

NUTRITION AND PATIENTS WITH HIV/AIDS

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Immune status of an individual depends on the organism's nutritional status as well as on the choice of nutrients that enter the body. Malnutrition and HIV progression are closely linked and require an active cooperation between infectious disease physicians and nutritionist. It has been noticed that patients with HIV that receive antiretroviral therapy have a significantly greater loss of body weight, and therefore need an adequate diet modification. Oxidative stress represents an important etiological factor in diseases of immune deficiency, so that antioxidant agents (Vitamin A, Vitamin E, Vitamin B12 and certain minerals, such as zinc and selenium) are crucial factors in HIV dietotherapy. Polyphenols from cocoa beans as well as from green and black tea (catechins and teaflavins) have an important role in disease progress modification as well as disease transmission prevention. The patients also need their probiotic intestinal flora to be encouraged to grow properly in order to prevent opportunistic infections. All of these nutrition elements are already in use in prevention, therapy and alleviation of HIV symptoms, and further science development will make a personal diet modification for each patient possible. *Acta Medica Medianae 2011; 50(3):63-68.*

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Introduction

Nutrition and intake of bioactive nutrients have important roles in the immune homeostasis preservation. Epidemiological and clinical studies have pointed out that nutritive deficiencies interfere with organism's immunocompetence and increase the risk of infections. This is the characteristic of the whole population. The importance of nutrition status for the function of immune system is reflected in the fact that primary malnutrition leads to lymph organs atrophy, T-lymphocyte deficiency, as well as to an increased sensibility to pathogenic agents, reactivation of viral infections and development of opportunistic infections. Malnutrition is also considered to be responsible for the development of secondary immunodeficiency (1-3).

Bioactive nutrients may have a preventive effect on emerging of infections and tumors, gastrointestinal disorders and asthma. The immune system disorder has a significant impact on the etiology of these diseases and that is why scientists explore the immunostimulatory effect of these nutrients (4). Researches have shown that: lipids (fatty acids, cholesterol, fat soluble

vitamins), glucose and oligoelements (zinc, iron and copper) have the greatest impact on immune system (3). Immune system requires a high level of energy, so it uses glucose for starting and maintenance of its function (4).

Nutrition and bioactive nutrients have an impact on individual's genetic status on daily basis. Biological active components in nutrition have an active impact on genes that code transcriptional factors, pro-inflammatory cytokines and heat shock proteins which have an impact on efficiency of immune response. Immune response weakened by irregular food intake is not capable of coping with the attacks of viruses and pathogen agents (5).

Modern researches emphasize the importance of the association between pharmacology and nutrition integration with the aim of making the therapy of these diseases more efficient; further investigations in the field of nutrigenomics will give more detailed recognition of possible ways to efficiently use nutrition with the aim of prevention. Nutritional and pharmacologic regimes frequently used today and uniformly for all patients will not be acceptable in the future, while nutritive prevention of secondary effects of pharmacotherapy or multi-target combination of both therapies will be possible. Diseases that could be efficiently treated with combinations like these are: metabolic syndromes, immune system diseases and HIV infection (5).

Viral infections represent a significant global problem. The number of patients with HIV, tuberculosis and malaria in underdeveloped countries is increasing every year. Therefore, the Global Fund to

Fight AIDS, Tuberculosis and Malaria was formed in 2002, as well as the Global Alliance for Improved Nutrition in affected countries. There is also an increasing number of people infected with HIV in developed countries, while experts consider that irregular and inadequate nutrition represent an important precipitating factor (6, 7).

Malnutrition in HIV/AIDS and its nutritional prevention

Immune system of people infected with HIV is being slowly weakened over the years so that the symptoms develop progressively. HIV infection can develop slowly or rapidly until the occurrence of early symptoms of infection, after which HIV infection or AIDS develops. In case of developed AIDS, opportunistic infections can occur, which is not characteristic of healthy people (8). Nutrition plays an important role in the maintenance of the immune system and nutrition disorders may contribute to faster progression and even to patient's death. In patients with HIV/AIDS, malnutrition is hard to escape, since the symptoms like nausea, diarrhea, vomiting, lesions in esophagus and mouth cavity, decreased appetite, malabsorption and lipodystrophy are frequently encountered. That is why it is needed to detect malnutrition in the early stage, treat it properly and control it frequently with the aim to improve metabolic response to aggressive therapy and decrease unwanted effects of malnutrition. The efficiency of monitoring depends on the type and length of therapy, as well as the previous nutritional status and its maintenance. In patients with AIDS, it is of vital importance to preserve body weight (even the increase is desirable), blood supply of tissues and possibility of immune system's cells to get to specific tissues (8).

