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Metabolic Alterations of HIV Infection

E.F. Silva

*Federal University of São Paulo – São Paulo,
Brazil*

1. Introduction

Changes in lipid profile, like increased serum triglycerides (TG) and decreased cholesterol levels have been described in patients with HIV infection before the introduction of highly active antiretroviral therapy (HAART) (Constans et al., 1994; Grunfeld et al., 1991; Shor-Posner et al., 1993). However, with the widespread use of HAART it has been worsening. After the introduction of protease inhibitors (PIs) in 1996, patients developed a syndrome of fat redistribution with peripheral loss and central gain, generally associated with metabolic abnormalities and insulin resistance (lipodistrophy syndrome) (Carr et al., 1998). High levels of TG and total cholesterol (TC) concentrations are well known and often associated with abnormal body fat distribution and glucose metabolism disturbs (Carr et al., 1998). On persons treated with HAART, TG and TC elevations are associated with the use of protease inhibitors/nonnucleoside reverse transcriptase inhibitor (PIs/NNRTI) regimens (54 and 44% respectively), followed by PIs regimes (40 and 27% respectively) and NNRTI-containing combinations (32 and 23% respectively) (Friss Moller et al., 2003). All these symptoms are related to metabolic syndrome that could act to increase the cardiovascular risk in HIV-infected patients. Another aspect of these metabolic alterations is non-alcoholic fatty liver disease. Its prevalence is higher in HIV infected patients (30-40%) than in general population (14-31%) (Crum-Cianflone et al., 2009; Guaraldi et al., 2008). It is believed that there is a potential role of the antiretroviral therapy in the pathology of non-alcoholic fatty liver disease due to its negative effects on glucose control, lipid metabolism, body fat redistribution, insulin resistance and mitochondrial toxicity (Crum-Cianflone et al., 2009; Guaraldi et al., 2008).

HAART has change dramatically the natural history of HIV-infection, leading to a notable extension of life expectancy and decline in mortality (Palella et al., 1998). Thus, mortality rates in HIV-infected patients who have experienced a CD4 recovery (> 500 cells/mm³) on long-term treatment resemble that of the general population (Lewden et al., 2007). However, prolonged metabolic imbalances could act on the long-term prognosis and outcome of HIV-infected persons. There is an increasing concern about the cardiovascular risk in this population despite the virological control (Graham, et al., 2000; Manfredi et al., 2000; Palella et al., 1998). Cardiovascular disease is emerging as one of the most important co morbidity and cause of death (Sackoff et al., 2006). Early identification and proper management of traditional cardiovascular risk factors, such as smoking, overweight or hypertension is imperative (Barbaro, 2006; Triant et al., 2007). As the prevalence of metabolic disorders is age-related their incidence will increase as HIV population becomes older (Triant et L., 2007). Thus, active prevention, together with prompt diagnosis and management of cardiovascular risk factors must be integrated on the routine of HIV care.

2. Dyslipidemia and antiretroviral therapy

The degree of dyslipidemia and lipid changes is different among the several classes of antiretroviral drugs and even among the individual drugs within each class. Furthermore, the magnitude of lipid changes varies widely among patients on the same antiretroviral regimen, reflecting the likely important role of host genomics. While the PI and NNRTI have well-described effects on lipids, there have been no reported significant changes in lipid profiles or cardiovascular risk associated with the new classes of antiretroviral such as, fusion inhibitors (enfuvirtide), CC chemokine receptor type 5 (CCR5) receptor inhibitors (maraviroc) or integrase inhibitors (raltegravir) as described in table 1. Nonnucleoside reverse transcriptase inhibitors are also associated with lipid abnormalities, but to a lesser extent than PIs. Nucleoside reverse transcriptase inhibitors have been associated with mitochondrial toxicity and insulin resistance, but the lipid changes associated with them are normally less significant than those caused by PI or NNRTIs (Malvestutto & Aberg, 2010, Hammond et al., 2004).

