Nutritional management of HIV in the era of highly active antiretroviral therapy: a review of treatment strategies

Dannae Brown and Marijka Batterham

Abstract The introduction of highly active antiretroviral therapy (HAART) has resulted in marked improvements in HIV disease outcome with improved long-term survival. These changes in disease treatment have necessitated changes in nutritional management strategies. Weight loss continues to occur in the HAART era and dietary counselling, oral supplementation, enteral and parenteral nutrition and pharmacological agents are treatment options. The introduction of HAART has been complicated by drug and nutrient interactions, the load of pills to be taken and side effects that all need to be considered in a dietary assessment. HAART has been associated with peripheral lipodystrophy or fat redistribution syndrome—a syndrome characterised by various combinations of hyperlipidaemia, insulin resistance, loss of peripheral fat stores, visceral adiposity and/or dorso-cervical fat accumulation. This syndrome has complicated the nutritional management of HIV and potential treatments and may require dietary modification, exercise and pharmacological treatments. Each patient could have a combination of different abnormalities all requiring an individually modified treatment strategy. Nutritional management of people with HIV/AIDS has become extremely complex and knowledge of conventional and current issues is essential to assist people maximise nutritional status. (Aust J Nutr Diet 2001;58:224–235)

Key words: HIV, AIDS, nutritional management, weight loss, highly active antiretroviral therapy

Introduction

The aim of this paper is to address the current nutritional management guidelines for people with HIV/AIDS. The treatments discussed here are complimentary to the nutritional issues discussed in the previous paper (1).

Weight loss

Treatments for HIV-associated weight loss

Weight loss still occurs in people with HIV/AIDS even in patients receiving highly active antiretroviral therapy (HAART) although the prevalence is not clear. Many people with HIV/AIDS already had advanced disease before HAART was introduced, and even in those who respond to treatment, viral resistance may develop thus reducing the effectiveness of the drugs. Due to the side effects of HAART and lifestyle changes necessary to take this treatment effectively, some people choose not to take therapy or, despite a good virological response, do not tolerate therapy. For these people with HIV/AIDS, nutritional management remains focused on maintaining nutritional status and treating the symptoms of disease. Management strategies for weight loss have progressed since they were last published in this Journal (2) and so they are discussed in detail below.

Dietary counselling

Intensive nutritional intervention is recommended early in the course of HIV infection to maintain nutritional status (3,4). When weight loss has occurred, nutritional intervention with or without oral supplementation (3,5–7), enteral-nasogastric nutrition (8), percutaneous endoscopic gastrostomy nutrition (9,10) and parenteral nutrition (11–14) has been trialled with varying degrees of success in increasing weight and improving body composition.

Few studies have examined the effect of nutritional counselling alone to improve dietary intake and weight in people with HIV/AIDS. Dowling et al. (5) conducted a prospective study to investigate the effect of dietary counselling on dietary intake, weight and body composition in 34 people with HIV/AIDS over 12 weeks. While nutrient intake increased, body composition was not significantly altered. Chlebowski et al. (6) examined the effect of dietary counselling in 108 people with HIV/AIDS over a six-month period in a prospective cohort study. Weight declined despite adequate energy intake. Van Niekerk and colleagues (15) investigated the effectiveness of nutritional counselling for treating weight loss in people with HIV/AIDS not receiving antiretroviral therapy. A mean weight increase of 3.5 kg was seen in 32 of the 60 subjects versus a mean weight increase of 2.0 kg in only six of the 28 matched controls.

Other research has investigated the role of oral nutritional supplementation in addition to nutritional counselling. Rabeneck et al. (7) compared dietary counselling with oral nutritional supplementation (treatment group) to dietary counselling without nutritional supplementation (control group) over a six-week period in 118 people with HIV/AIDS who had lost weight. They found no significant differences in the change from baseline in weight or body composition between the two groups; mean weight decreased by 0.1 kg in both groups; fat free mass increased in the treatment group by 0.9 kg and decreased in the control group by 0.4 kg (P = 0.077). Around 50% of patients in each group were able to...
achieve their recommended dietary intake for weight gain. Stack et al. (3) investigated the effects of dietary counselling including the provision of a high energy, high protein supplement for approximately six weeks in 17 people with HIV/AIDS. Twelve of 17 people were able to maintain or gain weight (mean gain 1.1 kg). However, the remaining five continued to lose weight.

Schwenk et al. (16) examined the effects of dietary counselling to increase intake with and without the addition of oral supplements. They found a significant increase in fat free mass over eight weeks in both groups. However, the weight change was not significant. Berneis et al. (17) also investigated the effects of nutritional supplements with dietary counselling (n = 8) or dietary counselling alone (n = 7) on body composition and whole body protein catabolism in people with HIV/AIDS. In contrast they found only the group receiving the oral supplement with dietary counselling had significant increases in fat free mass (2%) and a significant reduction in protein catabolism.

