Healthy lifestyle interventions in general practice: Part 9: Lifestyle and HIV/AIDS

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Introduction

This article forms the ninth part of the series on the role of lifestyle modification in general practice with specific reference to patients living with HIV/AIDS. AIDS continues to be a major global health priority. The global prevalence of HIV-1, the aetiologic agent responsible for AIDS, has stabilised at 0.8%, yet the number of people living with HIV worldwide continues to grow. In 2008, there were 33.4 million people living with HIV/AIDS, 2.7 million new infections, and 2.0 million AIDS related deaths. Heterosexual spread is the main mode of transmission in sub-Saharan Africa, which remains the most affected geographical area, with 67% of the global burden.[1] Whilst rates of infection are declining in some geographical areas, including some of the most heavily affected countries in Africa, they are increasing elsewhere including Eastern Europe and central Asia. Recent HIV epidemiologic research findings include new insights into the role of HIV viral load, co-infection with sexually transmitted infections, male circumcision, antiretroviral treatment, and superinfection in HIV transmission and prevention.[1;2]

South Africa continues to be home to the world's largest population of people living with HIV – 5.7 million in 2007. Based on the 2008 HSRC survey the national prevalence of HIV seems to have stabilised at around 11% of the population. However, HIV is a heterogeneous disease with varying prevalence by age, sex and province.[3] The prevalence is disproportionately high amongst females with about twice as many females as males affected in the age group 20–29. The peak prevalence amongst females is in the age group 25–29 with one in three females HIV-positive. Amongst males, the peak prevalence is in the age group 30–34, with about one in four males HIV positive. The prevalence of the disease has dropped from 5.6% in 2002 to 2.5% in 2008 amongst children aged 2–14 years. This is attributed largely to more effective prevention of maternal-child transmission. The incidence and prevalence of the disease also appears to be decreasing amongst 15–20 year olds.[3]

The clinical profile of HIV infection has changed substantially since the advent of highly active antiretroviral therapy (HAART). Whilst HIV infection was once viewed as an illness progressing steadily towards death, it is nowadays viewed as a chronic and episodic disease for patients who have access to and tolerate HAART. Thus morbidity is lower and functional capacity and quality of life issues have become paramount for patients living with HIV/AIDS. Therefore exercise training and physical fitness, healthy nutritional interventions and psychological interventions can play an important role in the management of patients living with HIV.

Physical activity in patients with HIV/AIDS

There is much scientific evidence that indicates that exercise training is not only appropriate but also warranted for patients with HIV/AIDS. Results from various meta-analyses suggest that constant or interval aerobic exercise at 60–80% of maximum heart rate, or a combination of aerobic exercise and progressive resistance exercise for at least 20 minutes, three times a week for a minimum period of four weeks is beneficial and appears to be safe for adults living with HIV/AIDS.[4,5] Furthermore, immunological and virological measures appear to be unaffected by aerobic exercise which is an important consideration for those patients starting an exercise programme. There are also documented improvements in cardiopulmonary fitness and improved psychological outcomes including improved quality of life amongst exercisers.[5,6] This suggests that adults living with HIV could expect many of the well established benefits of exercise.[6,7] However, a limitation of studies to date is that less information is known regarding participants who drop out of programmes or who are at more advanced stages of immunosuppression. A summary of the

Table I: Benefits of exercise at the three clinical stages of the disease

	Stage I	Stage II	Stage III
Clinical Characteristics	Asymptomatic HIV seropositive	Early symptomatic HIV	AIDS
Effects on Exercise Response	No limitations during graded exercise testing	Reduced exercise capacity	Dramatically reduced exercise capacity
	All metabolic parameters normal	Reduced submaximal VO_2 and VO_2 max	More severe VO_2 limitations
		Reduced heart rate reserve	Altered neuroendocrine response
Effects of Exercise Training	Increase in CD4+ cells	Lesser increase in CD4+ cells	Unknown effects on CD4+ cells
	Possible delay in onset of symptoms	Possible diminished severity and freq of symptoms	Inconclusive effects on symptoms
	Increase in muscle function and size		

benefits of exercise at the three clinical stages of the disease is presented in Table I.