PI	Lipid Change
Atazanavir	No change
Atazanavir/ritonavir	↑ LDL-c, TG and no change HDL-c
Darunavir/ritonavir	↑ TC, LDL-c, TG and no change HDL-c
Fosamprenavir/ritonavir	↑ TC, LDL-c, TG and no change HDL-c
Indinavir	↑ TC, LDL-c, TG and
Lopinavir/ritonavir	↑ TC, LDL-c, TG and no change HDL-c
Nelfinavir	↑ TC, LDL-c, TG and no change HDL-c
Ritonavir	↑ TC, LDL-c, TG and ↓ HDL
Saquinavir/ritonavir	↑ TC, LDL-c, TG and no change HDL-c
Tipranavir/ritonavir	↑ TC, LDL-c, TG and not known in HDL-c
ITRN	
Stavudine	↑ TG
ITRNN	
Efavirenz	↑ TC, LDL-c, TG and HDL-c
Nevirapine	↑ TC, LDL-c, TG and HDL-c
Etravirine	No change
Integrase Inhibitor	
Raltegravir	No change
Fusion Inhibitor	
Enfuvirtude	No change
CC Chemokine receptor	
Maraviroc	No change

Table 1. Lipid changes with antiretroviral therapy.

3. Cardiovascular risk evaluation

Primary prevention must be indicated and periodic assessment could be done every 3-6 months in HIV-infected person on treatment and annually in patients not treated (Blanco et al., 2010). Factors to be evaluated include: age, smoking habit, diet, physical activity, alcohol consumption, personal and family history of coronary heart disease, hyperlipidemia, diabetes mellitus and hypertension (Adult Treatment Panel III, 2002). In women, the menopausal status is relevant. Baseline blood pressure, body mass index and waist circumference should be recorded together with lipid profile, glucose and renal function (Blanco et al., 2010). In addition, virologic control with HAART use may also decrease the risk of noninfectious co morbidities including cardiovascular disease.

To predict the cardiovascular risk, Framingham Risk Score could be use (Anderson et al., 1991). Using this score, which includes: age, gender, TC, HDL-c, systolic blood pressure and smoking, an individual could be stratified into three risk categories: low (<10%), medium (10-20%) and high risk (> 20%) in 10 year. The extent to which this model could be used from the general population to HIV-infected people is still under discussion. The Framingham Risk Score has not been specifically validated for HIV-infected subjects and factors related to the HIV/AIDS could not be adequately evaluated, but until more evidence is available, management strategies for cardiovascular risk proposed for the general population could be applied to HIV-infected subjects. In the D:A:D study (Data Collection on Adverse events of Anti-HIV Drugs), myocardial infarction rates seen in HIV-infected person treated and untreated were higher and lower respectively, than those predicted with Framingham Risk Score. Nevertheless, it predicted cardiovascular events at increased rates in parallel with time exposure to antiretroviral treatment (Friss-Moller et al., 2003). According to these findings, Framingham Risk Score may be useful for an initial estimation of cardiovascular risk in HIV-infected persons, although a more accurate model needs to be developed.

To contribute with the discussion about HIV and cardiovascular risk, it was recently showed by the Kaiser Permanent Members that HIV infection confers a high independent risk for coronary heart disease (Klein et al., 2011). They matched HIV-infected adults of Kaiser Permanent California health plan with HIV negative members (1:10 ratio) on age, sex, medical center and start year follow-up. The cohort was followed from first Kaiser Permanent enrollment in 1996 until the end of December 2008. Coronary heart disease rates among HIV-infected members stratified by antiretroviral use and the most recent and lowest CD4 cell counts recorded were compared with rates among HIV negative members- Adjusted rate ratios (RRs) for any CHD diagnosis and for MIs were obtained from Poisson regression models adjusting for age, sex, race, tobacco use, alcohol/drug abuse, obesity, diabetes, and use of lipid lowering and hypertension therapy. 20,775 HIV-infected and 215,158 HIV negative members contributed to 90,961 and 1,133,333 persons-years (py) respectively. HIV-infected and not infected individuals had respectively 399 (447/100,00 py) and 3,463 (311/100,00 py) coronary heart disease events and 248 and 1,825 myocardial infarction. In the HIV-infected group, the only significant HIV-related factor associated with an increased risk of coronary heart disease was the lowest CD4 \leq 200 cells/mm³ recorded (relative risk = 1.3 [95% CI: 1.0-1.6, p = 0,022) (Klein et al., 2011). HIV-infected patients on antiretroviral therapy and with CD4 count > 500 cells/mm³ (recent or lowest) had similar coronary heart disease risk compared with HIV negative group. These findings support

early initiation of antiretroviral therapy and aggressive management of cardiovascular disease risk.