In most cases dietary counselling for weight gain was described as education regarding a high energy, high protein diet with individual modifications to minimise symptoms (e.g. foods low in fat and insoluble fibre in order to minimise diarrhoea) (3,5,7,18). In some of these studies the education was poorly described and referred to as following standard nutritional principles (6,19).

In one study parenteral nutrition has been shown to significantly increase weight (+8 kg), fat free mass (9%) and body cell mass (15%) in malnourished people with HIV/AIDS when compared with dietary counselling in which weight decreased by 3 kg, fat free mass decreased by 5% and body cell mass decreased by 12% (13). In contrast Kotler et al. (11,20) found no significant increase in body cell mass in people with HIV/AIDS receiving total parenteral nutrition. The weight gain in both these studies was primarily attributable to an increase in fat mass.

Percutaneous endoscopic gastrostomy feeding has been shown to increase weight (3.3 kg), although the mean increase in body cell mass was not significant (10). However, some subjects had opportunistic infections and experienced decreases in body cell mass while the others had a significant mean increase of 1.2 kg (10). Another study demonstrated significant increases in both body cell mass and fat mass in clinically stable people with HIV/AIDS fed through a percutaneous endoscopic gastrostomy tube (9).

Specialised supplements have also been trialled for their effectiveness in promoting weight gain and immune improvement in people with HIV/AIDS. A small pilot study in three HIV-positive subjects showed weight gains of 2 kg to 7 kg over three months when taking whey protein supplements (21). Whey protein supplementation for 14 weeks resulted in significant increases in weight (both fat free and fat mass) in HIV-positive women (22). A combination of β-hydroxy β-methylbutyrate, glutamine and arginine has also been shown to increase weight and fat free mass when compared with placebo in a double-blind study of HIV-positive people with weight loss over an eight-week intervention period (23). Another randomised double-blind placebo-controlled study showed that a combination of glutamine and anti-oxidant supplement resulted in a significant increase in the body cell mass in the treatment group compared with the placebo group after a 12-week period (24). In contrast, a study comparing two oral liquid supplements with and without arginine and n-3 fatty acids for six months showed similar body weight increases in both groups (25). A study investigating the effects of n-3 fatty acids over a ten-week period after a ten-week control period showed no significant change in body weight or composition with supplementation (26).

Some of these results are promising but further research regarding the doses and optimum regimens is required before these supplements could be routinely recommended for treating weight loss in people with HIV/AIDS.

Pharmacological agents in the management of HIV-associated appetite and weight loss

Several pharmacological agents, usually marketed for some other conventional use, have been investigated for their capacity to stimulate appetite and/or promote therapeutic weight gain in people with HIV/AIDS.

Hormonal agents with anabolic action

Testosterone

Hypotestosteronaemia was a frequent finding in HIV-positive men prior to the HAART era. Pre-HAART estimates suggested approximately 50% of HIV-positive males were likely to experience hypogonadism related to undernutrition, chronic illness or medications (27). Data relating to the degree of hypogonadism since the HAART era are limited but Berger et al. (28) suggest the prevalence of hypogonadism may be diminishing with more effective therapy (17.3% of 127 studied).

Grinspoon et al. (29) demonstrated an increase in fat free mass of 2.0 kg in hypogonadal men with wasting receiving 300 mg of testosterone every three weeks for six months versus a decrease of 0.6 kg of fat free mass in the placebo group (P < 0.05). There was no significant change in weight or exercise capacity. Treatment at this dose for 12 months resulted in a mean increase in fat free mass of 3.7 kg. More recently this same group of researchers demonstrated that weekly treatment with 200 mg testosterone for 12 weeks resulted in an increase in muscle mass assessed using computed tomography (30).

Dehydroepiandrosterone

Dehydroepiandrosterone (DHEA) is produced by the adrenal glands and converted to androgens and/or oestro gens in target tissues. Concentrations have been shown to decrease in people with HIV/AIDS and to be related to the amount of weight lost (31). A pilot study of the effectiveness of dehydroepiandrosterone in 32 people with HIV/AIDS showed significant improvements in mood and body cell mass over an eight-week treatment period (32). While this treatment warrants further investigation, it is not currently available in Australia for routine use.

Nandrolone decanoate

Prior to the introduction of recombinant human erythropoietin, nandrolone decanoate (a testosterone analogue) was used for the treatment of anaemia associated with chronic renal failure. Nandrolone decanoate use in men
with HIV/AIDS has been reported to result in significant increases in both weight (range 1.6 to 4.9 kg) and lean body mass (range 1.9 to 3.9 kg) (33–36).

