REVIEW PAPER

Effect of diet on lipid profile in HIV-infected patients

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Abstract

The implementation of highly active antiretroviral therapy has increased the life expectancy of people living with human immunodeficiency virus (HIV), thus reducing the number of deaths from acquired immune deficiency syndrome. Nowadays life expectancy of HIV(+) patients is comparable to those who are not infected. However, due to the use of antiretroviral therapy and the persistent immune activation and inflammation caused by HIV, other negative events may occur including dyslipidaemias, cardiovascular disorders, chronic kidney disease, early ageing, and neurocognitive impairment. It also increases the risk of developing metabolic syndrome and becomes a risk factor for cardiovascular disease: e.g. hypertension, brain stroke, and heart infarct. Comprehensive care of HIV patients with disturbed lipid profile includes lifestyle modifications such as dietary changes along with smoking cessation and has a beneficial effect on the lipid profile (total cholesterol, LDL, HDL, triglyceride levels). Therefore, it can reduce the risk of cardiovascular disease, allows the patients to avoid additional pharmacotherapy, and can eliminate drug-drug interactions with antiretroviral drugs.

There are a lot of data showing that early dietary intervention and consistent diet control have a beneficial effect on lipid disorders in HIV-infected patients. Clinicians should be aware of it. In view of the benefits that can be gained by people living with HIV from dietary intervention, it is appropriate to include dieticians in a panel of specialists who take care of HIV(+) patients.

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Introduction

Highly active antiretroviral therapy (HAART) has reduced the number of acquired immune deficiency syndrome (AIDS) diagnoses and extended lives of seropositive patients. Human immunodeficiency virus (HIV)-infected people are now able to reach old age [1]. Similarly to the general population, controlling civilizational and metabolic diseases, especially cardiovascular disease (CD), which increase the risk of early death but are not directly associated with AIDS, has become a clinical problem [2].

Although extremely effective at combatting AIDS, antiretroviral drug (ARV) therapy can still have side effects, including metabolic disorders [3]. Adverse effects of combined antiretroviral therapy (cART) on lipid profile are well known [4]. They manifest as increased triglycerides, total and LDL cholesterol levels, as well as decreased HDL cholesterol levels [5]. The pathomechanism of these changes is complex, and one of the postulated factors is mitochondrial toxicity [2]. Viral replication can also modulate lipid and lipoprotein concentrations and accelerates the development of arterial disease [3].

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Comprehensive care for patients with lipid disorders, especially HIV(+) patients, requires a multi-pronged approach as well as lifestyle changes, including proper diet and pharmacological treatment. Improving lipid profile through lifestyle modification, particularly by following a diet plan, could limit the need for additional pharmacotherapy and minimise the risk of drug-drug interactions or other undesired effects [3, 6].

Risk factors for cardiovascular disease

Besides classical risk factors of cardiovascular disease, HIV is an additional factor raising the risk by causing persistent immune activation and enhancing atherogenesis [7, 8].

Hypercholesterolaemia in HIV-positive individuals

Based on the NATPOL 2002 and 2011 studies, the prevalence of hypercholesterolaemia in the Polish population (aged 18-79 years) reached levels as high as 61% (approximately 18 million people).

Attention has also been drawn to the unfavorable phenomenon of the falling percentage of people in Poland with high HDL levels. Very low HDL levels have been reported in WOBASZ study of the general population and among HIV positive persons not on cART from POLCA cohort [9]. In other countries elevated LDL was reported in 35% of patients [10]. Hypercholesterolemia is more commonly observed among patients on cART and depends on the class of drugs used [11]. Particularly protease inhibitors (PIs) such as indinavir and lopinavir increase LDL and HDL cholesterol levels. In this class of drugs only atazanavir is associated with minor changes in lipid profile [12]. Among Polish patients treated with antiretroviral drugs, abnormal levels of total and LDL cholesterol were 37% and 47%, respectively [9].

