence of severe diarrhea or clinical evidence of malabsorption. As a result, few patients met the criteria for aggressive dietary counseling or intervention. A downward fluctuation of serum albumin level within the normal range was also observed. A progressive, significant decrease in serum cholesterol level occurred despite stable or increasing daily dietary intake of energy, fat, and cholesterol. As a result, dietary saturated fat intake was *inversely* related to serum cholesterol level ($r=.56$, $P<.01$) in this HIV-infected population (Figure 1).

With respect to clinical outcome, life-table analyses (Figure 2) indicated strong clinical benefit associated with favorable ratio of CD4 to CD8 (median event-free survival > 900 days vs 266 days for favorable vs unfavorable tertile groups; $P<.0001$); weight maintenance (median event-free survival=656 days vs 301 days for low vs high tertile percentage usual body weight; $P<.01$); and high serum cholesterol level (median event-free survival=915 days vs 254 days for high vs low tertile groups; $P<.001$). A multivariate analysis using 16 variables including immunologic status (CD4, CD8, lymphocyte count, ratio of CD4 to CD8), serum immunoglobulins (IgA, IgG), nutritional status (percentage usual body weight; serum albumin level; energy, fat, and protein intakes), and major infections or malignant complications was conducted to determine the best predictor for event-free survival. The ratio of CD4 to CD8 ($P<.001$) and percentage usual weight loss ($P<.001$) were identified as independent factors best predictive of event-free survival.

DISCUSSION

In this study, baseline nutritional status (as manifested by percentage usual body weight) was an independent factor for predicting clinical outcome in patients with HIV. In addition to the strong ($P<.01$) association seen in life-table analyses, percentage usual body weight emerged as a significant ($P<.001$) predictor of clinical outcome in a multivariate analysis. These results expand

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Mary Grosvenor, MS, RD, is a research nutritionist in the Division of Medical Oncology at Harbor-UCLA Medical Center, Torrance, Calif. At the medical center, Grosvenor and her coauthors were reminded of how much patients with the human immunodeficiency virus (HIV) look like cancer patients — they were all losing weight and the more sick they became, the more weight they lost. Grosvenor and her colleagues began the research for this article when they could find little research written on the relationship between HIV and weight loss. Grosvenor et al examined, through a National Institutes of Health grant, how intake relates to an HIV patient's nutritional status and clinical course.

The following are Grosvenor's tips for dietitians who counsel persons with HIV and AIDS.

- *Intervene at an early stage.* Do not wait until patients look like they need nutrition intervention. Once patients need hospital care or receive a physician referral, it's too late — the patients are too sick and the disease has progressed too far for nutrition intervention to do much good. Catch patients early on even if they have not lost weight or if they seem to be eating an adequate diet.

- *Maintain cholesterol and fat intakes.* HIV patients typically have low serum cholesterol levels. We have shown an inverse relationship between dietary fat and cholesterol and serum cholesterol levels. HIV patients with low serum cholesterol levels should be closely monitored; associations have been found between hypocholesterolemia and adverse clinical outcomes.

- *Increase micronutrient intake.* Take a careful look at the patient's diet and make sure he or she is consuming at least 100% of the Recommended Dietary Allowance (RDA) for all vitamins and minerals. In our study we found that patients were consuming less than the RDA for vitamin B-6, zinc, and folic acid. Additionally, dietitians may recommend a multivitamin/mineral supplement.

- *Increase energy intake.* A study that we did with Ross Laboratories on enteral supplements showed that patients who consume an adequate diet (30 to 35 kcal/kg) could consume an additional 400 kcal/day and maintain their body weight. I would recommend that HIV-infected persons consume a few hundred more kilocalories per day.

- *Consume more and frequent meals.* To keep energy intake up, I would advise consuming many meals, snacks, and enteral supplements throughout the day. Enteral supplements may also help increase protein levels; low protein levels are a problem with many HIV patients who lose lean body mass first and fat second.

inferences based on observations from pilot studies in patients with advanced AIDS; in those studies severe reduction in albumin level (5) and lean body mass (6) were associated with decreased survival time (23,24). Such observations highlight the potential importance of dietary interventions directed at weight maintenance in patients with HIV.

In patients with HIV infection, weight loss is independently prognostic of clinical outcome and development of a low serum cholesterol level is not favorable

In this prospective study, most HIV patients who were free of chronic diarrhea had energy intakes calculated as being adequate to prevent weight loss, based on 30 kcal/kg usual body weight. This experience in a large patient sample in which intake was assessed using 7-day food records agrees with observations made by three other groups that used 3-day food records (9,25,26) and by one group that used the food frequency for intake assessment (27). In these studies, differences in intake were not observed when patients with HIV infection (with or without AIDS) and HIV-free controls were compared, despite the common occurrence of weight loss in HIV populations. Thus, the observation of good energy intake in ambulatory patients in the early stages of HIV infection has general support, although some contrary data have been reported (28). The observed intake deficiencies of micronutrients (zinc, folate, and vitamin B-6) reported here are also consistent with other reports (29-32). Because such levels of micronutrient intake may result in clinical deficiency syndromes, they represent appropriate counseling targets. Nevertheless, their presence cannot explain the progressive weight loss seen during the course of HIV disease.