Effects of physical exercise on the immune system

A review of the effects of exercise training on the immune system suggests that exercise training facilitated no decline in CD4+ counts in any of the studies regardless of initial stage of disease, level of CD4+ cells or symptomatology; a trend towards increased numbers of CD4+ cells with more significant increases seen in those subjects at earlier stages of the disease.[8] Furthermore, progressive resistance training with or without endurance training has shown to increase strength, improve fitness and improve CD4+ and CD4+/CD8+ counts in HIV positive elderly patients.[9]

Cardiovascular system

HIV disease and the treatment thereof (HAART) is associated with cardiovascular and autonomic dysfunction. This may be measured and monitored in the form of post exercise heart rate recovery.[10] Exercise training improves arterial compliance, baroreflex sensitivity and autonomic profile in HIV positive individuals[11] as well as reduces the traditional risk factors for cardiovascular disease.[12]

Metabolism

Central fat accumulation is increasingly recognised as a clinical issue for patients with HIV infection, particularly since the advent of HAART. The term "lipodystrophy" has been used to describe the changes in body composition and metabolic abnormalities commononly seen in these patients.[13] These include increased visceral adipose tissue accumulation, serum lipid abnormalities and insulin resistance. It has been shown that regular physical activity contributes towards prevention of fat accumulation in patients with HIV/AIDS,[14] lowers total cholesterol, low-density lipoprotein cholesterol, free fatty acid and highly sensitive C-reactive protein concentrations and improves insulin resistance and concentrations of high-density lipoprotein cholesterol.[15,16]

Skeletal muscle

Skeletal muscle structure and function might be impaired by HIV/Aids or the pharmacological treatments used in the management of the patients or a combination thereof. Furthermore there is evidence to suggest that there are central inhibitory factors associated with HIV/Aids that might be responsible for muscle atrophy and functional incapacity.[17] Resistance exercise is useful to induce skeletal muscle hypertrophy and can counteract the muscle wasting effects of HIV/Aids or associated therapeutic agents.[18]

Other benefits of physical exercise training in patients with HIV/AIDS include:

- Improved joint range of motion, increase in muscle strength and endurance capacity.
- Improved quality of life, self-esteem, improved fitness, mood and functional capacity with respect to activities of daily living.
- Modest reduction of fatigue, enhanced body image and sense of control

Yet, despite the abovementioned benefits of exercise training, more than one in four patients with HIV/Aids fail to meet the recommended level of suggested exercise or participate in any form of structured exercise.[19] This is thought to be even greater in rural communities.[20] Further research is therefore required to identify barriers to participation and interventions that would lead to increased exercise.

Primary prevention? Future directions

Although more studies are required, there is interesting preliminary data that show that athletically fit HIV negative individuals have a high serum reactivity with peptide NTM1, confirming that aerobic exercise training stimulates the

production of natural autoantibodies which could block the superantigenic site on the HIV-1 gp120 which could slow down disease progression. These exciting studies suggest that exercise training may be a promising, inexpensive adjunct anti-HIV therapy.[21]

Practical considerations in prescribing exercise for patients with HIV/AIDS

- Intense exercise or very long duration exercise > 90 min can depress immune function acutely in HIV negative individuals (decreased nasal and salivary IgA, decreased mitogen-induced lymphocyte proliferation, decreased natural killer cell cytotoxic activity, low lymphocyte blood counts induced by high concentrations of plasma cortisol). Therefore exercise bouts should not be intense (> 80% max) or last over 90 minutes due to the potential immunosuppressive effect.
- Exercise training should be individualised and should be increased in duration and intensity at a gradual rate.
- Fatigue is common and may signify progression of HIV, opportunistic infection or thyroid disease.
- Ongoing monitoring of body composition is desirable
- Anaemia is common and might lead to increased submaximal heart rate and fatigue
- Chronic diarrhoea can cause hypovolaemia, hyponatraemia and hypoglycaemia
- An acute change in general health status since the last exercise session is a contraindication to exercise.
- Many of the medications used might affect the exercise response e.g. AZT/DDI can cause anaemia and affect the body as described above
- Tai Chi has been shown to be an effective exercise intervention in patients with HIV/AIDS[22]
- Walking might be a useful intervention for peripheral neuropathy associated with antiretroviral therapy.[11]

Psychosocial interventions

The data linking psychosocial phenomena and immunity is well-described in the integrative field of psychoneuroimmunology. Psychological stress, trauma and depression in particular have been examined with respect to their impact on various immune parameters, the mediating neural, hormonal and peptidergic pathways of communication as well as impact on disease progression.[23] Given the centrality of immunity in HIV and its progression to AIDS, the implication of these data for HIV is significant.

The fact that HIV is immunosuppressive over time and stress is immune-modulatory (chronic stress being predominately suppressive as well), the variability evident in progression of HIV to clinical AIDS, even with the use of HAART, may be explained through stress-induced psychoneuroimmune pathways.[24]

The large body of data linking psychosocial phenomena and differential progression of HIV is not restricted to stress, but includes trauma (as defined in the DSM4) and depression as well.[25]

The question of which physiological pathways transmit the psychosocial influences and which aspects of viral pathogenesis are influenced by biobehavioural processes is currently being examined.

