Chapter

Nutrition Habits in People Living with HIV/AIDS in Bulgaria: Review of Current Practice and Recommendations

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Abstract

The innovations in the medical science and development of new biotechnology medicines changed significantly the course of the human immune-deficiency virus (HIV) infection toward a chronic condition. Along HAART, habits in nutrition place an important role in the improvement of the health status of people living with HIV. Proper diet and nutrition may enhance the adherence and concordance to prescribed therapy and its effectiveness, to reduce the risk of adverse drug events and to boost the immune function. In the resent years a tendency towards increased food supplements consumption is observed, especially in patients with chronic diseases. There is a risk of possible interactions between selected dietary supplements with the antiretroviral medicines which may result in decrease of the drug concentrations in the blood plasma and subsequent decreased therapeutic effect and increased risk of viral resistance. Still there are gaps in respect with such information in the guidelines and recommendations for treatment, monitoring and nutrition in HIV. More studies are needed to fully evaluate such interactions and to put recommendations both for the healthcare professionals and for the people living with HIV for their use in order not to compromise HAART and to maintain the desirable therapeutic outcome.

Keywords: HIV, nutrition, food supplements, highly active antiretroviral therapy, interactions

1. Introduction

The innovations in the medical science and development of new biotechnology medicines changed significantly the course of the human immune-deficiency virus (HIV) infection towards a chronic condition. The advancement of the highly active antiretroviral therapy (HAART) led to significant increase in the life expectancy allowing people living with HIV to have a near-normal life-expectancy while meeting a variety of acute and chronic care needs [1].

Along HAART, nutrition habits place an important role in the improvement of the health status of people living with HIV. Proper diet and nutrition (food-based attitude and micronutrient supplementation) may enhance the adherence and concordance to prescribed therapy and its effectiveness, to reduce the risk of adverse drug events and to boost the immune function. On the other side, one of

the main concerns in terms of nutrition habits, especially food supplement intake, is related to possible interactions with the antiretroviral medicines which may result in decrease of the drug concentrations in the blood plasma and subsequent decreased therapeutic effect and increased risk of viral resistance [2]. In this respect there are still gaps of scientific evidence for the antiretroviral drug-to-supplement interactions and only a few dietary supplements (i.e., Ca, Mg, Fe supplements) have been evaluated in combination with the currently available on the pharmaceutical market antiretroviral medicines [3, 4]. While, there is a tendency towards increased consumption of food supplements among patients with chronic diseases, healthcare providers should monitor their patients for potentially important drug—supplement interactions. People living with HIV should also be willing to communicate with their healthcare providers any administration of dietary supplements and special nutrition regimes in order to optimize their intake in compliance with the prescribed HAART and to avoid possible undesirable interactions.

It is a matter of national practices of the competent authorities and healthcare providers to provide reliable knowledge and adequate nutrition habits in people living with HIV to assure increased compliance and to maintain the effectiveness of the therapy.

2. Nutrition recommendations and habits of people living with HIV

In the recent years a tendency towards optimization of the HAART due to the development of new drug formulations, including fixed dose combinations led to decease in the "pill burden" and increase in the tolerability due to better safety profile [5]. Improvements in the drug supply process led to better access to HAART. Along with this there are growing evidences for the influence of lifestyle habits and nutrition on onset and progression of different chronic and socially important diseases. Due to these reasons nutrition recommendations and guidelines are created to help the competent national authorities, healthcare providers and people living with HIV to create overall care plan.

Literature search of published recommendations and habits for nutrition and HIV was performed in the scientific databases PubMed, Google Scholar, Scopus, Research gate using key words—nutrition, recommendations, guidelines, HIV.

2.1 Nutrition recommendations

Literature search aimed to find and review the scope and recommendations in published guides and scientific manuscripts for nutrition and HIV.

2.1.1 Guidelines for nutrition and HIV

Since 2002, the World Health Organization has issued a set of guidelines and manuals on nutritional care and support for people living with HIV/AIDS, nutrient requirements, regional consultations on nutrition, and integrated approaches to nutritional care of HIV-infected children [6–8].

