Effect of antiretroviral therapy on metabolism and body composition in HIV-infected patients

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ABSTRACT

The PhD study was carried out as a collaborative research project between the Department of Infectious Diseases, Skejby Hospital and Department of Nutritional and Metabolism, Massachusetts General Hospital, Boston. The dissertation consists of three publications and a summarizing review.

The introduction of highly active retroviral therapy (HAART) has markedly improved the prognosis for HIV-infected patients. However, accumulating data suggest that HIV-infection and HAART can cause a syndrome of lipodystrophy associated with metabolic abnormalities contributing to increased mortality in HIV-patients. The main focus of this thesis was to further understand how HIV-lipodystrophy affects reproductive indices and cardiovascular risk in HIV-infected women. This was assessed in a cohort of 200 HIV-infected women and matched controls. To separate the effect of HIV from that of HAART the effect of stavudine treatment for a month on mitochondrial number and activity in skeletal muscle of healthy adults were investigated as well as how mitochondrial changes influenced overall insulin sensitivity. This was done in a placebo-controlled prospective randomized study.

Changes in body composition were seen in approximately two-thirds of HIV-infected women and rates of impaired glucose tolerance and hyperinsulinemia were also significantly increased. The numbers of women identified with polycystic ovaries were identical in the two groups but levels of sex hormone binding globulin were significantly increased in the HIV-infected women. This may be one factor contributing to the absence of polycystic ovaries in hyperinsulinemic and centrally obese HIV-infected women. Carotid intimal media thickness (IMT), a surrogate marker of atherosclerosis, was increased significantly in the protease-inhibitor treated HIV-infected women; however no correlation between HIV-infection and carotid IMT was found.

In the randomized prospective study of the effect of stavudine in healthy adults, we found a reduction of mitochondrial DNA as well as a reduction in insulin sensitivity in the stavudine treated group compared to the placebo treated group. Additionally a correlation between insulin sensitivity and mitochondrial function was found suggesting a mechanism by which NRTI can induce insulin resistance in HIV-infected patients.

These findings adds to the current knowledge of the occurrence of HIV-lipodystrophy and associated metabolic disturbances and how this may affect important risk factors for disease such as diabetes, heart disease, metabolic syndrome, and reproductive function. Further large scale epidemiological studies and prospective randomized controlled studies are needed to establish how changes in metabolism and body composition in HIV occurs.