While data are incomplete, the evidence supports the theory that CNS-induced alterations in neural and hormonal activity regulate aspects of leukocyte functioning which in turn affects HIV replication and pathogenesis of immunodeficiency-related illness. For example, studies have consistently linked activation of the sympathetic nervous system (a feature of the stress response) with HIV-1 pathogenesis: SNS activity is hypothesised to enhance viral replication (thereby accelerating disease) by inhibiting interferons which consequently impairs resistance to viral gene expression and enhances cellular vulnerability to infection.[26]

Biobehavioural interventions have been examined with respect to their impact on HIV progression in particular. It is worth considering that, as for much of the psychosocial interventional research, the data are conflicting, probably as a result of relatively low patient sample numbers, methodological flaws, and in the case of HIV, variability of time of intervention (i.e. at time of testing, time of receiving serological diagnosis, latent period and presence of AIDS-related symptoms). Furthermore, some studies were conducted pre-HAART and some post. Finally, it is of particular relevance in the South African context that most psychosocial interventions which have assessed biological markers of disease – primarily CD4+ levels and viral load – have taken place in first-world countries. Given the complexity of the disease in this country, we should be cautious in extrapolating these data to our context.

In a review of randomised controlled trials of psychosocial interventions in HIV, roughly half had a demonstrable effect on the standard immunological parameters of disease. Invariably, where there was a significant impact on psychological states and adjustment there was an improvement in immune status and vice versa. Interventions described were predominately 6–12 week cognitive behavioural stress management programmes (which included various forms of relaxation, imagery and cognitive re-appraisal), but also included individualised interpersonal psychotherapy and journaling.[27] The simplicity and effectiveness of the latter intervention is worth mentioning, in that patients were asked to write about a highly stressful event for 20 minutes a day for four consecutive days (compared to controls who wrote about trivial events). Those writing about their worst stressor had reduced viral load at two weeks post randomisation and increased CD4+ counts over a six month follow-up compared with controls.[28]

Mindfulness-based stress reduction (MBSR), an eight week intervention which is being increasingly utilised in clinical settings worldwide has been shown to have significant salutary effect on humoral immunity in the context of a shift in dominance to the left prefrontal cortex versus controls.[29] These data led researchers to examine the potential of this programme to positively impact HIV-1 progression. A promising initial pilot study[30] led to a randomised controlled trial which demonstrated that this eight week mindfulness meditation training can buffer CD4+ T lymphocyte declines in HIV-1 infected adults.[31]

Dietary interventions for patients living with HIV/AIDS

The association of malnutrition, micronutrient deficiencies, weight loss and muscle wasting with the increased morbidity and mortality is clearly present in patients living with HIV/AIDS.[32,33] Factors resulting in a compromised nutritional status include reduced food intake, increased nutrient losses, drug-nutrient interactions and malabsorption as a result of gastrointestinal involvement and increased nutritional needs due to fever and infection. Further confounding factors include resource-limitations, food unavailability, and areas where a sub-optimal nutritional status is the norm.

Malnutrition results in an immunocompromised state, and also contributes to the severity of opportunistic infections often seen in persons with HIV/AIDS, and is a major factor in survival, as a body cell mass less than 54% of ideal body weight could result in death.[34] Furthermore, for patients on HAART, adequate nutrition is essential if the benefits of antiretroviral drugs are to be optimised, and essentially, prolong lives of HIV-positive individuals.[35]

Assessing nutritional status and dietary recommendations

It is important that the treating clinician refers the patient for formal assessment of nutritional status, which forms the foundation for effective dietary management. Components of the assessment include a diet history, anthropometric measurements, specified laboratory results and a thorough family and medical history, where the risk for other chronic and lifestyle-related disease is to be established.

Dietary recommendations

It is essential to maintain an adequate intake of macro- and micronutrients to restore malnutrition-related immune dysfunction. HIV-associated wasting is a clear indication that macronutrient requirements are not being met.