The main scope of these guidelines and manuals is to promote proper nutrient requirements in people living with HIV and to focus on the need of adequate nutrition and access to food in all regions, especially in the developing countries. The guidelines give detailed information on the recommended daily intake of different micronutrients (i.e., vitamin A, C and E and B-complex vitamins, iron-folate supplementation, to boost the immune system and to meet the increased energy requirements of people living with HIV, sets of recommendations for appropriate food intake and the importance of the type of food for the effect of the antiretroviral therapy [9].

The WHO guides recommend that all national health authorities should provide counseling on the management of the long-term nutritional aspects of the antiretroviral therapies. It is also recommended that healthcare providers should improve the attention of people living with HIV that diet and nutrition may enhance the acceptability of their prescribed HAART and to improve adherence and effectiveness of therapy.

In 2001, a guide for nutrition care and support in HIV/AIDS was published thanks to the Food and Nutrition Technical Assistance Project of the Office of Health, Infectious Disease and Nutrition and the Bureau for Global Health at the US Agency for International Agreement. This document provided guidance on general nutrition care and support of people living with HIV, the role and source of selected micronutrients [10]. In 2004, this report was updated with information concerning mainly different types of important drug-drug interactions, food-medication interactions, and their impact on the effect of the antiretroviral therapy and detailed recommendations on how to avoid such interactions depending on the prescribed antiretroviral medicines. The guide also focuses on the need to identify reliable sources (i.e., Ministries of health, drug product information, pharmaceutical services, journals and patient organizations) of easy to comprehend information in the light of improved access to existing and new antiretroviral medicines, possible important drug-drug and drug-food/food supplement interactions [11].

In their latest updates the Guidelines of the U.S. Department of Health and Human Services and of the European AIDS Clinical society (v.9.1) for the treatment and monitoring of HIV/AIDS set list of recommendations and cautions possible interactions and effects between food and Ca, Mg and Fe supplements with the antiretroviral medicines [12, 13]. The guidelines also focus that the healthcare providers should always monitor their patients in terms of any food supplement intake for possible interactions with their prescribed HAART, not only in case of therapeutic failure.

2.1.2 Published articles for nutrition recommendation

The guidelines on treatment, monitoring and nutrition and HIV discussed above put more focus on the needs for adequate and proper nutrition and give practical advices for dietary regimes and micronutrient daily needs. Special focus is put also on the interactions between food and Ca, Mg and Fe supplements and antiretroviral medicines interactions.

However, there are still gaps of information in the guidelines concerning possible interactions between some food supplements, containing herbal products (i.e., St. John's wort, *Echinacea*, ginkgo) and the antiretroviral medicines and their impact on the therapeutic effect. For this reason the second part of the literature search focused on recommendations on nutrition and HIV from published scientific articles evaluating this type of interactions.

Results from systematic review published in 2017 show that the most frequently reported food supplement-antiretroviral medicine interactions in the literature from herbal origin are with St. John wort, ginkgo, milk thistle and cat's claw [14]. The proposed mechanism of action was examined mostly in pharmacokinetic studies and case-reports. It is considered that most probably these food supplements interact with the antiretroviral medicines on CYP450 enzyme system level either inhibiting or inducing different CYP 540 enzymes thus causing adverse events or reduced therapeutic response respectively. In the systematic review are included also studies evaluating the interactions between some micronutrients like vitamin C, ferrous fumarate, calcium carbonate, zinc sulfate and multivitamin. The latter are considered to form chelation with entry inhibitors (maraviroc), integrase inhibitors

(dolutegravir, raltegravir), protease inhibitors (atazanavir, darunavir, lopinavir, ritonavir, etc.), non-nucleoside reverse transcriptase inhibitors (efavirenz, etravirine) and nucleoside reverse transcriptase inhibitors (abacavir, emtricitabine, lamivudine, tenofovir) thus causing reduction in the therapeutic effect. The systematic review found also that for some of the dietary supplements there were controversial results but statistically significant interactions with selected antiretrovirals were found for St. John's wort, vitamin C, zinc sulfate, ferrous fumarate, calcium carbonate, multivitamins and some forms of ginkgo, garlic, and milk thistle [4, 15–17]. With this respect people living with HIV, who are prescribed HAART, should better avoid taking them. Cat's claw and evening primrose oil are found to increase significantly the levels of selected antiretrovirals and close monitoring for adverse effects is recommended [18, 19].

