The future of HIV vasculopathy when our patients are on antiretroviral therapy

RENA LD B AR RY, M.M.E D.
Department of Surgery, University of the Free State, Bloemfontein

Summary
South Africa was one of the last countries in Africa to be affected by the HIV epidemic, but currently has one of the highest prevalences in the world. Antiretroviral therapy (ART) was recently introduced in South Africa, and as of December 2007 antiretroviral treatment coverage in this country was about 25% (UNAIDS, 2008). There is a well-documented relationship between vascular disease and HIV infection. This HIV vasculopathy may manifest as arterial aneurysms, occlusive disease or complications of hypercoagulability. The question to be asked is “What is the future of HIV vasculopathy when our patients are on antiretroviral therapy?”

The HIV epidemic
The global percentage of people living with HIV has stabilised since 2000. However, the overall number of people living with HIV has increased as a result of the ongoing number of new infections each year and the beneficial effects of more widely available ART. Sub-Saharan Africa remains the part of the world most heavily affected by HIV, accounting for 67% of all people living with HIV and for 72% of AIDS deaths in 2007. In South Africa the prevalence of HIV infection is about 30% among pregnant women attending antenatal clinics. The epidemic stabilised in South Africa between 2004 and 2007, but at an unacceptably high level.

Antiretroviral therapy
Currently available antiretroviral drugs inhibit enzymes of the human immunodeficiency virus. The antiretroviral drug classes are the nucleoside analogues, such as zidovudine (AZT), the non-nucleoside reverse transcriptase inhibitors, such as nevirapine, and the protease inhibitors, such as indinavir and atazanavir. Antiretrovirals may be used to prevent infection (following exposure or to prevent transmission from mother to child) or to treat established infection. The pathogenic mechanisms of this disease are not completely understood. However, opportunistic infections may present with false aneurysms or thrombotic occlusion. The treatment of HIV vasculopathy has the triple objective of controlling the HIV infection, curing the vasculitis and managing the aneurysms and occlusive disease. Suppressing HIV replication is best done using three or more antiretroviral agents. Deciding how to treat the vasculitis is not easy, because its pathogenesis is not completely understood. However, opportunistic infections should be treated. Some success has been reported with plasmapheresis. The rationale behind plasma exchange is the presence of circulating immune complexes in patients with HIV vasculitis. Treatment with steroids and cytotoxic agents (mainly cyclophosphamide) is controversial. It may
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be helpful in the short term, but in the long term can lead to relapses and complications due to virus persistence. The preventive effects of antiretroviral drugs and prophylactic antibiotics with regard to the development of HIV vasculopathy are not known. However, since HIV vasculopathy is probably due to HIV replication, opportunistic infections and/or immune mechanisms, antiretroviral drugs and antibiotics should decrease its incidence.

**Late metabolic and atherogenic consequences of HIV infection**

HIV infection causes metabolic changes that may accelerate atherosclerosis. The metabolic changes of concern include raised triglycerides, decreased HDL, raised C-reactive protein, raised fibrinogen and increased plasminogen-activating inhibitor activity. Also, a number of studies in Western populations showed a higher prevalence of smoking in HIV-infected people when compared with the general population. The metabolic changes associated with HIV infection have been shown to increase coronary artery disease complications.

**Late metabolic and atherogenic consequences of antiretroviral drugs**

Protease inhibitors have been associated with a range of metabolic side-effects, including the metabolic syndrome (hyperlipidaemia, central fat accumulation and insulin resistance), that have been implicated in the pathogenesis of atherosclerosis. The nucleoside analogues can cause lipoatrophy and damage to mitochondria. These metabolic derangements caused by the protease inhibitors and nucleoside analogues have contributed to the rationale that the start of ART should be deferred until it is clearly necessary and that protease inhibitors should be avoided as long as possible. Cardiovascular risk is a concern. In a large, multicohort study, combination ART was associated with a 26% increase in the risk of myocardial infarction per year of regimen exposure. Atazanavir, a new protease inhibitor, has into reduced cardiovascular risk with this drug compared with the other protease inhibitors.

**Future of HIV vasculopathy when our patients are on antiretroviral drugs**

Treatment of patients with antiretroviral drugs will reduce their viral load and improve their immunity, which should result in less arterial damage and fewer patients with acute HIV-related vasculopathy. Control of their disease should also improve the metabolic derangements seen in HIV patients. However, the antiretroviral drugs, and especially the older protease inhibitors with their metabolic side-effects, can result in vascular damage and accelerated long-term atherosclerotic cardiovascular disease. This problem is best managed by treating the modifiable risk factors of atherosclerosis (particularly smoking and hypertension), and it is hoped that new protease inhibitors with a more favourable risk profile for metabolic derangements will be developed.

The author has attempted to show the various factors involved in changing the cardiovascular status of patients infected with HIV. It is difficult to predict the end result. However, treatment with potent combination ART has transformed HIV infection from a rapidly fatal disease into a chronic illness that some patients can live with for more than two decades. In future, when most of our patients are on antiretrovirals and the percentage of our people living with HIV has stabilised, South African vascular surgeons will probably manage fewer acute HIV-related aneurysms and thrombotic occlusions but perhaps more chronic peripheral arterial disease.

**REFERENCES**

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