Hypertriglyceridaemia in HIV-positive patients

Hypertriglyceridaemia was seen in 20% of women and 31% of men in the WOBASH population [13]. In the SCOLTA project, it was noted that this relationship, where men were more likely to develop hypertriglyceridemia, can also be attributed to the HIV population [14]. The exact pathomechanism linking hypertriglyceridaemia with cardiovascular risk is still being investigated [15]. As with hypercholesterolaemia, hypertriglyceridaemia is dependent on the class of drugs and, in the case of the combined use of nucleoside reverse transcriptase inhibitors (NRTIs) with PIs, its prevalence reaches almost 60% [16]. A positive note from the study is that among patients undergoing dietary intervention only 16% of seropositive individuals developed hypertriglyceridaemia, compared to 50% of those without dietary intervention [17]. Among Polish HIV(+) patients receiving antiretroviral therapy the prevalence of hypertriglyceridaemia can reach as much as 48% [9]. It is worth pointing out that some PI-based therapies can induce or exacerbate hypertriglyceridaemia. Non-nucleoside reverse transcriptase inhibitor (NNRTIs) therapy also significantly increases serum triglyceride levels, but to a lesser extent than PIs [18].

Metabolic syndrome

Decreased HDL cholesterol and elevated triglyceride levels may be part of metabolic syndrome (MS) [10]. Low HDL cholesterol level and insulin resistance are consequences of consuming excessive amounts of easily digestible carbohydrates. Abdominal obesity (waist circumference > 88 cm for women and > 94 cm for men in the European population) [19] with insulin resistance play an important role in the development of MS; therefore, weight reduction is very important. Many studies have shown that elevated HDL cholesterol levels are associated with weight loss [20, 21].

It was observed by Mondy *et al*. that the incidence of metabolic syndrome was similar in HIV-infected patients and in a healthy NHANES group [22]. Other studies conducted with HIV(+) and non-infected individuals from different parts of the world have shown that MS is significantly more common in HIV-infected patients [23].

Some studies evaluating the incidence of metabolic syndrome in the HIV-infected population showed lopinavir/ritonavir (PI), indinavir/ritonavir (PI), and stavudine (NRTI) as factors associated with MS [23]. Indinavir and stavudine are no longer used in Poland.

Reduction of cardiovascular risk

Recommended procedures for people with lipid disorders have been published in the Report of the National Cholesterol Education Program (NCEP), known as the Adult Treatment Panel III [ATP III] [20]. A group of researchers from the Cardiovascular Subcommittee of the AIDS Clinical Trials Group adjusted recommendations for HIV-infected patients. Special attention has been placed on preventive actions aimed at reducing cardiovascular risk. HIV(+) individuals should be evaluated and treated according to NCEP ATP III guidelines, with particular emphasis on potential drug interactions with cART and maintenance of HIV virological control [10]. In addition, the Polish Forum for Prevention of Cardiovascular Diseases (PFP) recommends implementation of nonpharmacological intervention including diet changes, increased physical activity, weight loss, and quitting smoking in patients with dyslipidaemia [21]. Moreover, the European AIDS Clinical Society (EACS) recommends lifestyle modifications (diet changes, regular exercise, smoking cessation, etc.) in order to improve lipid profile. If these changes are unsuccessful, consideration should be given to cART modification and introduction of lipid-lowering drugs [24].

Treatment of hypercholesterolaemia

Non-pharmacological interventions are essential for hypercholesterolaemia management and should be imple-

mented before drug therapy, except when there is an urgent need for pharmacotherapy [10, 25]. LDL cholesterol level is highly dependent on nutrition and increases when nutrients such as saturated fatty acids (SFA), trans isomers of unsaturated fatty acids, and cholesterol are consumed. LDL cholesterol levels decrease when monounsaturated fatty acids (MUFA) and omega-3 fatty acids are introduced, dietary fibre intake (soluble fraction) is increased, plant stanols are supplemented, dietary intake of cholesterol is reduced, and weight loss is achieved [17, 20, 21].

The most important dietary intervention is to reduce the intake of SFA and trans isomers. Saturated fatty acids intake should be reduced to 7% of required energy needs, while cholesterol should not exceed 200 milligrams per day for those who need to lower their LDL cholesterol levels. Meta-analysis of intervention studies shows that following adherence to these recommendations in the general population can reduce LDL cholesterol by an average of 16% [20, 21].

Dietary intervention is particularly recommended for HIV-infected individuals who need to lower their lipoprotein levels, as well as weight [10]. Studies have found that proper diet and regular exercise result in a statistically significant 11% reduction in cholesterol levels in HIV-infected patients [10, 26].

One randomised study looked into the effect of dietary intervention for the prevention of dyslipidaemia in HIV-1 infected patients on HAART. The best results were achieved in the group with dietary intervention with reduced calories, cholesterol, and fat intake (mainly SFA) along with increased carbohydrate and dietary fibre intake. At the end of a one-year period, hypercholesterolaemia was diagnosed in 14 (39%) patients from the control group and only three (7%) from the study group [17] (Figure 1).