The occurrence of weight loss despite apparently appropriate energy intake, together with the absence of clinical malabsorption in our population, support a role for other factors in HIV-associated weight loss, such as altered metabolism. Although moderately increased energy expenditure (33,34) and metabolic abnormalities (9,11,35) have been described in patients with advanced AIDS, recommendations for determining appropriate energy intake targets in patients with HIV are not available, especially for asymptomatic patients early in their disease course.

The striking inverse association between intake of dietary saturated fat and serum cholesterol level may well represent the convergence of two events: the observed stable or increasing dietary fat intake and the metabolic disturbance in lipid or cholesterol control mechanisms. In our study, low serum cholesterol level was related to adverse patient outcome. For patients with HIV, hypocholesterolemia has also been associated with increased β_2-microglobulin levels, a recognized indicator of HIV disease progression (36). From a clinical dietitian's standpoint, development of a low serum cholesterol level in an HIV-infected patient (36-40) should not be considered favorable, because associations between hypocholesterolemia and adverse clinical outcome from a variety of clinical conditions have been well described (40-46).

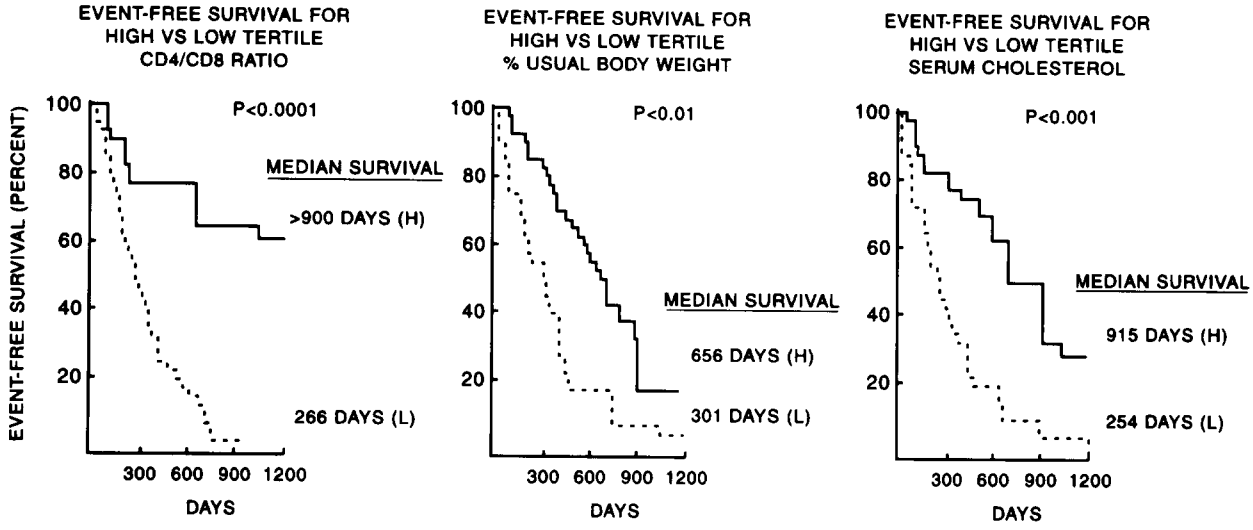

FIG 2. Life-table analyses of the influence of favorable immunologic status (ratio of CD4 to CD8), weight maintenance, and serum cholesterol level on clinical outcome in patients infected with human immunodeficiency virus H=high; L=low.

The difficulty in reliably determining energy intake in a population with changing intakes (eg, patients with a complicated HIV disease course) is well recognized (15,16). Seven-day food records were selected as the method best able to capture the dietary detail needed to estimate total energy intake. Because of the limitations of any method selected to accurately assess energy intake, implications regarding the mechanisms underlying the development of malnutrition in this population must be guarded. Practical inferences can be made, however, from the lack of success of the "standard" dietary counseling approach used for this prospective patient cohort. In our experience, even use of 7-day food records to identify energy intake deficiency for guiding timing and level of dietary counseling was inadequate to prevent progressive weight loss. These results are similar to those of Ysseldyke (47) who reported that malnutrition commonly developed in an HIV-infected patient population despite the use of "nutritional support" (of a nature not clearly specified) in 68% of patients. Thus, dietary interventions based solely on identifying problems with nutrient intake are not likely to be successful. If the goal of dietary intervention is to prevent weight loss and mitigate its adverse clinical consequences, new strategies based on early intervention to increase energy intake should be considered.

Several groups have demonstrated the feasibility of increasing energy intake in ambulatory HIV patients by means of dietary counseling combined with supplement use (48-51). Preliminary evidence also supports the concept that early nutrition intervention in patients with HIV infection can favorably influence nutritional and clinical outcomes. In a randomized trial, Chlebowski and coworkers (52) reported that before identification of intake deficiency, use of supplements — in excess of calculated need and provided as an enterotropic peptide-based formula in addition to regular dietary intake — was associated with body weight maintenance and fewer hospitalizations compared with supplementation with a standard enteral formula in a patient in the early stages of HIV infection. Such results support further research (53) to evaluate similar dietary interventions in the early stages of HIV infection.

APPLICATIONS

In patients with HIV infection, weight loss is independently prognostic of clinical outcome and development of a low serum cholesterol level is not favorable. As weight loss progresses despite apparently adequate energy intake, use of conventional criteria to identify energy requirements for counseling will be unlikely to prevent weight loss and to improve clinical outcome. Dietary interventions early in the disease course combined with increased target levels for energy intake should be considered. ■

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