2.1.3 Nutrition guidelines and recommendations in Bulgaria

Bulgaria is a country with low HIV infection prevalence in the general population (2.8 per 100,000) but still there is a risk of rapid spread of epidemics in certain "most-at-risk" groups-injecting drug use and sex between men. There is already an epidemiological evidence for these groups and the main concern is the possibility of transmission of the infection to the general population [20]. In the resent years there is also a tendency in increase in the transmission via heterosexual contact (39% for 2016). The most affected age group is 30–39 years and the number of man is almost five times higher than the women [21].

In 2016, the Ministry of Health published two methodology guides - one for antiretroviral treatment and monitoring of adult people living with HIV. The guidance is based on the European guidelines for treatment and monitoring of HIV of the European AIDS Clinical Society from 2015 and gives straightforward recommendations and cautions for interactions between food and Ca, Mg and Al containing anti-acid medicine with selected available on the pharmaceutical market antiretroviral medicines and recommendations to the healthcare professionals to pay attention to possible drug-food and drug-food supplement interactions in case of treatment failure [22]. The other is a methodology guidance on prophylaxis of HIV transmission from mother to child was also published. This guidance gives nutrition recommendations for the children [23].

2.2 Nutrition habits

Nutrition habits and lifestyle play an important role in the overall care process of different chronic diseases and can contribute to the compliance to the prescribed pharmacotherapy [24].

Healthy diet, physical activity and proper micronutrient supplementation consistent with HAART can boost immune response, reduce side effect of medicines, improve the health status and can help people living with HIV to adhere better to therapy.

Studies have shown that people living with HIV tend to use dietary supplements as a part of their treatment care plan – mostly antioxidants and supplements from herbal origin. These patients are also more likely to use internet for searching and sharing health-related information. This hides a risk of misinformation from non-reliable sources of health information [25].

Competent healthcare authorities together with different non-profit and patients' organizations have developed online sources for health information with advices for nutrition habits, healthy lifestyle and dietary regimes [26–28].

Most of these sources of information, however, focus on the importance of nutrition, pay attention on the daily micronutrient intake, energy consumption

and provide ready dietary recipes. Still there is lack of information concerning the concordance of different micronutrient supplements with the prescribed antiretroviral therapy.

An ongoing study in Bulgaria among people living with HIV and their healthcare providers is evaluating the tendency for utilization of dietary supplements, the knowledge for possible dietary supplements-drug interactions and the sources of respective health-related information.

Preliminary results show that 50% of the people living with HIV, participating in the inquiry, are following healthy lifestyle including active physical activity and dietary regimes rich in proteins, fats and vegetables. Half of the inquired use dietary supplements mostly are proteins, amino-acids, vitamin C, vitamin D, fatty acids and multivitamins.

About 88% of the inquired agree that the balanced healthy dietary regime is important to boost the immune system and are aware of possible interactions between the prescribed therapy and the dietary supplements they are taking, 62% believe that the nutrition is important for HAART adherence.

The preliminary results also show that people living with HIV tend to use internet for health related source of information—86% use internet as a main source of information concerning nutrition and its impact on the health status and prescribed therapy. About 71% of these patients rely mostly on the information presented on the websites of patients' organizations.

The healthcare providers follow the methodology guidance for treatment and monitoring of adult people living with HIV issued by the Ministry of health. They also pay attention to the people living with HIV who are prescribed HAART not to take St. John's wort and ginkgo due to negative impact on the therapeutic effect of the antiretroviral medicines.

These preliminary results are consistent with those found in the literature and show the increasing tendency of administration of food supplements and the related with this search of health related information in internet.

3. Practical advices for nutrition and HIV for the Bulgarian health care setting

3.1 Practical advices for use of dietary supplements

The review of literature shows that the Bulgarian methodology guidance for treatment and monitoring of HIV in adult people is consistent with the European guidelines but since 2016, it has not been updated. The latest version (9.1) of the European guidelines for treatment and monitoring of HIV in adults gives information for some possible interactions between the antiretrovirals and Ca, Mg, and Fe supplements and multivitamins.