Recombinant human growth hormone

Schambelan et al. (37) conducted a randomised placebo-controlled study of growth hormone at a dose of 0.1 mg per kilogram per day in 178 people with HIV/AIDS with weight loss. Weight (mean ± sd, 1.6 ± 3.7 kg) and fat free mass (3.0 ± 3.0 kg) increased significantly and fat mass decreased significantly (1.7 ± 1.7 kg) in the treatment group. On the basis of these results recombinant human growth hormone is available for use in the USA for HIV-associated wasting on a compassionate basis, and is currently available as part of a clinical trial for HIV-associated wasting in Australia.

Hormonal agents without anabolic action

Megestrol acetate

Megestrol acetate, a synthetic progesterone analogue, was initially used in the early 1980s as a treatment for advanced breast cancer. Weight gain and appetite stimulation were noted as unwanted side effects in many patients at conventional doses.

Three large randomised placebo-controlled studies (38,39) have investigated the effectiveness of megestrol acetate, at various doses, for treating HIV-associated weight loss. Significant weight increases of about 2 kg to 3 kg were found at doses of 800 mg per day. The body composition assessments conducted in two of the three studies showed an increase in weight, primarily in fat mass (38,39). One group also reported a significant mean increase in fat free mass of 1.14 kg in the treatment group compared with a decrease in the placebo group (38). However, the change in fat free mass was not significant in the other study (39).

Glucocorticosteroids

Glucocorticosteroids are used for the treatment of steroid responsive conditions such as inflammation, and also as appetite stimulants in oncology patients (40).

Prednisone (metabolically inactive) is converted to prednisolone (metabolically active) in the liver. Anecdotally, Coodley (41) reports doses of 40 mg to 80 mg per day of prednisone have been useful in improving weight in an HIV-positive patient population. Dexamethasone is a high potency corticosteroid that has also been used to increase appetite but not weight in cancer patients (42). A small study of dexamethasone in five people with HIV/AIDS with disseminated mycobacterium avium complex infection and progressive weight loss, as an adjunct to their antimicrobial therapy (43) demonstrated substantial weight gain (12% to 50% body weight prior to steroid treatment, P < 0.03) in all subjects.

It is likely that the increase in weight experienced with glucocorticosteroids is primarily fluid retention resulting from the mineralocorticoid actions (44), although body composition has not been assessed.

Non-hormonal agents

Dronabinol

Dronabinol (delta-9-tetrahydrocannabinoil) contains the neuroactive part of the marijuana plant and was trialled initially as a therapy for nausea and vomiting associated with cancer chemotherapy, following anecdotal reports of efficacy (45). This treatment is approved for use in HIV-associated wasting in many countries including Australia, but it has been taken off the market by the distributor.

Although dranabinol has been found to be an effective antiemetic agent, randomised controlled studies were unable to demonstrate a significant effect on weight in wasted people with HIV/AIDS (45,46). Dronabinol use was associated with a high incidence of neuropsychological side effects including dizziness, euphoria and confusion and limit the acceptability of this agent (45,46).

Smoked marijuana is also currently under clinical investigation in the United States as an appetite enhancing agent for people with HIV.

Cyproheptadine

Cyproheptadine is an antihistamine with antiserotonergic properties. The conventional use is for the treatment of acute and chronic allergies, pruritus and vascular headaches. It has previously been used as an antidepressant and to promote weight gain for patients with anorexia nervosa (47–49).

Summerbell et al. (50) observed weight gain (mean 3.1 kg) in only three of seven people with HIV/AIDS-associated weight loss treated with cyproheptadine but the increases in appetite and intake were significant. The authors concluded that cyproheptadine should be the first line of treatment for HIV-related weight loss as it produced an increase in appetite and moderate weight gain in some patients without the side effects of megestrol acetate.

Treating weight loss

Dietary counselling should be trialled as the first line of management for people with HIV-associated weight loss. As there is some discrepancy in the literature about the effectiveness of dietary counselling alone or in combination with oral supplements, it is important that practitioners consider studying and documenting the effectiveness of their interventions.

Nandrolone decanoate and testosterone are often prescribed for treating HIV-associated weight loss. Although formal protocols do not exist, other treatable causes of weight loss should be excluded and dietary counselling trialled before the use of these agents is contemplated. Presently the literature indicates that testosterone should be prescribed where there is evidence of hypogonadism, and nandrolone decanoate should be used in eugonadal men with wasting (51). Although nandrolone decanoate has previously been used in women, there is no literature regarding the effectiveness of this agent in women with HIV. Testosterone supplementation has been studied with success at low doses in women with HIV/AIDS (52).

Megestrol acetate is an effective appetite and weight-promoting agent in people with HIV/AIDS. It is, however,
associated with side effects related to its glucocorticoid activity, particularly with long-term use (38).