A different study evaluated the effect of omega-3 fatty acids supplementation on lipid profile in HIV-positive patients and did no show statistically significant changes in LDL and HDL cholesterol levels [27]. A lack of significant changes in total cholesterol levels was observed in both the study population and in non-infected individuals. In addition, LDL-cholesterol and HDL cholesterol increased by 5-10% and 1-3%, respectively. Therefore, it could be assumed that the use of omega-3 acids did not result in the expected reduction in total and LDL-cholesterol, and in the case of HDL cholesterol the increases were not significant [28].

On the other hand, a lipid-lowering diet that entails reducing cholesterol intake to 300 milligrams a day, decreasing energy value of meals, replacing animal fats with vegetable fats, and introducing dietary fibre [28] in combination with physical exercise (for example three times a week) showed success by significantly reducing total cholesterol levels by 18% [10, 26].

Treatment of hypertriglyceridaemia

As in the case of hypercholesterolaemia management with dietary therapy should also be the first-line intervention. Elevated triglycerides levels should prompt diet modification. One study has shown that adherence to a recommended diet is beneficial for triglyceride levels, reducing them by 23% in six months. Dietary counselling combined with supervised exercise three times a week and cycling reduced triglyceride levels by 25% [10].

Smoking cessation also helps to lower triglyceride levels and improve the overall risk of cardiovascular disease. Therefore, physical activity, smoking cessation, and weight reduction in obese patients should be encouraged [10].

Irrespective of the cause of hypertriglyceridaemia, which may be endogenous (elevated VLDL-TG levels) or exogenous (increased chylomicron triglycerides levels), an important component of diet therapy is to limit or completely eliminate alcohol intake because it is a potent agent of hypertriglyceridaemia [20].

Patients with hypertriglyceridaemia should reduce their intake of fat and highly processed products and increase their intake of complex carbohydrates, including dietary fibre. Restrictions should be made on the consumption of easily digestible carbohydrates such as sucrose and fructose, which are substrates for triglyceride synthesis in the liver. This in effect leads to a decrease in triglycerides and HDL cholesterol levels [17, 20].

It is additionally important to replace saturated fatty acids and monounsaturated fatty acids with polyunsaturated omega-3 fatty acids. As recommended by the Consensus of the Editorial Board of the Polish Forum for Prevention of Cardiovascular Diseases, on the principles of proper nutrition, an n-6/n-3 fatty acid ratio of 4 : 1 should be provided [29, 30]. Large amounts of omega-3 fatty acids (EPA and DHA) are present in fresh, greasy fish and vegetable oils (mainly flaxseed oil and cold pressed rapeseed oil). It is recommended 2-4 g of these fatty acids be ingested daily, for example in the form of fish oil supplements [20]. The mechanism by which omega-3 fatty acids cause a decrease in tri-

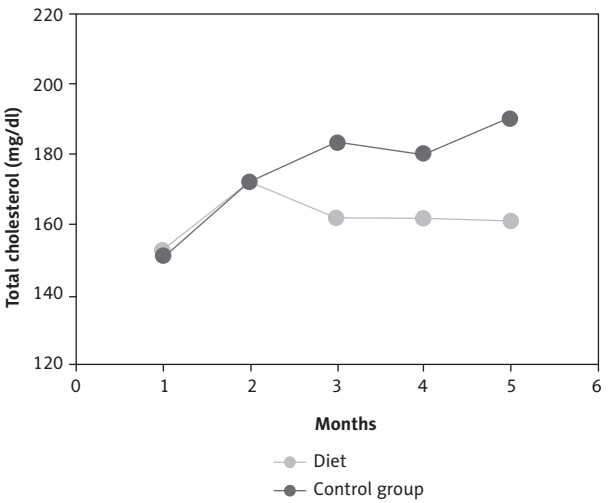

Fig. 1. Effect of 12-month dietary intervention on total cholesterol concentration (mg/dl) [17]

