

ADVANCES IN NUTRITION SUPPORT FOR TREATMENT AND MANAGEMENT OF HIV INFECTION

*Chinmaya keshari sahou¹, Surepalli Ram Mohan Rao², Muvvala Sudhakar³, Uttam Prasad Panigrahy⁴, Satyabrata Bhanja⁵

¹Department of pharmaceuticals, Osmania University College of Technology, Osmania University, Hyderabad, Telangana, India.

²Professor, Mekelle Institute of Technology, Mekelle University, Mekelle, Ethiopia.

³Professor and Principal, Department of pharmaceuticals, Malla Reddy College of Pharmacy, Maisammaguda, Secunderabad, Telangana, India.

⁴Assistant Professor, Department of pharmaceutical Analysis and Quality Assurance, Malla Reddy College of Pharmacy, Maisammaguda, Secunderabad, Telangana, India.

⁵Associate Professor, Department of pharmaceuticals, Malla Reddy College of Pharmacy, Maisammaguda, Secunderabad, Telangana, India.

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ABSTRACT : Acquired immunodeficiency syndrome (AIDS) is an epidemic, severe and fatal disease which is caused by human immunodeficiency virus infection (HIV). HIV infection decreases immunity and increases number of other risk factors such as opportunistic infection, malnutrition, wasting syndrome and oxidative stress. Weight loss, lean tissue depletion, lipodystrophy, loss of appetite, diarrhea, and the hyper metabolic state each increase risk of death in HIV infection. The optimization of nutritional status, intervention with foods and supplements, including nutrients and other bio-active food components are needed to maintain the immune system. The nutrient may reduce the incidence and severity of infectious illnesses by forms of bio-protection which include reduced oxidative stress due to reactive oxygen species which stimulate HIV replication and AIDS progression. Hence nutritional management, counseling and education should be beneficial to the quality and extension of life in AIDS patients. This review gives idea about possible benefits of nutrient supplementation in the treatment and management of HIV infection and AIDS.

Key words: AIDS, HIV infection, Weight loss, oxidative stress, nutrient.

Introduction:

AIDS is considered one of the most dangerous¹ and a pandemic disease and has a great effect on society such as an illness, a source of discrimination and economic² condition of people. AIDS is the most serious infectious disease and actively spreading worldwide among humankind. Human immunodeficiency virus infection/acquired immune deficiency syndrome (HIV/AIDS) is a disease of human immune system caused by infection with human immune deficiency virus.

*Address of correspondence:

Chinmaya keshari sahou

Department of pharmaceuticals, Osmania University College of Technology, Osmania University, Hyderabad, Telangana, India.

AIDS is diagnosed when a person infected HIV has a CD4+ count of less than 200 cells/ μ L³. There are two types of HIV that cause AIDS such as HIV type 1 (HIV-1) and HIV-2. HIV-1 strain is closely related to the SIV (Simian immunodeficiency virus) that infects the Chimpanzee subspecies *Pan troglodytes troglodytes* or Gorillas (*Gorilla gorilla gorilla*). HIV-2 strain is closely related to SIV smm that infects sooty mangabey (*Cercocebus atys atys*) HIV is transmitted primarily via unprotected sexual intercourse such as heterosexual route⁴, homo sexual route⁵, anal sexual route⁶ and even oral sex etc., contaminated blood⁷ transfusions, hypodermic needles and from mother to child during pregnancy, delivery or breastfeeding⁸. Prevention⁹ of HIV infection

primarily through safe sex, male circumcision, use of diaphragms, substance abuse prevention and treatment, condom use, use needle exchange programs are key strategies to control the spread of disease and may lead to a near normal life expectancy. Antiviral agents¹⁰ with good micronutrient supplement have made HIV/AIDS a more manageable disease in some industrialized nations and several vaccines are about to enter phase III clinical trials. The micronutrient deficiencies are common in most HIV-infected people interfere with immune responses, weaken epithelial integrity and are linked to accelerated HIV disease progression. The potential of micronutrient supplementation with antiretroviral drugs plays a vital role for improving immune status, reducing HIV disease progression, improving nutritional status and possibly in reducing vertical transmission of HIV. Micronutrient¹¹ supplementation can play a vital

role in reducing the burden of HIV infection, improve quality of life and contribute to the improvement of nutritional status of people living with HIV/AIDS. The use of vitamins, minerals or other supplements¹² is considered to be a popular complementary therapy by people living with chronic diseases such as HIV/AIDS and even by the general public. It is reported that since the beginning of the HIV/AIDS epidemic, the use of vitamins/ minerals and other nutritional supplements has been one of the methods adopted by people living with HIV/AIDS as a complementary therapy to improve their general health status and quality of life as well as possibly reverse or slow down HIV disease progression and increase their survival¹³ rate. The present review gives idea about malnutrition, oxidative stress and micronutrient supplement for managing AIDS patients.