Recently, we conducted a controlled open label study to compare the effectiveness of nandrolone decanoate, megestrol acetate and dietary counselling in people with HIV/AIDS-associated weight loss (36). Weight gain was significant in all three groups (dietary counselling mean +1.1 kg, nandrolone decanoate +4.0 kg, megestrol acetate +10.2 kg). However, increases in fat free mass were significant only in the nandrolone decanoate (3.5 kg) and megestrol acetate arms (mean 2.8 kg) over the 12-week treatment period. The increase in percentage body fat mass was significant only in the megestrol acetate arm (+7.8%). We concluded that when dietary counselling fails, megestrol acetate should be the treatment of choice in palliative cases where weight and appetite increase were desirable. However, nandrolone decanoate was the preferred treatment for those with asymptomatic disease where an increase in fat free mass was the primary aim.

Due consideration must be given before the decision to recommend one of these agents is made. The weight gain achieved using the pharmacological therapies is usually only a few kilograms, and the long-term consequences of using these agents have not been evaluated. The treatments also differ significantly in their cost to the patient. Currently used agents, usual dose and costs are shown in Table 1.

At present there is no literature demonstrating improved survival with increasing weight or changes in body composition. However, it is assumed that increased survival will be the benefit of reversing losses in weight and fat free mass. Therefore the choice of intervention rests on the benefits to quality of life, enhanced performance, physical function and the potential to increase survival time. In palliative patients or those with advanced disease the focus of dietary counselling and treatment should be on quality of life and therefore weight gain and appetite should be maximised regardless of the composition of the change. In those with moderate disease and a long life expectancy, increases in fat free mass are desirable to maximise the potential survival benefit, while at the same time improving quality of life and enhancing performance and physical function (53,54). As the natural course of HIV disease progression seems to result in a decrease in fat free mass, even small gains or maintenance may provide survival benefit over a period of years.

Exercise
One study investigating the association between HIV disease progression and exercise in a cohort of 156 people with HIV/AIDS found that moderate physical activity (three to four times a week) may slow HIV disease progression (55). Resistance exercise has been shown to improve muscle mass in men with HIV/AIDS (30,56). Aerobic exercise has been shown to decrease fatigue and improve aerobic capacity (57–59). However, a recent Cochrane review concluded that most studies investigating aerobic exercise interventions in people with HIV were underpowered because of small sample sizes and high drop out rates and that it was difficult to make firm recommendations about an adequate regimen for effect (60). Nevertheless, current research suggests exercise should be recommended for people with HIV/AIDS and an appropriate regimen discussed with an experienced HIV physiotherapist or exercise scientist.

HAART-related nutritional issues

Drug and food interactions
Most antiretroviral therapies require dietary modification to maximise absorption (see Table 2). Indinavir, a protease inhibitor, is perhaps the most restrictive. This medication takes three times daily, eight hours apart. For one hour

Table 1. Dose, approximate cost and availability of pharmacological agents for treating HIV-associated weight loss in Australia (adapted from 97)

<table>
<thead>
<tr>
<th>Name</th>
<th>Usual dosage</th>
<th>Daily cost to patient (approximate $AUD)</th>
<th>Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testosterone</td>
<td>200–250 mg intramuscular per 2–3 weeks</td>
<td>$1.60–$2.00</td>
<td>Yes</td>
</tr>
<tr>
<td>Dehydroepiandrosterone (DHEA)</td>
<td>200–500 mg per day as 2–5 capsules</td>
<td>$2.00–$6.00</td>
<td>No (only available through special access scheme by application to the Therapeutic Goods Administration)</td>
</tr>
<tr>
<td>Nandrolone decanoate</td>
<td>100 mg intramuscular per 2 weeks</td>
<td>$2.80 ($76 for 4 × 50 mg)</td>
<td>Yes</td>
</tr>
<tr>
<td>Recombinant human growth hormone</td>
<td>1.4–6 mg subcutaneous per day</td>
<td>$260 ($1000 US per week)</td>
<td>No (placebo-controlled studies at some Australian centres)</td>
</tr>
<tr>
<td>Megestrol acetate</td>
<td>400–800 mg per day as 4–5 tablets</td>
<td>$5.00–$10.00</td>
<td>Yes</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>(not available)</td>
<td>$7 on PBS(a)</td>
<td>Yes</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>0.5–4 mg per day as 2–4 mg tablets</td>
<td>$0.15 on PBS(a)</td>
<td>Yes</td>
</tr>
<tr>
<td>Dronabinol</td>
<td>2.5–5 mg per day as 1–2 tablets</td>
<td>$4.00–$8.50</td>
<td>Yes, with special approval. Although no longer sold in Australia, some patients import this treatment.</td>
</tr>
<tr>
<td>Cyproheptadine</td>
<td>12–32 mg per day as 3–8 tablets</td>
<td>$0.30–$0.70</td>
<td>Yes</td>
</tr>
</tbody>
</table>