Based on this and the preliminary results from the inquiry, the advices for use of dietary supplements, which interact with available on the Bulgarian pharmaceutical market antiretrovirals, could be summarized in the following table (**Table 1**).

It should be noted that the European guidelines for treatment and monitoring of HIV in adults give detailed information on the potent interactions between micronutrients and particular HAART regime, while those interactions published in the literature from pharmacokinetic and case-report studies are only for selected antiretrovirals. That is way when healthcare professionals evaluate the risks of possible interactions should consider each of the antiretrovirals included in the HAART. For those possible interactions between medicines and food supplements for which an advice for use in concordance with HAART or recommendation for

Dietary supplement	Antiretrovirals	Potential outcome	Caution	Source
Micronutrient supplements				
Multivitamins and Al/Ca/Mg supplements	Dolutegravir/abacavir/lamivudine	Reduced therapeutic effect	Take separate in time (2 h after or 6 h before)	[14]
Multivitamins and Al/Ca/Mg supplements	Tenofovir disoproxil fumarate/ emtricitabine, tenofovir alafenamide/ emtricitabine	Reduced therapeutic effect	Take separate in time (2 h after of 6 h before)	[14]
Multivitamins and Al/Ca/Mg supplements	Dolutegravir	Reduced therapeutic effect	Take separate in time (2 h after of 6 h before)	[14]
Multivitamins and Al/Ca/Mg supplements and high doses Ca	Raltegravir 1200 mg once daily	Reduced therapeutic effect	Not recommended. Instead administer raltegravir 400 mg twice daily	[14]
Zinc sulfate	Efavirenz, etravirine, raltegravir, dolutegravir, abacavir, emtricitabine, tenofovir, zidovudine, lamivudine	Reduced therapeutic effect	Chelation suspected	[15]
Vitamin C	Atazanavir, darunavir, fosamprenavir, lopinavir, ritonavir, saquinavir, efavirenz, etravirine, dolutegravir	Reduced therapeutic effect	CYP3A4 induction suspected	[15]
Dietary supplements of herbal origin—potential CYP3A4 induction mechanism				
St John's wort	Atazanavir, darunavir, fosamprenavir, lopinavir, ritonavir, saquinavir, efavirenz, dolutegravir	Reduced therapeutic effect	CYP3A4 induction	[15]
Ginkgo	Atazanavir, darunavir, fosamprenavir, lopinavi, ritonavir, saquinavir, efavirenz, etravirine, dolutegravir	Reduced therapeutic effect	CYP3A4 induction	[15]
Garlic	Atazanavir, darunavir, fosamprenavir, lopinavir, ritonavir, saquinavir	Reduced therapeutic effect	CYP3A4 induction	[15]
Milk thistle	Atazanavir, darunavir, fosamprenavir, lopinavir, ritonavir, saquinavir, efavirenz, etravirine, dolutegravir	Reduced therapeutic effect	CYP3A4 induction	[15]
Dietary supplements of herbal origin—potential CYP3A4 inhibition mechanism				
Cat's claw	Atazanavir, darunavir, fosamprenavir, lopinavir, ritonavir, saquinavir, efavirenz, etravirine, dolutegravir	Adverse effects	CYP3A4 inhibition	[15]
Evening primrose Oil	Atazanavir, darunavir, fosamprenavir, lopinavir, ritonavir, saquinavir, efavirenz, etravirine, dolutegravir	Adverse effects	CYP3A4 and CYP2D6 inhibition	[15]

Table 1.
Potential interactions between antiretrovirals and micronutrients and dietary supplements of herbal origin available on the Bulgarian pharmaceutical market.

no use at all is not reported yet, it is advisable healthcare professionals and people living with HIV should monitor for possible effects on the therapeutic outcome and for adverse events.

As the national guidance is not updated in the same pace as the international ones it is recommendable healthcare professionals to be up-to-date with the most current recommendations and guidelines.

It is advisable people living with HIV to communicate with their healthcare professionals possible use of dietary supplements and micronutrients in order to not to interfere negatively with their prescribed therapy.