Malnutrition in AIDS patients:

Malnutrition¹⁴ is considered to be the most common cause of immunodeficiency worldwide. Malnutrition elicits dysfunctions in the immune system and promotes increased vulnerability of the host to infections. These immune dysfunctions are known as nutritional-acquired immune deficiency syndrome (NAIDS)¹⁵. Nutrition plays an important role in maintaining the immune system. Imbalance of nutritional status is a main cofactor in HIV infection and can contribute to death during AIDS progression¹⁶. Malnutrition and wasting

syndromes in AIDS sufferers are difficult to avoid when there is nausea, vomiting, diarrhea, thrush, esophageal and oral lesions, decreased appetite, lower absorption and lipodystrophy. Hypermetabolic states and drug-treatment side effects also contribute to body weight loss, a decrease in lean body mass. These nutritional situations create a high risk of death for AIDS patients. Malnutrition should be detected¹⁷ early, treated and monitored in order to improve the ability to respond to therapies as well as survival and quality of life.

PEM:

Protein-energy malnutrition (PEM) is known as protein-energy under nutrition¹⁸. PEM is an energy deficit due to chronic deficiency of all macronutrients. PEM causes widespread atrophy of lymphoid tissues, particularly T-lymphocyte areas in children. There is reduction in the thymus-derived lymphocyte growth and

maturation factors, arrest of lymphocyte development, reduced numbers of circulating mature CD4 helper cells and impairment of antibody production to T-dependent antigens in thymus. In malnourished children changes such as dermal energy, loss of delayed dermal hypersensitivity (DDH) reactions and loss of the ability of killer lymphocytes¹⁹ to recognize and

destroy foreign tissues were noted. In adequately nourished children they are usually huge but are virtually undetectable in children with severe PEM. This would indicate atrophy in the child's thymus, spleen, and lymph nodes, and severely compromised cell-mediated immunity. It is found that on malnourished patients have shown depletion of the thymolymphatic system and

severe depression of cell mediated immunity. Chronic thymic atrophy with peripheral lymphoid tissue wasting along with depletion of paracortical cells and loss of germinal centres was observed. This is confirmed to have led to various types of infections from which these patients died.

Essential fatty acids:

The deficiency of essential amino acid can suppress the synthesis of proteins responsible for production of cytokines released by lymphocytes, macrophages, and other body cells, complement proteins, kinins, clotting factors and tissue enzymes activated during acute phase responses. The deficiency of Arginine reduces the production of nitric oxide. Arginine also enhances phagocytes of alveolar macrophages, depress T suppressor

cells and stimulate T helper cells. The nonessential amino acid glutamine is necessary for lymphocytes and other rapidly growing cells. Particularly the omega-3 fatty acids²⁰, serve as the key precursors for the production of eicosanoids like prostaglandins, prostacyclins, thromboxanes, and leukotrienes that play a variety of host defensive roles. Thus their deficiency in the diet can impair cytokine synthesis.

Micronutrient supplementation multi-vitamins²¹

Vitamin C

Phagocytic cells cannot produce tubulin in the deficiency of vitamin C. Hence with impaired chemotaxis, microorganisms cannot be engulfed and destroyed. Higher intakes than the recommended daily allowance (RDA) vitamin C²² provides a unique pharmacological function, displaying the potential to serve as an antioxidant under conditions of drug induced glutathione (GSH) deficiency or free radical toxicity. People living with AIDS causes GSH deficiencies and often exhibit symptoms of acute scurvy characterized by life threatening weight loss, brittle bones and swollen glands. It is reported that GSH deficiency can result from changes in dietary vitamin C intake. Administration of a vitamin C rich diet (250

mg/dl) in the same study resulted in restoration of plasma GSH concentration^{11,23}. The high concentrations of vitamin C can act as a direct scavenger of free radicals as well as being able to convert oxidized forms of non-enzymatic scavengers (tocopherol and GSH disulphide) to their reduced states. Continual ROS production in HIV-infected persons may cause the biological system to consume antioxidants (free radical scavengers) at an increased rate which may lead to depletion of vital antioxidants such as vitamin C in the body. It is reported that in a population with a limited access to antiretroviral therapy, the findings that nutrient supplementation maintained the body mass index (BMI) as well as lean body mass (LBM) indicates a contributing role of nutritional supplements²⁴ on the quality of life and the general well-being of HIV positive patients.