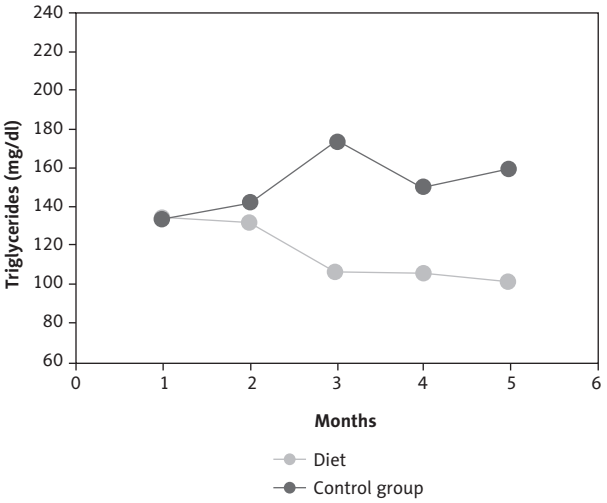

Fig. 2. Effect of 12-month dietary intervention on triglyceride concentration (mg/dl) [17]

glyceride levels is probably related to inhibition of enzymes involved in TG synthesis in the liver, competition between fatty acid oxidation and triglyceride biosynthesis, and increased triglyceride clearance due to endogenous lipoprotein lipase activity stimulation [24].

Severe hypertriglyceridaemia and hyperchylomicronaemia require low dietary fat content (less than 30% of energy intake, including < 7% SFA) [20], avoidance of simple sugars, and reduction or elimination of alcohol consumption. In cases where triglyceride levels are extremely high (> 2000 mg/dl or > 1000 mg/dl in patients with pancreatitis) it is justified to use nonpharmacological intervention together with pharmacotherapy [10, 20].

Omega-3 fatty acids as well as fibrates and statins significantly reduce triglyceride levels. Delivering high doses of omega-3 fatty acids is associated with a decrease in TG levels of between 25% and 30%. Statins and fibrates reduce TG concentrations by 7% to 30% and by 20% to 50%, respectively. The greatest reduction was seen among people with advanced hypertriglyceridaemia. Numerous studies have shown measurable benefits from incorporating omega-3 supplementation into pharmacotherapy [27] also in the HIV population [25, 28, 31-34]. However, benefits of supplementation have not been established for protease inhibitors [10]. The importance of dietary intervention in terms of maintaining normal levels of triglycerides in HIV(+) patients can also be seen in a study from southern Brazil [17] (Figure 2).

The key approach to controlling triglyceride levels in HIV(+) patients should include dietary changes and increased physical activity and in certain cases fibrate therapy and omega-3 supplementation [24].

Mediterranean diet

A Mediterranean diet contains a small amount of saturated fatty acids (≤ 7-8% energy) and is characterised by high intake of olive oil, vegetables, fruit, grain products, and legumes, average consumption of milk products, alcohol, and fish, and low intake of animal fat and meat. The rule is to create a diet from products available on the local market that will be rich in monounsaturated fatty acids, omega-3 fatty acids, antioxidant vitamins, flavonoids, and fibre and low in saturated fatty acids and cholesterol [34].

One of the studies has shown that consumption of olive oil and nuts reduces LDL cholesterol levels and therefore atherosclerosis risk [35]. The effectiveness of the Mediterranean diet in terms of cardiovascular risk reduction was also examined among HIV-infected people during the first year of HAART. The study did not show a statistically significant difference between serum lipids levels and compliance with the Mediterranean diet. Consumption of olive oil was not associated with a decrease in lipid levels, and moderate alcohol consumption had no effect on total cholesterol, LDL cholesterol, and triglycerides. Similar results were obtained in the healthy population. It is thought that the protective effect of a Mediterranean diet is not related to total plasma cholesterol, LDL, and HDL cholesterol but with changes observed in fatty acid concentrations. Controlled dietary studies have shown that a Mediterranean diet in which the consumption of MUFA and PUFA (polyunsaturated fatty acids) was relatively high lowered LDL cholesterol and TG levels and increased HDL cholesterol levels. In addition, randomised trials have shown that patients on PI-containing cART using pravastatin and dietary advice tend to have lower cholesterol levels, while diet only did not affect lipid levels [36].

Conclusions

Dietary counselling for HIV-infected people is effective and can bring measurable benefits: it can significantly reduce total cholesterol and increase HDL cholesterol levels, thus reducing cardiovascular risk. Monitoring of lipid parameters by diet can help to avoid pharmacological therapy and the risk of interactions with cART.

Supplementation with omega-3 fatty acids seems to be advantageous due to their ability to reduce serum triglyceride levels.

In view of the benefits that can be gained by people living with HIV from dietary intervention, it is appropriate to include dieticians in the panel of specialists who take care of HIV(+) patients.

Conflict of interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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