Revista da
ASSOCIAÇÃO MÉDICA BRASILEIRA
www.ramb.org.br

Review article

Lipid profile of HIV-infected patients in relation to antiretroviral therapy: a review☆

Suelen Jorge Souza[a], *Liania Alves Luzia*[a], *Sigrid Sousa Santos*[b], *Patrícia Helen Carvalho Rondó*[a,*]

[a] *Nutrition Department, School of Public Health, Universidade de São Paulo (USP), Sao Paulo, SP, Brazil*
[b] *Department of Medicine, Center of Biological Sciences and Health, Universidade Federal de São Carlos, São Carlos, SP, Brazil*

ARTICLE INFO

Article history:
Received 5 April 2012
Accepted 4 November 2012

Keywords:
Human Immunodeficiency Virus
Acquired Immunodeficiency Syndrome
Antiretroviral therapy
Highly active antiretroviral therapy
Dyslipidemia

ABSTRACT

This study reviewed the lipid profile of human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) patients in relation to use of antiretroviral therapy (ART), and its different classes of drugs. A total of 190 articles published in peer-reviewed journals were retrieved from PubMed and LILACS databases; 88 of them met the selection criteria and were included in the review. Patients with HIV/AIDS without ART presented an increase of triglycerides and decreases of total cholesterol, low density lipoprotein (LDL-c), and high density lipoprotein (HDL-c) levels. Distinct ART regimens appear to promote different alterations in lipid metabolism. Protease inhibitors, particularly indinavir and lopinavir, were commonly associated with hypercholesterolemia, high LDL-c, low HDL-c, and hypertriglyceridemia. The protease inhibitor atazanavir is apparently associated with a more advantageous lipid profile. Some nucleoside reverse-transcriptase inhibitors (didanosine, stavudine, and zidovudine) induced lipoatrophy and hypertriglyceridemia, whereas abacavir increased the risk of cardiovascular diseases even in the absence of apparent lipid disorders, and tenofovir resulted in lower levels of cholesterol and triglycerides. Although non-nucleoside reverse-transcriptase inhibitors predisposed to hypertriglyceridemia and hypercholesterolemia, nevirapine was particularly associated with high HDL-c levels, a protective factor against cardiovascular diseases. Therefore, the infection itself, different classes of drugs, and some drugs from the same class of ART appear to exert distinct alterations in lipid metabolism.

Perfil lipídico de pacientes infectados pelo HIV em relação à terapia antirretroviral: uma revisão

Palavras-chave:
Vírus da Imunodeficiência Humana

RESUMO

Este estudo faz uma revisão sobre o perfil lipídico de pacientes com vírus da imunodeficiência humana/síndrome da imunodeficiência adquirida (HIV/AIDS) em relação ao uso da terapia antirretroviral (TARV), e suas diferentes classes de fármacos. Um total de 190 artigos

☆ Study conducted at Faculdade de Saúde Pública da Universidade de São Paulo, São Paulo, SP, Brazil.

* *Corresponding author.* Nutrition Department, School of Public Health, University of São Paulo, Avenida Dr. Arnaldo, 715, Cerqueira César, São Paulo, SP, 01246-904, Brazil.
E-mail: phcrondo@usp.br (P.H.C. Rondó).

0104-4230
http://dx.doi.org/10.1016/j.ramb.2012.11.003

Síndrome da Imunodeficiência Adquirida
Terapia antirretroviral
Terapia antirretroviral de alta potência
Dislipidemia