High connection between malnutrition and HIV/AIDS has been noticed by the experts with the occurrence of first epidemics (9, 10). The lack of food has become one of the leading causes of the occurrence of HIV epidemics around the world and an important cause of disease progression in infected people (11, 12). The research conducted on HIV-infected subjects that were either homeless or had temporary shelters in San Francisco have shown that human organism becomes more vulnerable to the outside agents (including HIV) when food is not always available (53.6% of subject did not have permanent access to food, and 32.4% of subjects were extremely jeopardized) (12). In the rural part of South Africa, there is a statistically significant difference when it comes to infants because they are being fed with their mothers' milk or milk formulas if they are accessible (13).

Severe malnutrition in HIV-infected individuals is closely associated with mortality. According to researches conducted in the eighties, death occurred when body mass fell under 66% of ideal body mass (of a healthy person, same age and nutritional needs) (9, 10). Researches are being

conducted all over the world with the aim of discovering food (functional food) that can promote health status and increase body mass index (BMI) in infected people. In one of the researches, the patients with HIV received a special spread (paste made of peanuts, rich in fat, resistant to bacterial contamination), while the control group received the mixture of corn and soya beans. Changes in BMI and free fat in the blood, survival of CD⁺ cells, disease activity and reaction of antiretroviral therapy were observed after 3.5 months. Nutrition of patients that were fed with peanut paste resulted in the greater increase in BMI as well as in increase of free fats in blood and larger circumference of the upper arm than in the controls (14). The aim of our study was to improve nutritional status in patients with HIV with the whey intake. In randomised study, the patients had an intake of: 40g whey proteins, 20.5g carbohydrates and 4g of fat in 280 calory meal, while the other (control) group took isocaloric food without whey proteins. Whey proteins did not increase body mass, but a significant increase of CD⁺ cells in blood was noticed (15).

A significantly higher loss of body mass was noticed in patients that received a highly active antiretroviral therapy (16, 17). This therapy interacts with nutrition in many ways. Nutrition can have an impact on absorption, metabolism, distribution and excretion of medications in positive and negative ways, and vice versa. Secondary effects of medical therapy (changes of taste, loss of appetite, vomiting, diarrhoea) may have a negative impact on intake and absorption of food. The combination of medicaments and certain food can have harmful effects that further jeopardize health (18). Nowadays, an incidence of severe malnutrition in patients that receive antiretroviral therapy can be decreased by adequate dietetic consulting. Severe malnutrition and progression of disease is possible to be prevented in the properly treated HIV-infected individuals that also have an adequate diet (19). Studies conducted on patients with HIV had an aim to evaluate the impact of the so-called Mediterranean diet on HIV progression in patients that receive therapy. The results have shown a positive correlation of MedDiet score and height of HDL-cholesterole in blood, so it is concluded that Mediterranean diet decreases the risk for cardiovascular diseases occurrence in these patients. Mediterranean diet has an impact on patient's metabolism, but these studies did not give answers to the question if this diet affects the immune system and, therefore, further investigations are needed (20, 21).

Impact of antioxidative agents on HIV progression

Studies have shown that certain changes are present in immune cells that are caused by oxidative stress, that is by an increased level of ROS (reactive oxygen species). It is concluded that oxidation represents a key factor in HIV pathogenesis, so a special attention is paid to adequate nutrition modification with the aim of

introducing antioxidant agents into organism. In the organisms of patients with developed disease as well as in the case of some asymptomatic patients, an increased level of antioxidative vitamins, total glutathione and decreased SH potential are noticed. Malnutrition and diarrhoea represent the symptoms of patients with developed AIDS, so that decreased level of antioxidative vitamins and components that include SH group can to some extent be their consequence. A few studies have shown that deficiency of vitamin A (liver, carrot, brocoli), beta carotene (palm oil, mango, carrot), vitamin E (nuts, tomato, sunflower oil), vitamin B12 (meat, eggs, milk) and certain minerals (zinc, selen) in blood, as well as decreased anti-oxidative status of organism is present in asymptomatic patients as well. Further research should give more details about other causes of deficiency, besides malnutrition and diarrhoea (8, 22, 23).