(a) PBS, Pharmaceutical Benefits Scheme which provides a discount for patients receiving social security benefits.
before and two hours after each dose (i.e. nine hours of the day) only snacks less than 1200 kJ, with less than 2 g of fat and 5 g of protein are allowed. Missed doses are associated with reduced drug efficacy (61). Often more than one HAART medication requires dietary adjustments. These changes may be overwhelming for the patient, particularly if they are taking antiretroviral medications for the first time. Dietitians working with this group should be aware of the dietary specifications and design an appropriate meal plan that both maximises nutritional intake and drug absorption. Liaising with the pharmacist to ensure the patient receives consistent and accurate information is important, for example, sometimes ritonavir can be prescribed with indinavir to eliminate the dietary restrictions.

Antiviral pill load

Some commonly prescribed HAART regimens contain up to 34 tablets per day (excluding prophylactic or other therapeutic agents) and some of the tablets and capsules are large and difficult to swallow. Most antiretroviral medications are taken two or three times a day, and it can take up to 15 minutes each session to take the pills. The efficacy of the regimen is reduced if medications are not taken to a strict schedule. All of this must be considered in a dietary education session. Achieving an adequate dietary intake with these restrictions is often challenging. Careful meal planning around the times of the day when appetite is great and consideration of the food specifications for particular medications is essential.

Side effects

Most antiretroviral treatments are associated with side effects. In our patient population in Sydney, Australia, 66% (n = 99) of those surveyed reported diarrhoea, 48% (n = 72) nausea and 45% (n = 67) loss of appetite (62). Most of these patients (84%) were receiving HAART and most attributed their symptoms to their therapy (62). Reijers et al. (63), reported side effects in patients receiving quadruple antiretroviral therapy and found diarrhoea present in 49 (lasting for an average of 98 days) and nausea in 13 out of 65 patients. Seven patients had to change their HAART medication for reasons of toxicity within the first 26 weeks of treatment.

Diet sheets providing information on symptom management (e.g. nausea, diarrhoea and loss of appetite) are available from the Dietitians Association of Australia NSW HIV/Oncology Interest Group. However, there are some points worth mentioning here about nausea and diarrhoea specific to HIV in the HAART era. (The Dietitians Association of Australia NSW HIV/Oncology Interest Group can be contacted through the national office of the association at 1/8 Phipps Close, Deakin ACT 2600.)

Nausea and loss of appetite

Nausea is listed as a potential side effect of most antiretroviral agents and is often the cause of a reduced appetite in those taking HAART. Maintaining nutritional intake can be difficult, particularly in patients with chronic daily nausea. In some cases adhering to food specifications can be helpful, for example the manufacturers recommend ritonavir, a protease inhibitor, be taken with food, to avoid nausea. When standard nutritional interventions fail, pharmacological antiemetics and/or an appetite stimulant (e.g. megestrol acetate, cyproheptadine) should be considered.

Diarrhoea

Diarrhoea is also commonly listed as a side effect of antiretroviral medications. It appears to be more prevalent in those people with HIV/AIDS receiving protease inhibitors (particularly ritonavir or nelfinavir) as part of their antiretroviral regimen. In some severe cases, this can be extremely debilitating. Standard anti-diarrhoeal medications can be helpful. However, issues concerning increased pill load and rebound constipation are commonly reported.

Dietary intervention can help, in some cases, to alleviate symptoms. Soluble fibre supplementation, in the form of psyllium husks, is usually the first line of dietary treatment and has been shown to be successful (64,65). There is anecdotal evidence that treatment with one or two heaped teaspoons of psyllium husks twice a day, with around 300 mL of water has been successful. Fat intolerance is often reported with nelfinavir-induced diarrhoea, and symptoms can be significantly reduced with a reduction of dietary fat, but care needs to taken to avoid weight loss. With chronic diarrhoea, lactose intolerance should also be considered.

Other treatments reported in the literature for controlling diarrhoea induced by protease inhibitors include calcium supplementation (66), pancreatic enzymes (67), and oat bran (68). The cost, availability and burden of pills all need to be considered when selecting a particular intervention.

Peripheral lipodystrophy syndrome or fat redistribution syndrome

As discussed in the previous article lipodystrophy is common in people with HIV/AIDS in the HAART era. The long-term implications of lipodystrophy are not established, although it is likely that hyperlipidaemia and hyperglycaemia will have negative consequences if uncontrolled. Of equal importance, particularly in the short term, is the impact these body shape changes have on quality of life, self-esteem, body image and drug compliance.

At present there are no effective treatments for lipodystrophy. As the underlying mechanism is unclear, most treatment strategies are based on symptom control. More research is needed in this area to ascertain the safety and efficacy of specific interventions. Potential intervention strategies are discussed below.