3.2 Practical advices for use of health-related sources of information

The preliminary results from the inquiry show that people living with HIV are more likely to use internet health-care related sources of information related to nutrition and lifestyle. In this respect, in order to prevent misinformation, it is advisable to recognize reliable sources like websites of the patients' organizations and trusted health websites. Most of these websites, however, do not present information about drug-drug and drug-micronutrient and dietary supplement information. That is way it is advisable that people living with HIV to communicate with their healthcare providers the nutrition and lifestyle habits as well. Healthcare professionals can discuss with them trusted sources of health-related information and recommend such.

4. Discussion

The literature search on the nutrition habits and HIV shows that the competent health authorities worldwide consistently issue recommendations and guidelines which could be implemented on national level.

On the basis of the increased need for healthy lifestyle as an important component of the treatment process of many chronic diseases and the increased consumption of food supplements [29], more studies with higher significance of the results should be performed in order to fully evaluate the possible interactions between different medicines and available food supplements and micronutrients.

The study on the current practice on nutrition habits and HIV in Bulgaria shows that people living with HIV acknowledge the importance of nutrition and healthy lifestyle for the adherence and the overall effect of the antiretroviral therapy and the majority of them are informed about possible interactions between the prescribed antiretroviral therapy and the dietary supplements and micronutrients they are taking, mostly from internet. These results are consistent with those published in the literature.

The study has this limitation that the current results are preliminary as it is still ongoing.

The Bulgarian guidelines for treatment and monitoring of HIV in adults are consistent with the European ones but are not updated and the same pace and currently do not give information on food supplement-drug interactions. However, they recommend that healthcare professionals should be aware of such in case of treatment failure.

Patients' organizations in Bulgaria are very active and maintain up-to-date websites and other sources of information like brochures and periodic initiatives and meetings but still there is a lack of information about the potent interactions between drugs and dietary supplements in the light of increased consumption of food supplements in the overall population [30].

It is advisable that people living with HIV communicate more with their healthcare professionals in respect to their nutrition habits in order not to compromise the therapeutic effect of their prescribed therapy.

5. Conclusion

The innovations in the medical science and development of new biotechnology medicines changed the course of the human immune-deficiency virus (HIV) infection towards a chronic condition and increased significantly the life expectance.

People living with HIV are more likely to follow healthy lifestyle and build proper nutrition habits but are also willing to use food supplements and micronutrients as a part of their care plan. They acknowledge that nutrition habits place an important role in the improvement of the health status, enhance the adherence and concordance to prescribed therapy and its effectiveness, reduction in the risk of adverse drug events and to boost the immune function. However, there is a risk of possible interactions with the antiretroviral medicines which may result in decrease of the drug concentrations in the blood plasma and subsequent decreased therapeutic effect and increased risk of viral resistance.

International guidelines are issued periodically to help competent health authorities and healthcare professions in the process of care of people living with HIV. The guidelines for treatment and monitoring of HIV in adults and those for nutrition and HIV already present information about potent interactions between selected micronutrients and antiretrovirals, but still there are gaps of information concerning possible interactions between drugs and food supplements from herbal origin.

People living with HIV are also more likely to use internet for nutrition and health-related sources of information. In this light competent authorities, healthcare professionals and patients' organizations should place info-vigilance strategies to monitor the reliability of health-related information in order to protect consumers from misinformation. People should be advised to use only trusted medical websites and have closer communication with their healthcare professionals. They should be also educated how to monitor their health status and what possible outcomes to expect when using food supplements and micronutrients (desirable or negative) alongside the prescribed antiretroviral therapy and should always communicate with their healthcare professionals (physicians and pharmacists) any changes in their nutrition habits. Healthcare professionals should follow the most up-to-date recommendations in order to individualize and assure proper nutrition habits as a part of the total treatment plan of people living with HIV.

More studies are needed to fully evaluate the possible interactions between the different medicines and available food supplements and micronutrients and propose mechanism of action in order not to optimize and not to compromise the desired therapeutic outcomes.

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Conflict of interest

The author declares no conflict of interest.

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