Progression of disease can in certain patients be a consequence of oxidative stress and apoptosis that are caused by higher levels of toxic drinks and food intake, but also of the impact of toxic chemicals, herbicides, alcohol and tobacco on patient's organism. It has been noticed that there is a variance between food intake and weight gain in infected people that take narcotics intravenously, irrespective of their regime of food intake and nutrition quality. Narcotic intake causes lower food intake, and thereby makes the immune system weaker, while new infections increase the organisms' need for adequate food intake, and that makes further discrepancy between the need for food and food intake. These facts show that protective agents should be focused on when it comes to apoptosis as well as the education of patients about decreasing of alcohol, tobacco and toxic materials intake besides antioxidative strategy for food intake (8, 18). Researches have shown that children of mothers that smoke are exposed to carcinogenic elements through breast milk, so it is needed to educate mothers whose infants are infected by HIV that intake of these factors can have further negative impact on infant's immune system (24, 25). In organism of people with HIV, there is a permanent deficiency of micronutrients even when their intake is in accordance with recommendations for certain population group. The cause of this occurrence is not completely clear, but it is sure that it has a great impact on variations in disease severity, chronic inflammation and organism's reaction to therapy; therefore, it has become clear that HIV infection requires specific nutrition in different disease stages (19). Keeping a normal nutritive status of HIV-infected patients requires consultations with dietitians. It is possible to satisfy almost two thirds of nutritive needs by oral intake of nutrients, so that the enteral and parenteral nutrition should be applied. It is recommended to determine organism's need for intake of minerals and vitamins in these patients and optimal diet should be prescribed only based on laboratory markers. High doses of vitamins (A, B1, B2 and folic acid, C, E and D), antioxidants and minerals are recommended to persons whose organism is conti-

nously exposed to infective agents as well as to oxidative stress, and should be considered while making diets for HIV patients. There is a strategy based on the theory that HIV patients should be fed with a large spectrum of macro- and micronutrients. However, there is an open question about correct doses of vitamins and antioxidants that should be recommended (8).

Catechins (antioxidants that can be found in cacao beans) and teaflavins (antioxidants that can be found in leaves of green and black tea) are two groups of natural polyphenols. The most active and most effective catechin in green tea is epigallocatechin gallate (EGCG). Besides its biomodulative quality, EGCG also has anti-inflammatory effects, such as inhibition of allergic response type IV and inhibition of histamine release. Also, antioxidative, antitumorigenic and antiviral activity can be seen as a consequence of EGCG intake. The researches conducted so far have shown that it is possible to use these active substances as a successful anti-HIV therapy, by prevention of glycoprotein 120 HIV binding to CD4 receptor (23). Another very important function has been noticed in investigation about the impact of effective components of green tea (EGCG) on HIV transmission. Peptide fragments that originate from prostatic acidic phosphatases are secreted in large amounts into sperm and form amiloid fibrilles. These structures capture HIV viruses inside themselves and take them directly to target cells. It has been proved that EGCG dissolves these fibrilles, and therefore reduces the possibilities of infection transfer (26).

When it comes to organism's need for micronutrients, there is a hypothesis that organisms defence of intestinal infections depends on the intake of micronutrients. A randomised controlled trial has been conducted, where HIV-infected individuals received one tablet a day that contained 15 micronutrients. Diarrhoea, respiratory infections, nutritive status, CD+ cells count and mortality were observed. Results have shown that supplementation resulted only in a partial reduction of severe diarrhoea and decreasing of death cases (27).

Prevention of opportunistic infections

In HIV-infected individuals, there is a permanent risk of opportunistic infections that are caused by pathogenic agents such as Salmonellosis, Listeriosis, Cryptosporidium, Mycosporidiosis, Mycobacterium avium complex (MAC) and Candidiasis. Regarding this fact, it is needed to consider food safety carefully, as well as to evaluate if and to what extent food promotes growth of useful intestinal flora, and in to what extent it promotes growth of pathogenic microorganisms. Bacteria that can asymptotically be found in the human organism (*E. Coli*) can act like opportunistic infections in people with compromised immune system (like patients with HIV) so infections like these can be prevented by routine intake of milk products with probiotic cultures that produce lactic acid. Bacteria from species *Lactobacillus*

can support mucosis surface integrity, improve immune response and improve white blood cells proliferation. Growth of probiotic intestinal flora can also be stimulated by addition of probiotics in the form of indigestible carbohydrates or oligosaccharides to food or drink (8).

Microbiological contamination of food can represent a severe health problem even in healthy infants (28, 29). When it comes to infected children, a special regime of nutrition is recommended with the aim of avoiding organism's defence system weakening and pathogenic bacteria attack. In these children, avoiding of fresh or insufficiently boiled food (eggs, meat, seafood, poultry, bean sprouts) is recommended. The intake of nonpasteurised milk products is forbidden, as well as the intake of nonpasteurised fruit juices. There is a great danger of secondary bacterial contamination (30, 31).