Vitamin E

Vitamin E is necessary for the proper functioning of the immune system which increases humoral and cell mediated immune responses, antibody production, phagocytic and lymphocytic responses and exhibit resistance to viral and infectious diseases. The oxidative

stress created by HIV infection and related opportunistic infections increase the utilization of antioxidant vitamin E²⁴. Vitamin E deficiency may weak the immune system, increasing the susceptibility of people with AIDS to opportunistic infections.

B vitamins

B-group vitamins²⁵ like thiamin, riboflavin, pantothenic acid, biotin, folic acid and cobalamin can influence humoral immunity by diminishing antibody production. Pyridoxine deficiency is associated with reduced cell-mediated immunity. Folic acid and vitamin B₁₂ are essential to cellular replication. The deficiencies of these vitamins were reported to interfere with both replication of stimulated leukocytes and antibody formation. In anemia due to folic acid deficiency cell-mediated immunity is suppressed. The intake of thiamine,

riboflavin, niacin and vitamin B₁₂ were positively associated with improved CD4+T-cell counts and inversely associated with HIV disease progression in male patients¹¹. Vitamin B₁₂ deficiency is relatively uncommon in healthy populations but low serum vitamin B₁₂ concentrations are common among asymptomatic HIV-infected persons. Low B₁₂^{26,27} concentrations are associated with neurological and immunological abnormalities such as neuropathy, myelopathy, impaired cognition, reduced CD4+ T-cell count, increased bone marrow toxicity and increased mortality²⁶.

Beta carotene

The dietary intake of beta carotene^{28,29} was not associated with immunologic and clinical

progression of HIV-infected subjects. It reported that increased beta carotene intake improved survival rate in HIV positive subjects.

Vitamin A

Vitamin A³⁰ helps in nucleic acid synthesis and its deficiency is characterized by lymphoid tissue atrophy, depressed cellular immunity, impaired IgG responses to protein antigens and pathologic alterations of mucosal surfaces. Vitamin³¹ A deficiency decreases thymus and spleen sizes, reduced natural killer cell, macrophage and lymphocyte activity, lower

production of interferon and weak response to stimulation by mitogens. It is reported that vitamin A intake was positively associated with the CD4+T-cell count as well as a slower progression to AIDS³². It is reported that a decrease in serum vitamin A concentration was related to a decrease in CD4+T-cell count among HIV-positive drug-users^{33,34}.

Minerals

Selenium and immune function

Selenium³⁵ serves as an antioxidant and contributes to antibody responses and cytotoxicity of natural killer cells. In children with HIV infection, selenium concentration in plasma appeared to correlate with their immune functions. Selenium deficiency appears to enhance the virulence³⁶ or progression of some viral infections and that the increased oxidative stress resulting from selenium deficiency may induce mutations or changes in the expression of some viral genes. Selenium deficiency results in decreased activity of glutathione peroxidase with

a resultant increase in oxidative damage and the likelihood of mutation in the viral genome. Coxsackie virus is isolated from the blood of some sufferers of Keshan's disease suggesting that it may be a cofactor in the development of the cardiomyopathy associated with selenium deficiency in humans³⁷. Selenium deficiency is associated with impaired function of the immune system. Selenium plays a vital role in regulating the expression of cell signaling molecules such as cytokines, which orchestrate the immune response.

Zinc and HIV infection

Zinc is the fundamental component of thymic hormones and shares a similar role as vitamin A in nucleic acid synthesis. Zinc³⁸ deficiency influences both lymphocyte and phagocyte cell functions and affects more than 100 metallo enzymes that are zinc dependent. During infections reticuloendothelial cells sequester iron from the blood and phagocytes release lactoferrin with a higher iron binding capacity than bacterial siderophores. The net effect is to deprive the infectious agent of iron for its

replication and inhibit the spread of infection. Adequate intake of zinc is essential for maintaining immune³⁹ system function. HIV-infected individuals are particularly susceptible to the effects of zinc deficiency. A decreased serum zinc concentration is associated with advanced disease and increased mortality in HIV patients. Daily dietary supplementation with 45 mg/day of zinc for one month decreased the incidence of opportunistic infections when compared to the effects of a placebo⁴⁰.

Iron and its function

Iron serves as an antioxidant and contributes to antibody responses and cytotoxicity of natural killer cells⁴¹. Iron deficiency results in impaired

phagocytic killing, less response to lymphocyte stimulation, fewer natural killer cells and reduced interferon production.

