Improved Lipid Profiles and Maintenance of Virologic Control in Heavily Pretreated HIV-Infected Patients Who Switched from Stavudine to Tenofovir Treatment

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A retrospective chart analysis of 66 human immunodeficiency virus type 1 (HIV-1)–infected patients whose treatment was switched from stavudine to tenofovir without any other treatment changes was conducted. The mean total cholesterol values decreased significantly within 3 months after the tenofovir substitution and remained significantly less than baseline values during 18 months of follow-up (mean decrease, 36 mg/dL; P = .002). Regimens containing tenofovir provided effective control of HIV-1 infection, with stable CD4+ cell counts and continued suppression of plasma HIV-1 level following the treatment switch from stavudine.

Previous studies have suggested that antiretroviral regimens that include tenofovir may be associated with beneficial effects on blood lipids in HIV-1–infected individuals, compared with regimens that include stavudine [1–5]. To investigate the impact of replacing stavudine with tenofovir in combination antiretroviral regimens, we conducted a retrospective, computerized chart analysis of patients from 2 HIV treatment centers caring for 1860 patients in Hamburg, Germany (Praxis St. Georg), and Pavia, Italy (IRCCS Policlinico San Matteo Hospital).

We identified 66 HIV-1–infected patients whose treatment had been switched from stavudine to tenofovir without any additional changes to either their antiretroviral regimen or their concomitant lipid-lowering therapy. No change in lipid-lowering treatment was allowed within 1 month prior to the switch from stavudine to tenofovir, and patients had to have been receiving stable stavudine treatment for at least 1 month. The first switch was performed in August 2001, at which time tenofovir became available within an expanded access program in Germany. Patients were observed until any change in their combination antiretroviral regimen occurred. They were monitored at the time of treatment switch (baseline) and every 3 months thereafter. The time point of the last observation included in the current analysis was 1 August 2004. Plasma HIV-1 RNA load was measured using the Roche Cobas Amplicor HIV1 Monitor 1.5 (lower limit of detection, 50 copies/mL), and CD4+ cell count was measured using flow cell cytometry. Cholesterol (total, high-density lipoprotein and low-density lipoprotein) and triglyceride serum levels were determined using standard laboratory methods. Changes in quantitative variables were assessed using Student’s t test for paired observations. Pairwise McNemar tests with respect to baseline values were performed to assess the change in viral load (<50 copies/mL vs. >50 copies/mL and <400 copies/mL vs. >400 copies/mL). Two-sided P-values were calculated.

The 58 men and 8 women had a mean age of 46 years (range, 28–62 years). Forty patients (60%) had advanced HIV-1 disease, defined as Centers for Disease Control and Prevention stage C or a CD4+ cell count nadir of <200 cells/μL. The median duration of prior antiretroviral therapy was 8.7 years (range, 1–13.5 years). The patients were treated with stavudine for a median duration of 54 months (range, 1–95 months; mean, 48.2 months). Reasons for switching therapy from stavudine (>1 reason may apply per patient) included lipodystrophy (32 patients), polyneuropathy (21 patients), hyperlipidemia (11 patients), elevated liver function test values (10 patients), and an elevated plasma viral load (10 patients). Some degree of physician-defined lipodystrophy was present in 79% of patients. Ten patients received concomitant lipid-lowering therapy for a median duration of 18 months (range, 4–47 months).

At the time of treatment switch, 49 patients received protease inhibitor–sparing regimens (comprising tenofovir, 1 or 2 nucleoside reverse-transcriptase inhibitors, and 1 nonnucleoside reverse-transcriptase inhibitor; 27 patients received efavirenz, and 22 patients received nevirapine), 17 patients received regimens containing a protease inhibitor (14 received lopinavir/ritonavir), and 2 patients received regimens containing 3 classes of antiretroviral drugs. The median duration of follow-up after the treatment switch from stavudine to tenofovir was 18 months (range, 4–36 months; mean, 21 months). At the time...
of the switch, the mean CD4⁺ T cell count was 597 cells/µL (range, 86–1237 cells/µL), and CD4⁺ T cell counts remained stable throughout the 18 months following the switch to tenofovir, as shown in figure 1A. The median plasma viral load was <50 copies/mL at the time of switch, with 51 patients (77%) having a load of <50 copies/mL. The proportion of patients with a plasma viral load of <50 copies/mL increased to 91% six months after switching to tenofovir ($P = .039$). The proportion remained >90% until 18 months after the switch, although these data did not achieve statistical significance because of the smaller patient numbers at later time points (figure 1B).

Figure 1. A, Mean CD4⁺ cell counts, with 95% CIs, for the 18 months following the switch from stavudine to tenofovir. B, Proportion of patients, with 95% CIs, with an HIV-1 load (VL) less than the limit of detection (<50 copies/mL).

At the time of the treatment switch to tenofovir, the mean total cholesterol value was 227 mg/dL, and 67% of patients had total cholesterol values greater than the normal level (200 mg/dL). Mean total cholesterol values decreased significantly (mean decrease, 18 mg/dL) within 3 months after substituting tenofovir for stavudine ($P = .003$) and remained significantly lower than baseline values during the 18 months of follow-up (mean decrease, 36 mg/dL; $P = .002$), as shown in figure 2A.

Two of 10 patients were able to discontinue lipid-lowering therapy. Low-density lipoprotein cholesterol values decreased

Figure 2. Mean total cholesterol (A) and triglyceride (B) values, with 95% CIs, for the 18 months following the switch from stavudine to tenofovir.
antiretroviral therapy or had documented resistance to nucleoside analogues, no cases of viral rebound occurred following the switch to tenofovir.

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References