Nowadays, the recommendations suggest that HIV-infected people undergo evaluation and treatment on the basis of the Third National Cholesterol Education Program (ATP III) for dyslipidemia (Adult Treatment Panel III, 2002). Lipoprotein profiles should be done with at least 9 to 12 hours of fasting (Adult Treatment Panel III, 2002). Dyslipidemia is defined as TC \geq 200 mg/dL, LDL-c \geq 130 mg/dL, TG \geq 150 mg/dL, HDL-c $<$ 40 mg/dL and TC/HDL \geq 6.5. Therapeutic indications are made regarding the time for initiating specific lifestyle modifications and prescription of lipid-lowering therapy in order to achieve LDL-c goals (Adult Treatment Panel III, 2002). As for the general population, distinct drugs are suggested regarding the lipid alterations: hypercholesterolemia and/or hypertriglyceridemia. An update from ATP III (Grundey et al., 2004) included diabetes in high risk category for cardiovascular risk, and there is an additional benefit adding LDL-lowering therapy in this population.

4. Lifestyle interventions

Counseling on healthy diet habits, regular exercise, alcohol consumption and quitting smoking should be the first step to decrease cardiovascular risk. Hyperglycemia due to diabetes mellitus must be managed aggressively, with consideration of treatment with insulin sensitizers, such as metformin and thiazolidinediones when appropriate (Kalra et al., 2011).

Smoking is one well-know modifiable risk factor for coronary heart disease and its cessation leads to a decrease in cardiovascular and malignances risk (Mohiuddin et al., 2007). The smoking prevalence in HIV-infected patients is generally high, around 45-70%, much more than observed in uninfected controls (Friss-Moller et al., 2003; Mamary et al., 2002; Saves et al., 2003). Smoking cessation should be a priority in managing cardiovascular risk in HIV-infected persons.

The prevalence of hypertension in HIV-infected patients is around 25% (Glass et al., 2006; Jung et al., 2004). The current recommendations for general population should be followed for HIV-infected patients, considering drug-interactions between antiretroviral drugs and antihypertensive drugs, particularly calcium-channel blockers. The management of hypertension should include lifestyle modifications such as weight loss if needed, incorporating low total and saturated fat in the diet, reduction of dietary sodium to 2.5 g/day, aerobic exercise and decreasing alcohol consumption (Malvestutto & Aberg, 2010).

Diet and exercise could help improve dyslipidemia, high blood pressure and glucose metabolism (Barrios et al., 2002; Fitch et al., 2006). Comprehensive dietary interventions have been demonstrated to decrease LDL-c by 20% in short term interventions in which adherence is maximal (Jenkins et al., 2003; Skeaff et al., 2005). The majority of the cholesterol lowering effect may be achieved by substituting unsaturated fats for saturated fats and increasing intake of plant sterols to at least 1.5 g/day. Each strategy could decrease the levels of LDL-c around 10% (Clifton et al., 2009). Further cholesterol lowering is also possible through weight loss and increasing intake of soluble fiber and soy protein (Clifton et al., 2009). Replacing saturated and *trans* fats with unsaturated fats is therefore a key strategy for lowering serum LDL-c (Clifton et al., 2009). Weight loss in those who are overweight lowers serum TC, LDL-c and TG and increases HDL-c (Datillo & Kris-Etherton,

1992). Weight reduction should be strongly encouraged if obesity is present. There are several dietary components that may be protective against cardiovascular disease through known and unknown mechanisms and their consumption may be encouraged as part of a cholesterol lowering and cardiovascular protective diet such as fish oil, whole grains, fruit, vegetables and nuts. Low intake of alcohol may also be advised (Cheng et al., 2004; Clifton et al., 2009).