publicados em revistas indexadas foram selecionados das bases de dados PubMed e LILACS; 88 deles preencheram os critérios de seleção e foram incluídos nesta revisão. Pacientes com HIV/AIDS sem uso de TARV apresentaram aumento de triglicérides e diminuição dos níveis de colesterol total, lipoproteína de baixa densidade (LDL-c) e lipoproteína de alta densidade (HDL-c). Distintos regimes de TARV promoveram diferentes alterações no metabolismo lipídico. Inibidores de protease, particularmente indinavir e lopinavir, foram comumente associados com hipercolesterolemia, aumento de LDL-c, diminuição de HDL-c e hipertrigliceridemia. O inibidor de protease atazanavir aparentemente está associado a menores alterações do perfil lipídico. Alguns inibidores da transcriptase reversa análogos de nucleosídeos (didanosina, estavudina e zidovudina), induziram lipoatrofia e hipertrigliceridemia, enquanto o abacavir aumentou o risco cardiovascular mesmo na ausência de aparentes distúrbios lipídicos, e o tenofovir resultou em menores níveis de colesterol e triglicérides. Embora os inibidores da transcriptase reversa não análogos de nucleosídeos possam predispor a hipertrigliceridemia e hipercolesterolemia, a nevirapina, particularmente, foi associada a maiores níveis de HDL-c, um fator de proteção contra doenças cardiovasculares. Portanto, a própria infecção, diferentes classes de fármacos e alguns fármacos da mesma classe de TARV podem exercer distintas alterações no metabolismo lipídico.

Introduction

Patients with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) frequently present alterations in lipid metabolism due to infection with HIV itself, including elevated serum concentrations of triglycerides and low levels of total cholesterol.[1] The introduction of antiretroviral therapy (ART) in the mid-1990s led to substantial improvement in the prognosis of HIV/AIDS patients, with a reduction in morbidity and mortality due to opportunistic diseases and consequent improvement of the patient's quality of life.[2–7]

However, there is evidence that ART is associated with lipodystrophy syndrome, a disturbance of lipid metabolism characterized by insulin resistance, dyslipidemia, and fat maldistribution, usually presenting as visceral abdominal obesity and cervical fat pad accumulation (buffalo hump),[2,5,7–9] metabolic bone disease (osteopenia and/or osteoporosis), and lactic acidosis.[5,7,10–12]

ART-associated dyslipidemia is characterized by elevated serum concentrations of total cholesterol, triglycerides, low density lipoprotein (LDL-c), very low-density lipoprotein (VLDL), and apolipoprotein B (apoB), and low levels of high density lipoprotein (HDL-c), constituting an atherogenic lipid profile.[13,14] This lipid changes occurs within three months of initiating ART, and plateau after six to nine months.[15]

The prevalence of dyslipidemia and other risk factors for cardiovascular disease is significant in HIV/AIDS patients receiving ART, ranging from 20% to 80% depending on the study design and population investigated.[8] These lipid alterations were first described in patients who used antiretroviral regimens containing protease inhibitors, but also were later observed in patients who received regimens consisting of nucleoside reverse-transcriptase inhibitors (NRTI) and non-nucleoside reverse-transcriptase inhibitors (NNRTI).[16,17]

In view of the high prevalence of dyslipidemia and the increased risk for cardiovascular diseases among patients with HIV/AIDS, which is a matter of concern for public health, the present review aimed to describe the lipid profile of HIV-infected patients in relation to use of ART, and its different classes of drugs.

Methods

The PubMed (US National Library of Medicine, National Institutes of Health) and LILACS (Literatura Latino-Americana e do Caribe) databases were searched without restrictions on publication year or study design until August 2011. The keywords "HIV" [MESH] OR "Acquired Immunodeficiency Syndrome" [MESH] AND "Dyslipidemias" [MESH] were used for search in the PubMed database, and 169 articles were retrieved. The LILACS database was searched using "HIV and Dislipidemia", and 21 articles were retrieved. Thus, 190 articles were first selected, but one article appeared in both databases; therefore, 189 articles were selected for this review.

All studies investigating the association between lipid alterations in HIV/AIDS patients with or without treatment were identified and included in the review. Case report articles (12 articles from PubMed), articles related to lipid-lowering drugs (8 articles from PubMed), articles whose full text could not be accessed (35 articles from PubMed and five from LILACS), and articles not focusing on lipid alterations in HIV/AIDS patients (39 articles from PubMed and nine from LILACS) were excluded. 75 articles were thus selected from the PubMed database and six articles from the LILACS database. In addition, seven studies were identified in the references of these articles and retrieved for relevance, considering that the articles were useful to describe the possible metabolic mechanisms to explain the lipid alterations of the patients. Therefore, a total of 88 articles were included in the review (Fig. 1).

All the 88 articles were discussed in this review. Tables 1 and 3 presented the results of the original articles (n = 51) included in this search, excluding previously published reviews.