Children of HIV-infected mothers are in danger of virus transmission through breast milk and at the same time they are exposed to diseases which are characteristic of children of that age. These diseases can also be fatal if we consider these children's immune system status. It is now considered that it is the best for children in poor areas to be breastfed for six months, if it is not possible to safely introduce nutrition formula to these children (28). Recently, there has been a modification of recommendations when it comes to natural and artificial nutrition of infants. Researches have show that an infant is rarely infected with HIV that comes from mother's organism if it is fed only with mother's milk (32, 33). They become more frequently infected if they are fed with combined nutrition because foreign proteins or bacteria damage intestinal mucosa and then viruses can enter the organism more easily through these lesions. Therefore, it is recommended that HIV-infected mothers breastfeed their children and then suddenly stop if safe alternatives are available (32). Adequate nutrition of infant is crucial for regular growth and development. Therefore, HIV-infected women (especially in underdeveloped parts of the world) should suddenly stop breastfeeding only if they are advised by experts in which way it would be possible to replace breast milk and only if these methods of nutrition are always and surely available (34, 35). When it comes to older children from poor countries, it is concluded that they are more vulnerable to infection with HIV because of malnutrition, so that prevention strategy should be built only on adequate food providing (28, 29).

Damaged immune system and weak antioxidative response, which are connected with insufficient intake of selenium result in HIV infection worsening (36). One of selenium effects is protection of cell integrity, which results in immune system function enhancement and life prolongation of HIV-infected people. Selenium has a possibility of enhancing cellular and humoral immunity by increasing the activity of natural killer cells and cytotoxic T cells (37). Research in this area give encouraging results because in

vitro and in vivo studies have shown that selenium intake would make the immune system stronger and prolong life. It has also been shown that lower intake of selenium in patients with HIV is associated with severe cardiomyopathy (37, 38).

Research in the area of functional food give encouraging results when it comes to intake of food that would have an impact on organism's immune status improvement. A capability of tannin and other polyphenoles that come from cranberry to form uninformative complexes with viruses has been noticed (39). Biological components of whey (lactoferrin, beta-lactoglobulin, alpha-lactoglobulin, glycomacropeptide, immunoglobulin) have the ability to improve immunity. The mechanism of whey proteins' functions is in conversion of amino acid cysteine into glutathione, that represents an extremely active antioxidant. Numerous clinical trials have been conducted with the aim of lowering progression of viral infections (HIV, hepatitis B) and they gave remarkable results. Breast milk contains the ratio of whey/ casein 9:1 to 6:4 depending on the lactation period, while milk formulas contain the same ingredients in ratio 6:4 to 4:6 (40, 41). At the beginning of this century, extreme immunomodulatory and antitumor activities of *Grifola frondosa*, a mushroom, were reported. It grows in Japan and in north-eastern part of the USA. While exploring its capabilities, experts came to conclusion that it contains beta-glucanes that induce mytogenic activity and activate effective immune cells, like lymphocytes, macrophages and natural killer cells. They also stimulate the production of cytokines and chemokines such as interleukins and tumor necrosis factors (42).

Progress in etiology and HIV treatment understanding have made HIV infection a chronic disease that can be successfully treated. The risk factors, which include the lifestyle, especially diet, represent the important predisposing factors. Modification of HIV infection treatment has been followed with prolongation of life span of infected people, so there are new problems that include changes of taste and changes in appetite in elderly people, as well as difficulties in purchasing food and its preparation (32).

Conclusion

Modification and combination of pharmacological medicines and food have made it possible to improve prevention and therapy but also to alleviate the symptoms of HIV infection. Cooperation between infectious disease specialists and nutritionists is needed for obtaining the adequate results. A strong influence of certain nutritional and non-nutritional food components on the improvement of the immune system has been proven in prior studies, and development of new science of personalised medicine (nutrigenomics and nutrigenetics) opens space for more serious progress in this sphere.

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ISHRANA I OBOLELI OD HIV/AIDS-A

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Status imunog sistema individue zavisi u velikoj meri od nutritivnog statusa organizma kao i od izbora nutrijenata koji se unose u organizam. Malnutricija i progresija HIV-a usko su povezane, zbog čega je neophodna aktivna saradnja infektologa i lekara nutricioniste. Primećeno je da značajno veći gubitak telesne težine imaju osobe inficirane HIV-om koje primaju antiretroviralnu terapiju, te je kod njih potrebno adekvatno modifikovati ishranu. Oksidativni stres predstavlja važan etiološki faktor u bolestima imunodeficijencije, te antioksidativni agensi (vitamin A, Vitamin E, Vitamin B12 i određeni minerali, kao što su cink i selen) predstavljaju ključni faktor u dijetoterapiji HIV-a. Polifenoli iz zrna kaka, kao i iz zelenog i crnog čaja (katehini i teaflavini), pored efekata modifikacije toka bolesti, imaju ulogu u prevenciji transmisije bolesti. Kod obolelih je takođe potrebno podstaći rast probiotske crevne flore radi prevencije oportunističkih infekcija. Svi ovi elementi ishrane se već koriste u prevenciji, terapiji i ublažavanju simptoma HIV-a, a dalji razvoj nauke će omogućiti modifikaciju ishrane za svakog bolesnika posebno. *Acta Medica Medianae* 2011;50(3):63-68.

Ključne reči: *dijeta, HIV, SIDA, funkcionalna hrana, virusi*