Clinicians should be alert for potential exacerbating conditions, such as hypothyroidism, renal and liver disease and hypogonadism. They should also consider the effects of glucocorticoids, beta-blockers, thiazide diuretics, thyroid preparations and hormonal agents (such as androgens, progestins, and estrogens) on both cholesterol and triglyceride levels (Dube et al., 2003).

5. Lipid lowering therapy for HIV-infected patients

The benefits of lipid-lowering therapy interventions have been extended to HIV-infected persons. Enthusiasm for drug therapy for dyslipidemia should be tempered with the understanding that interventions for advanced immunosuppression, opportunistic infections, malignancies, and HIV-associated wasting, should be done during the initial stages of treatment. There is currently no basis for a more aggressive dyslipidemia intervention among HIV-infected patients than what is currently recommended for the general population. Due to a significant possibility for drug interaction between some lipid-lowering agents and antiretroviral drugs, special attention should be given to the choice of lipid-lowering therapy (Dube et al., 2003). Some advises should be instituted before pharmacological interventions as explained in life style modification section, except when there is an urgent need to prompt treatment (individuals with high risk for cardiovascular disease or with previous coronary heart disease or diabetes mellitus) (Adult Treatment Panel III, 2002).

5.1 Statins

The 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase enzyme catalyzes the first step of cholesterol synthesis in the mevalonate pathway. Statins lower LDL-c levels through the inhibition of this specific enzyme. The more potent statins have been shown to reduce LDL-c levels by up to 55%. In addition, they also decrease TG levels to a lesser extent (up to 20%), probably through the inhibition of its synthesis in the liver and increase of lipoprotein lipase enzyme activity in the adipocytes (Jones et al., 2003; Saiki et al., 2005). Furthermore, statins are known to modestly increase levels of HDL-c (up to 10%). The precise mechanism by which statins increase HDL-c levels is not known; however, it is thought to result from apolipoprotein A1 gene induction through the activation of peroxisome proliferator activated receptors (Yano et al., 2007). It is also postulated that statins have pleiotropic effects, (certain lipid-independent effects) that contribute to some degree to their antiatherothrombotic properties. Among the proposed mechanisms are modulation of inflammatory response, improvement of endothelial function and inhibition of coagulation factors (Ray & Cannon, 2005).

Lovastatin and simvastatin are highly metabolized through the cytochrome P450 (CYP3A4), which is inhibited by most PIs. Thus, their concomitant use is contraindicated to avoid serious side effects of statins overexposure such as rhabdomyolysis. Pravastatin and

fluvastatin appear to be safe for use in association with HAART (Dube et al., 2003). Pravastatin is eliminated mostly by glucoronidation, fluvastatin by CYP 2C9 isoform, and CYP 3A4 has no role in their metabolism (Willians & Feely, 2002). Table 2 has a summary of the lipid lowering therapy in HIV infected people.

Rosuvastatin and atorvastatin have higher efficacy than pravastatin in decreasing LDL-c. Due to partial metabolism of atorvastatin by CYP3A4, it must be used with caution when co administered with a PI, with hepatitis and myositis being potential toxicities. Rosuvastatin is the most potent statin to reduce LDL-c and TG, with serum levels being only slightly modified when co administered with a PI (Aslangui et al., 2010; Calza et al., 2008). It can also reduce TG and increase HDL-c. Moreover, pharmacokinetic studies have demonstrated that its metabolism is not dependent on the CYP 450 3A4 isoenzyme and its use could be considered in PI-treated individuals since the risk of drug-drug interactions are low (Martin et al., 2003). Only 10% of the administered dose is metabolized by CYP 2C9 isoenzyme into N-desmethyl rosuvastatin and its metabolite are 90% eliminated by the fecal route (Cheng, 2004; Martin et al., 2003; Willians & Feely, 2002). The usual recommended starting dose of rosuvastatin is 10 mg daily, but initiation at 5 mg daily may be considered for patients who have predisposing factors for myopathy or are taking cyclosporine. In subjects with severe renal impairment or taking fibrates, therapy with rosuvastatin should be used with great caution, daily dose should be initiated at 5 mg and not exceed 10 mg (Cheng, 2004).