Diet and exercise

As with the general management of hyperlipidaemia, diet and exercise have been suggested as the first line of treatment (69). A working group of the adult AIDS clinical trials group (AACTG) (70) has issued preliminary guidelines on the management of lipid abnormalities in adults with HIV/AIDS receiving antiretroviral therapy. Recommendations for dietary management based on the National Cholesterol Education Program (71) are outlined in Table 3.

It should be noted, however, that there are limited data to indicate the efficacy of dietary intervention on HAART-
associated hyperlipidaemia. In one study, diet (plus exercise) significantly reduced the cholesterol and/or triglyceride concentration in eight of 44 people with HIV/AIDS with HAART-associated hyperlipidaemia. Drug therapy was required in the remaining patients to decrease concentrations to within normal the range (72). Moyle et al. (73) report a comparison of dietary advice versus diet plus pravastatin (a statin) in patients on protease inhibitor therapy with cholesterol concentrations greater than 6.5 mmol/L. Decreases in serum cholesterol of 4% and 17% for diet and pravastatin, respectively, were reported.

We investigated the relationship between dietary saturated and total fat intake and serum lipids, insulin resistance and body composition in 100 people with HIV/AIDS including 44 reporting lipodystrophy (74). We found no significant difference in dietary saturated and total fat intake (adjusted for total energy intake) between people with and without lipodystrophy. There was no sig-

Table 2. Current antiretroviral therapies available for use in Australia (dosage and food intake restrictions)

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Generic name</th>
<th>Food restrictions</th>
<th>Potential side effects</th>
<th>Food restrictions</th>
<th>Potential side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nucleoside analogue reverse transcriptase inhibitors</td>
<td></td>
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</tr>
<tr>
<td>AZT</td>
<td>Zidovudine</td>
<td>Take with low fat meal</td>
<td>Anaemia, nausea, headache, fatigue, neutropenia, neuropathy, myopathy, diarrhoea, fever, anorexia, altered taste, dyspepsia, increased liver function tests, weight gain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3TC</td>
<td>Lamivudine</td>
<td>No restrictions</td>
<td>Nausea, fatigue, diarrhoea, vomiting, anemia, anorexia, abdominal pain, dyspepsia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AZT+3TC</td>
<td>Lamivudine</td>
<td>Take with low fat meal</td>
<td>Hyperglycaemia, diabetes mellitus, hypertriglyceridaemia, diarrhoea, abdominal pain, nausea, anaemia, hepatomegaly, bloating, peripheral neuropathy, pancreatitis, elevated uric acid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DDI</td>
<td>Didanosine</td>
<td>Take 0.5 hour before or 2 hours after a meal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DDc</td>
<td>Zalcitabine</td>
<td>Take on empty stomach</td>
<td>Oral ulcers, dysphagia, abdominal pain, constipation, hepatomegaly, peripheral neuropathy, pancreatitis, nausea, diarrhoea, anorexia, myalgia, fatigue, weight loss</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D4T</td>
<td>Stavudine</td>
<td>No restrictions</td>
<td>Nausea, vomiting, abdominal pain, diarrhoea, pancreatitis, increased liver function tests, peripheral neuropathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1592U89</td>
<td>Abacavir</td>
<td>No restrictions</td>
<td>Nausea, headache, asthenia, rash</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generic name</td>
<td>Food restrictions</td>
<td>Potential side effects</td>
<td></td>
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<tr>
<td>Protease inhibitors</td>
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<tr>
<td>Saquinavir hard gel capsule</td>
<td>Take with &gt;54 g fat</td>
<td>Diarrhoea, abdominal discomfort, nausea, hypoglycaemia, increased creatine phosphokinase</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Saquinavir soft gel capsule</td>
<td>Take with &gt;28 g fat</td>
<td>As above</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amprenavir</td>
<td>Avoid high fat foods</td>
<td>Diarrhoea, nausea, rash</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Ritonavir</td>
<td>Take with meals</td>
<td>Nausea, vomiting, diarrhoea, abdominal pain, anorexia, taste changes, dyspepsia, hyperlipidaemia, abdominal pain, elevated liver function tests, triglycerides, cholesterol, creatine phosphokinase and uric acid</td>
<td></td>
<td></td>
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<tr>
<td>Indinavir</td>
<td>Take 1 hour before or 2 hours after a meal, &lt;5 g protein and &lt;2 g fat within the dose window. Require &gt;1.5 L of fluid/day</td>
<td>Nausea, vomiting, abdominal pain, diarrhoea, fatigue, nephrolithiasis, pharyngitis, taste changes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nelfinavir</td>
<td>Take with meal or light snack</td>
<td>Mild to moderate diarrhoea, nausea, flatulence, abdominal pain</td>
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<td></td>
<td></td>
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<tr>
<td>Kaletra</td>
<td>Take with meal</td>
<td>Diarrhoea, nausea, pancreatitis, hyperlipidaemia</td>
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<td></td>
</tr>
<tr>
<td>Non-nucleoside reverse transcriptase inhibitors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nevirapine</td>
<td>No restrictions</td>
<td>Nausea, fever, elevated liver function tests, weight loss, rash</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delavirdine</td>
<td>No restrictions</td>
<td>Abdominal pain and distension, anorexia, aphthous ulcers, colitis, constipation, diarrhoea, intestinal inflammation, dry mouth, pancreatitis, anaemia, rash</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Efavirenz</td>
<td>High fat meals to be avoided at dosing time</td>
<td>Dizziness, insomnia, rash</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ribonucleotide reductase inhibitors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydroxyurea</td>
<td>No restrictions</td>
<td>Bone marrow suppression, aphthous ulcers, hair loss, peripheral neuropathy</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(a) Potential side effects are obtained from the manufacturers’ information.
(b) When indinavir is used with ritonavir, indinavir food (not fluid) restrictions are removed. Doses should be taken with food (as per ritonavir specifications) to reduce nausea.
(c) Hydroxyurea augments the effect of other antiretroviral therapies (DDI, d4T and possibly other nucleoside analogue reverse transcriptase inhibitors) without having a direct antiviral effect.
Lipid-lowering agents