Cytokine Abnormalities in HIV:

Cytokines are substances that play an important role in coordinating inflammatory response of the body to various external and internal stimuli. They may be pro inflammatory which are

essential to initiate defense against various pathogens and anti-inflammatory which downregulate the inflammatory process by suppressing production of the proinflammatory

cytokines and balance the inflammatory response. Excess production of both is counterproductive. The proinflammatory cytokines include IL-1 β , IL-6, IL-8, TNF- α , and IL-2, and the anti-inflammatory cytokines include IL-1 receptor antagonist, IL-4, IL-10, and IL-13. PEM diminishes immunoglobulin (IgA, IgM, and IgG) concentrations and cytokine production^{42,43}. Severe malnutrition alters the

ability of T lymphocytes to respond appropriately to IL-1 rather than simply affecting synthesis of this monokine. During catabolic states, interleukin 1 is released by a leukocyte which causes endocrine changes that lead to amino acid mobilization, primarily from skeletal muscle. These amino acids are used for gluconeogenesis in the liver, and the nitrogen released is excreted in urine⁴⁴.

Oxidative stress in patients

Oxidation is a critical factor in the pathogenesis of AIDS and HIV expression. AIDS patients have oxidative stress which is a condition caused by increasing ROS (reactive oxygen species) and decreasing antioxidants. Some asymptomatic HIV infected individuals and AIDS patients have decreased levels of antioxidant vitamins, sulfhydryl (SH) potential and total glutathione (GSH). These reducing equivalents are required by microorganisms for division and survival. A decrease in the level of vitamins and SH-containing compounds may also result from malnutrition and diarrhea. Opportunistic infections, diarrhea and malnutrition cannot fully account for the low level of GSH and cysteine (acid-soluble SH) found in HIV positive, but symptom-free and well-nourished patients⁴⁵. In the AIDS risk groups,

exposure to oxidizing agents such as tobacco smoke, drugs (paracetamol), paraquat, ethanol would lead to the oxidation of reduced glutathione (GSH) to oxidized glutathione (GSSG). GSSG is efficiently excreted from cells. Thus the systemic decrease of glutathione concentration in HIV+ may result from both decrease in synthesis [38] and increased degradation. The oxidative stress to which the AIDS patients are subject would lead to anomalies in many cells including lymphocytes, resulting in opportunistic infection, immunological abnormalities and neoplasia. It is reported that the blood levels of vitamin A, beta-carotene, vitamin E and the antioxidative status in AIDS patients significantly decreased compared to apparently healthy persons (Table 1).

Table-1. Comparison of effects of hiv infection and malnutrition on various parameters of the immune system^{44,47,48}

Immunological parameter	Effect of HIV infection	Effect of malnutrition	Nutrient deficiency
Total lymphocytes	Decreased	Decreased	PEM
T lymphocytes	Decreased	Decreased	PEM
CD4 T lymphocytes	Decreased	Decreased	PEM
CD8 T lymphocytes	Transient increase, then decrease	Relatively maintained	-----
CD4: CD8 T cell ratio	Inverted	Reversed	PEM
Cell mediated immunity	Compromised	Compromised	PEM, essential amino acids
B lymphocytes	Polyclonal activation	Maintained	-----
Immunoglobulin levels	Increased(IgA, IgG)	Reduced(IgA, IgG, IgM)	PEM, amino acids, vitamin B complex
Secretory IgA	Increased	Decreased	PEM
B- cell activity	Reduced	Reduced	PEM
Antibody response	Reduced	Reduced	PEM
NK cell activity	Increased	Reduced	VitaminA, C, Zn, Fe, Se
Serum complement	Increased	Reduced	PEM, essential amino acid
Serum β 2 microglobulin	Increased	Increased	PEM
IFN γ	Increased	Reduced	Amino acids
TNF α ,IL-6	Increased	Increased	PEM
Antiinflammatory cytokines (IL4)	Reduced	Increased	PEM
Soluble IL-2 receptor	Increased	Reduced	PEM
Antioxidants	Reduced	Reduced	Vitamin A,C,E
C reactive protein	Increased	Increased	PEM

Conclusion:

Antiviral agents with good micronutrient supplement may control AIDS. Nutrition intervention such as micronutrient supplementation is beneficial for people living with AIDS⁴⁹. Nutritional counseling can be effective and to influence health outcomes in HIV infection. It is reported that when dietary counseling is combined with nutritional supplements, it adds additional value and facilitates access to adequate dietary intake. Health professionals should provide information on alternative therapies cautiously and should

provide guidelines for home-based assessment. Nutritional intervention should begin early in patients diagnosed with HIV infection or AIDS evaluation of nutritional status should be conducted on a regular basis and nutritional supplementation should form an important and integral part of the clinical management of infected patients. Nutritional intervention can strengthen the immune system, replace lost micronutrients and reduce the severity or impact of opportunistic infections and may increase life span of patients.

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Conflict of interest:

The authors declare no conflict of interest.