Until recently, pravastatin and rosuvastatin were thought to be safer than other statins because their metabolism do not utilize the CYP450 3A4 enzyme system influenced by many antiretroviral medications. However, recent studies have demonstrated increased plasma levels (expressed as area under the plasma concentration-time curve [AUC] and maximum concentration [C_{max}] values) of these statins as a result of exposure to certain antiretroviral drugs (Busti et al., 2008; Calza et al., 2005; Mazza et al., 2008; Townsend et al., 2007). These increased levels may be the result of inhibition of the organic anion transporting polypeptide (OATP) 1B1 that facilitates statin uptake into the liver (Ray, 2009). The disposition of pravastatin and rosuvastatin may be more dependent than other statins on OATP1B1. In agreement with this theory, a study showed that atazanavir/ritonavir was associated with an increased in rosuvastatin levels. This finding led the authors to conclude that the maximum rosuvastatin dose with atazanavir/ritonavir should be 10-20 mg, similar to current recommendation of a maximum rosuvastatin dose of 10 mg when used with lopinavir-ritonavir (Busti et al., 2008). Although increased statins levels may enhance the effectiveness of these drugs, this benefit may come at the expense of an increase in toxicity. To date there is no known interactions between rosuvastatin and NNRTIs (Ray, 2009). Rosuvastatin may be a particularly good option in the setting of NNRTI-based therapy, given its greater effectiveness and lack of proven interactions, although additional pharmacokinetic studies would be useful (Ray, 2009).

Statins should be initiated at the lowest dose established for each agent. Subsequent, adjustments of dosing can be done according to response, and potential side effects must be closely monitored during follow-up, especially elevations in creatine phosphokinase and abnormal liver parameters (Blanco et al., 2010). Statins may improve abnormal baseline transaminases levels in patients with steatohepatitis (Millazo et al., 2007). Although the mechanism is not well defined, the removal of the lipids from the liver by statins might explain their benefits on liver function.

Goal	Lipid lowering therapy
Elevated LDL-c or non-HDL cholesterol with triglycerides level of 200-500 mg/dL	Statins: <ul style="list-style-type: none">- Pravastatin: 10-40 mg daily- Atorvastatin: 10-40 mg/daily- Fluvastatin: 20-40 mg/ daily- Rosuvastatin 5-20 mg- Lovastatin - not recommended with PI- Simvastatin - not recommended with PI- Ezetimibe: 10 mg daily
Triglycerides level > 500 mg/dL	Fibrates and Fish Oil: <ul style="list-style-type: none">- Gemfibrozil: 1200 mg daily- Fenofibrate: 200 mg daily- Omega-3 polyunsaturated fatty acids/fish oil: 3-5g (alternative treatment)

Adapted from Bader & Kelly, 2008; Bennet et al., 2007; Calza et al., 2003; Soler et al., 2006; Stebbing et al., 2009.

Table 2. Lipid lowering therapy for HIV-infected people.

5.2 Fibrates

For patients with triglycerides > 500 mg/dL, fibrates may be the first choice, especially in order to prevent pancreatitis (Dube et al., 2003). When extreme elevations are present (>1000 mg/dL in persons with a history of pancreatitis), it is reasonable to institute both drug and nondrug therapies concomitantly (Dube et al., 2003). Fibrates are metabolized by CYP4A, and there is less issue of interactions with antiretroviral drugs. They exert their effects by activating PPAR- α . These drugs reduce plasma TG between 30% to 50%, and raise the level of HDL-c by 2% to 20%. Their effect on LDL-c is variable, ranging from a small decrease around 10% to no change or even a slight increase (Barter & Rye, 2006). Gemfibrozil is generally initially recommended due to its efficacy in reducing TG. When concomitant hypercholesterolemia is present, statins can be added to fibrates, but the risk of rhabdomyolysis should be closely monitored (Henry et al., 1998). Clinicians treating HIV-infected patients must be aware of the interaction between Lopinavir/ritonavir and Gemfibrozil. Lopinavir/ritonavir decreases the systemic exposure to gemfibrozil by reducing the absorption of this drug (Busse et al., 2009). Fenofibrate is recommended by current guidelines for hypertriglyceridemia in antiretroviral treated patients. (Dube et al., 2003). Fenofibrate, could decrease triglyceride levels in HIV-infected persons on antiretroviral therapy, but only moderately (Aberg et al., 2005).