Gemfibrozil (a fibrate) has been used safely and has been shown to reduce levels of cholesterol, and particularly triglycerides, in people with protease inhibitor associated hyperlipidaemia (72). Although it appears that only a small number of people with HIV/AIDS will achieve concentrations within the normal range, the effect of even modest reductions in blood lipid concentrations on long-term morbidity and mortality should be considered. Fenofibrate is currently being investigated for use as a lipid-lowering agent.

Anabolic agents

Trials are currently under way to investigate the use of anabolic steroids for body composition changes in lipodystrophy. One study suggested that the incidence of body habitus changes in people with HIV/AIDS who were receiving steroids (testosterone, nandrolone decanoate, oxandrolone or growth hormone) was significantly lower than that reported elsewhere (84). However, the degree of virual control was lower in this group and this may have confounded the results. Some anabolic preparations are associated with increases in insulin resistance and serum lipids (85), although these changes have not been shown with injectable preparations such as nandrolone decanoate (86). Recently, we investigated the effect of high dose nandrolone decanoate on serum and body composition parameters in HIV-positive men with pre-existing lipodystrophy and showed no significant effects on serum lipids, glucose and insulin over an eight-week period (87). Waist circumference did not change. However, calf circumference and mid-upper arm circumference increased. These changes were viewed as favourable by the participants who felt the increases in arm and leg size gave a more balanced body morphology.

Growth hormone has been reported to significantly reduce visceral adiposity in lipodystrophy (88–90). It is
unknown whether growth hormone further decreases peripheral fat stores or increases blood lipid concentrations in people with HIV/AIDS. Also, positive effects on visceral adiposity seem to be lost once treatment has ceased. The cost of this agent may limit access in many centres. Further research is necessary to assess particular interventions with respect to efficacy, drug interactions and side effects.

Osteoporosis

A connection between the use of protease inhibitors and decreased bone mineral density has been proposed. Luna et al. (91) found decreased total body bone mineral density in a group of 17 HIV-positive men receiving HAART. More recently, Tebas et al. (92), examining whole body, lumbar spine and proximal femur bone mineral density, reported the prevalence of bone diseases such as osteoporosis was 50% in patients taking protease inhibitors. The risk of osteoporosis in subjects treated with the protease inhibitor was found to be twice that of people with HIV/AIDS not on protease inhibitors. These researchers also found a higher ratio of central to appendicular adipose tissue in the group treated with protease inhibitor but this was not found to correlate with bone mineral density, suggesting this to be an independent side effect of HAART. The role of diet has not been investigated in this context. Nevertheless, it would be prudent to ensure adequate calcium intake and, where possible, weight-bearing exercise by this patient group.

Assessing patients with HIV in the HAART era

Figure 1 shows the major reasons for referral of people with HIV/AIDS and suggested management strategies.

Weight and body composition

A history of weight changes and any changes in body composition should be documented. In particular, loss of peripheral or facial and gluteal subcutaneous fat and visceral adiposity should be noted as these are indicative of lipodystrophy. Body composition should be quantitatively assessed on a routine basis (about every three months), particularly prior to any changes in antiretroviral therapy. Bioelectrical impedance is useful for assessing fat free mass provided an appropriate prediction equation is used (93). Skinfold anthropometry is also useful for detecting site-specific changes in fat distribution. Multiple sites should be measured, but we have found the subscapular to triceps skinfold ratio particularly useful in predicting lipodystrophy (94). It is important to have serial measurements of body composition in order to distinguish between fat loss which may be related to lipodystrophy (95) and loss of fat free mass associated with HIV wasting. A dual energy X-ray absorptiometry scan to assess bone mineral content as well as body composition may be useful to assess potential osteoporosis.