Macronutrient requirements

- Energy

The progression of HIV affects both energy expenditure and caloric intake and often results in increasing energy requirements. The requirements for energy and protein should be based on individual requirements, and should consider the stage of HIV progression and other factors implicating the intake and use of nutrients.[36,37]

During the asymptomatic HIV stage, a 10% increase in energy intake is recommended in order to maintain body weight and physical activity. During the symptomatic stage and the stages thereafter that progress to AIDS, these requirements are increased to 20–30%.[36] Energy requirements are increased by up to 50–100% during opportunistic infections.[34] Research indicates that by increasing energy requirements to 500 kcal above estimated energy requirements (40 to 50 kcal/kg of current weight), HIV-wasting could be improved, if not reversed.[38]

- Protein

Negative nitrogen balance and weight loss are well correlated, with protein losses accounting for 80–90% of weight loss during acute events, with less lost during starvation. It therefore becomes vital to maintain body protein stores (body cell mass) as this affects the survival of HIV infected individuals. With regards to recommendations for protein intake, there is currently insufficient data to support increased protein requirements in HIV infected individuals.[36] However, increasing protein intake can result in a positive nitrogen balance and lean body mass repletion (for maintenance, 1–1.4 g/kg is recommended and for repletion, 1.5–2 g/kg), except for patients with renal or hepatic disease.[37]

- Fat

Tolerance to fat intake and individual symptoms, such as malabsorpotion and persistent diarrhoea, will vary between individuals and need to be considered when determining each patient's recommendations for fat intake.[36,37] Improvements in abdominal symptoms, the reduction in the number of bowel movements, and decreased stool fat and stool nitrogen content have been demonstrated with the intake of readily available fats such as medium chain triglycerides. However, evidence does not support specific recommendations for fat intake in HIV infected individuals.[36] Immune function can be improved by the intake of omega-3 fatty acids (found in fish oils such as sardines, salmon, mackerel and herring) by reducing possible inflammation caused by higher intakes of omega-6 fatty acids.[37] For patients on HAART, specific recommendations regarding fat intake might be necessary, including the intake of omega-3 fatty acids and monounsaturated fatty acids, in the

treatment of hypertriglyceridaemia and for the prevention of cardiovascular disease, both being common conditions in this group of patients.[36]

Micronutrients

Micronutrients are involved in essential metabolic processes and immune function and adverse health outcomes have been observed with mineral and vitamin deficiencies.[34,36]

Due to adverse outcomes being reported with vitamin A, zinc and iron supplementation in the HIV infected patients, safe upper limits need to be established prior to specific recommendations being made for daily micronutrient intakes for HIV infected individuals.[36] It is recommended that HIV patients use a multivitamin mineral supplement that provides 100% of the recommended daily allowances and, where specific micronutrient deficiencies exist, to provide specific supplementation when required.[8,34]

For patients on HAART, particularly in developing counties, multivitamin supplementation should be seen as a complementary intervention and part of the total care package, and not as an alternative to HAART.[33]

- *Fluids*

The fluid needs of individual living with HIV/AIDS are no different to those of healthy individuals (30–35 ml fluid per kg body weight per day), however, fluid and electrolyte losses resulting from vomiting, diarrhoea and fever should be replaced.[37]

- *Alternative therapies*

Unconventional therapies have often not been subjected to peer review and scientific evaluation.[35] In South Africa, African potato, virgin olive oil, onion, spirulina, garlic, sutherlandia, frutescens and certain phytoserols have been unconventional treatments highlighted by the South African HIV Clinical Society. Various herbs including, St John's wort and milk thistle[39] have been contraindicated when used with HAART.[37] Garlic supplementation has been shown to reduce blood concentrations of HIV treatment drugs and cause adverse side effects and should therefore not be recommended to patients with HIV infection.[40]

- *Alcohol*

Alcohol intake is common amongst people living with HIV/AIDS and is associated with reduced adherence to HAART.[41] Because alcohol intake can be seen as a modifiable risk factor for any adverse HIV-associated health outcomes, HIV infected patients should undergo routine screening. Research has indicated that alcohol intake may be implicated in the development of lipodystrophy.[41]

- *Food and drug interactions*

The absorption of HIV medications can be affected by food in the gastrointestinal tract.[34] The bioavailability, effectiveness and tolerability of HAART will be affected by food and drug interactions, resulting in altered drug concentrations.[34] The side effects of medication as well as complicated food and drug intake recommendations, could affect tolerability and compromise HAART adherence.[34] It is important for patients to be made aware of any drug-nutrient interactions when commencing a treatment regimen.

Conclusion

This article has provided an overview of the basic lifestyle modifications to consider in the management of patients with HIV/AIDS. A holistic view with respect to exercise training, dietary modification and psychosocial interventions are all important in patient management. General practitioners should particularly be aware of the benefits of exercise and healthy nutritional interventions and assist their patients by suggesting adherence to accepted physical activity and nutritional guidelines. All patients should therefore be afforded the time and interest of their general practitioner so that they may assist their patients in making well informed choices with respect to their lifestyle to promote health and manage disease.

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