5.3 Niacin

Niacin has also been used in HIV-infected persons to improve lipid profiles. In the AIDS Clinical Trials Group study A5148, hyperlipidemia was treated with long-acting niacin during 48 weeks. Treatment resulted in significant improvements in TG, TC, HDL-c, and LDL-c, but a transient worsening in insulin sensitivity was also observed (Dube et al., 2006). The use of niacin with antiretroviral drugs may reduce the effect of niacin (Martinez et al., 2008). Patients treated with niacin should have regular evaluation of fasting glucose levels, and a standard 75-g, 2-h oral glucose-tolerance test should be considered, particularly when lipodystrophy or traditional risk factors for type 2 diabetes mellitus are present (Dube, 2000; Schambelan et al., 2002).

5.4 Fish oils

The metabolic effects of N-3 polyunsaturated fatty acids (PUFAs) derived from marine sources (known as “fish oils”) have been demonstrated to reduce fasting and postprandial triglycerides levels in individuals without HIV infection (Simons et al., 1985). Omega-3 is considered an alternative treatment in non-HIV infected populations. It has been reported that 3-5 g per day of omega-3 fatty acids can reduce triglycerides by 30-50%, thereby potentially minimizing the risk of coronary heart disease and pancreatitis (O’Keefe & Harris, 2000). Treatment with fish oil is well tolerated, although potential effects on platelets must be checked, especially in persons taking drugs that may favor bleeding (Gerber et al., 2009).

5.5 Ezetimibe

Ezetimibe is the first lipid-lowering drug that inhibits intestinal uptake of dietary and biliary cholesterol at the brush border of the intestine, resulting in a reduction of hepatic cholesterol stores and an increase in clearance of cholesterol from the blood (Kosoglou et al., 2005). It doesn’t affect the absorption of fat-soluble nutrients and is an attractive option for HIV-infected patients because it lacks CYP P450 metabolism and therefore is not expected to interact with antiretroviral drugs (Kosoglou et al., 2005; Negredo et al., 2006]. The major metabolic pathway for Ezetimibe is the glucuronidation of 4-hydroxyphenyl group by uridine 5'-diphosphate-glucuronosyltransferase isoenzymes to form ezetimibe-glucuronide in the intestine and liver (Kosoglou et al., 2005). It reduces cholesterol absorption in the duodenum by approximately 50%, thereby attaining reductions in LDL-c of 20% (Gagne et al., 2002). This benefit is significantly greater when it is associated with any of the statins, achieving reductions in LDL-c of up to 50% (Bennett et al., 2007; Gagne et al., 2002, Pearson et al., 2005). This synergistic effect of the two drugs in combination results from the inhibition of duodenal cholesterol absorption by ezetimibe, together with the reduction of hepatic cholesterol production by statins (Kosoglou et al., 2005). The recommended dose is 10 mg/day, and can be administered in the morning or evening with or without food (Kosoglou et al., 2005).

Ezetimibe has a favorable drug-drug interaction profile. It does not have significant effects on plasma levels of statins (atorvastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, simvastatin), fibric acid derivatives (gemfibrozil, fenofibrate), digoxin, glipizide, warfarin and triphasic oral contraceptives (ethinylestradiol and levonorgestrel). Concomitant administration of food, antacids, cimetidine or statins had no significant effect on ezetimibe bioavailability (Kosoglou et al., 2005). For this reason, it could be recommended as a second line therapy for dyslipidemia associated with antiretroviral drug

use if hypercholesterolemia is refractory to statins or if patient does not tolerate statins. Its high tolerability and the lack of interactions with the CYP 3A4 indicate that ezetimibe will not increase the risk of toxicity or pharmacokinetic interactions with the use of antiretroviral medications. In HIV-infected patients ezetimibe results in a significant decrease in LDL-c, without significant changes in TG (Berg-Wolf et al., 2008; Chow et al., 2009). Creatine phosphokinase levels should be monitored due to potential risk of rhabdomyolysis.