Assessing dietary intake and social situation

Social supports, cooking skills, and financial situation should be assessed in addition to the adequacy of dietary intake. Long-term survivors with HIV may have lost most of their social network to the illness and be relying on social security benefits. Although the role of diet in treating lipodystrophy is unclear, focus should be given to the type of dietary fat consumed and its modification if necessary. However, the practicalities of cooking skills and the person’s living situation may take priority, particularly, in advanced disease where there is less concern over the long-term nutritional adequacy.

Assessing energy requirements

Although there is some discrepancy in the literature (discussed in the previous article) (1), resting energy expenditure and total energy expenditure (96) appear to be elevated in this population group. Energy intake has also been shown to be high in this patient group (74). Energy needs are 10% to 15% higher than that predicted by standard prediction equations and this should be taken into account when estimating energy requirements.

Biochemistry

In addition to any standard nutritional markers indicated by symptoms or disease, fasting measures of serum glucose, insulin, total and HDL cholesterol, and C-peptide should be measured routinely (95), particularly prior to and during treatment with antiretroviral therapy. In addition the CD4 T cell count and viral load should be documented as markers of HIV disease progression along with the length of HIV infection. These may affect the aggressiveness of treatment decisions.

Medications

Current and previous antiretroviral regimens should be documented and the restrictions associated with these medications incorporated into the dietary management plan. Other medications and drug-nutrient interactions or dietary restrictions should be considered.

Other risk factors

Documenting other cardiovascular or diabetic risk factors, such as smoking, family history and whether or not the patient exercises, may impact on the management plan. Although the metabolic abnormalities are usually associated with lipodystrophy, traditional risk factors can also result in lifestyle-related diseases in this population.

Conclusion

Nutritional management of people with HIV/AIDS has become an increasingly complex task. For dietitians working with this client group, knowledge of the current nutritional issues is essential to provide appropriate nutrition education and support. This paper has discussed current management strategies for managing some of the nutritional issues prevalent in people with HIV/AIDS in the HAART era. For those who may already have advanced HIV disease prior to commencing therapies, or for those people with HIV/AIDS who are not responding to, or cannot take, antiretroviral medications, it is also important to be aware of conventional nutritional issues concerning people with HIV/AIDS. It is crucial that dietary intervention is individualised to maintain and/or maximise the nutritional status and quality of life of each person positive for HIV.
Acknowledgment

The assistance of Sylvia Bridle, Pharmacist, The Albion Street Centre, in preparing the table referring to pharmacological agents is greatly appreciated.

References


Figure 1. Management schema for people with HIV/AIDS referred for nutritional counselling

- **Weight loss**
  - Assess cooking skills, food budget, social supports and dietary intake. Counsel on high energy, high protein diet (if on antiretroviral therapy avoid increasing saturated fat intake). Monitor weight and body composition.

- **HIV-positive patient referred for assessment and education**
  - In all cases assess:
    - weight history and body composition;
    - dietary intake, social situation;
    - energy requirements;
    - biochemistry and immune function;
    - antiretroviral and other medications; and,
    - symptoms or side effects of HIV and treatments.

- **Hyperlipidaemia**
  - Assess cardiovascular risk factors and dietary fat intake.
  - Modify fat and carbohydrate intake and encourage exercise.
  - Monitor body composition, lipids and insulin resistance.

- **Symptom management, e.g. diarrhoea, nausea, bloating**
  - Provide specific dietary intervention about foods which may exacerbate symptoms, e.g. moderate to high fat diets may exacerbate diarrhoea related to antiretroviral therapy.

- **Healthy eating**
  - Provide general dietary education and advice on specific food preferences, e.g. vegetarianism or alternative diets

- **If dietary counselling fails to increase weight,**
  - consider anabolic agents for those who are asymptomatic and megestrol acetate in those who are palliative. If recommending anabolic agents, check testosterone concentrations; if low, consider testosterone therapy, if normal consider nandrolone decanoate.

- **If dietary counselling fails to increase weight,**
  - consider anabolic agents for those who are asymptomatic and megestrol acetate in those who are palliative. If recommending anabolic agents, check testosterone concentrations; if low, consider testosterone therapy, if normal consider nandrolone decanoate.

- **If dietary counselling fails to increase weight,**
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Books received

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van Broekhoven-Grutters E, Gaasbeek D, Veninga-Verbaas M, Atlant Zorgroep, Apeldoorn, 2000, 70 pages, $30.00, ISBN 90-805882-1-0

Kids food health 1: nutrition and your child’s development: the first year

Kids food health 2: nutrition and your child’s development: from toddler to preschooler

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