Reductions in lipid levels with lipid-lowering therapy are greater in non-HIV infected patients than in HIV positive subjects (Martinez et al., 2008; Silverberg et al., 2009). Many studies that evaluated the effect of statins for the treatment of antiretroviral-associated dyslipidemia have shown only partial responses to such therapy, with total and LDL-c values being reduced by about 25% (Calza et al., 2003; Silverberg et al., 2009). The effectiveness and toxicity of statins among HIV-infected individuals may differ from those of the general population for several reasons. The patterns of dyslipidemia commonly seen among HIV-infected individuals are different from those observed in the general population (Riddler et al., 2003) and may be less responsive to treatment (Silverberg et al., 2009). Second, drug interactions between statins and antiretroviral drugs may impact the metabolism, effectiveness and toxicity associated with various forms of statins (Aberg et al., 2006; Gerber et al., 2005; Kiser et al., 2008, Ray, 2009). Response to any lipid lowering therapy must be evaluated after 3-6 months by repeating a fasting lipid profile.

6. Conclusion

Metabolic alterations and traditional cardiovascular risk factors are common in HIV-infected patients. Due to the success of antiretroviral therapy in the last years in reducing AIDS events and mortality, the population is aging and naturally the risk of cardiovascular disease increases. Early detection and management of cardiovascular risk factors is necessary to prevent coronary heart disease. All HIV-infected patients should have their fasting plasma lipid profile prior to starting antiretroviral treatment and then at every three or four months regularly. Efforts should be done including incorporating healthy diet habits, regular exercise, decrease alcohol consumption and smoking cessation prior to start of pharmacological interventions, to avoid excess medication and undesirable side effects. Virologic control and immune recovery should be the first priority in the management of HIV-infected patients due to their associations with high mortality.

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HIV Infection in the Era of Highly Active Antiretroviral Treatment and Some of Its Associated Complications

Edited by Dr. Elaheh Aghdassi

ISBN 978-953-307-701-7

Hard cover, 212 pages

Publisher InTech

Published online 14, November, 2011

Published in print edition November, 2011

Human immunodeficiency virus (HIV) infection is a complex illness affecting the immune system. Acquired immunodeficiency syndrome (AIDS) is an advanced form of HIV infection in which the patient has developed opportunistic infections or certain types of cancer and/or the CD4+ T cell count has dropped below 200/ μ L. More than 40 million persons around the world are infected with HIV, with approximately 14,000 new infections every day. The disease causes 3 million deaths worldwide each year, 95% of them in developing countries. Optimal management of human immunodeficiency virus requires strict adherence to highly active antiretroviral treatment (HAART) regimens, but the complexity of these regimens (e.g., pill burden, food requirements, drug interactions, and severe adverse effects) limits effective treatment. However, more patients with HIV are surviving longer today because of these drugs. This allows further study of commonly associated adverse effects. These may affect all body systems and range from serious toxicities to uncomfortable but manageable events. This book reviews some of HAART-related metabolic and neurological complications.

How to reference

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E.F. Silva (2011). Metabolic Alterations of HIV Infection, HIV Infection in the Era of Highly Active Antiretroviral Treatment and Some of Its Associated Complications, Dr. Elaheh Aghdassi (Ed.), ISBN: 978-953-307-701-7, InTech, Available from: <http://www.intechopen.com/books/hiv-infection-in-the-era-of-highly-active-antiretroviral-treatment-and-some-of-its-associated-complications/metabolic-alterations-of-hiv-infection>

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Phone: +86-21-62489820
Fax: +86-21-62489821

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