CONCISE COMMUNICATION

Higher efficacy of nevirapine than efavirenz to achieve HIV-1 plasma viral load below 1 copy/ml

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Objectives: To compare the level of HIV-1 residual viremia, defined by a viral load below 50 copies/ml in patients receiving a tenofovir/emtricitabine and nevirapine (NVP) or efavirenz (EFV)-containing regimen.

Design: One hundred and sixty-five HIV-1-infected patients were retrospectively included since they achieved virological suppression (viral load <50 copies/ml) for at least 6 months with a tenofovir/emtricitabine and non-nucleoside reverse transcriptase inhibitor-containing regimen (NVP, \( n = 75 \) and EFV, \( n = 90 \)).

Methods: Residual plasma viremia was measured using an ultrasensitive assay with a limit of quantification of 1 copy/ml. A Fisher’s exact test was used to compare the percentage of patients with HIV-1 RNA below 1 copy/ml between the two treatment groups. Logistic regression was used to search for factors associated with a viral load below 1 copy/ml among the different patient characteristics.

Results: Patients in the NVP group had more frequently a viral load below 1 copy/ml than patients in the EFV group (81.3 vs. 55.6%, \( P < 0.001 \)). In multivariate analysis, only NVP vs EFV (\( P = 0.005 \)) and duration of viral suppression under antiretroviral treatment (\( P = 0.005 \)) were independently associated with viral load below 1 copy/ml.

Conclusions: It is well known that NVP has a good penetration in anatomic compartments that could explain a deep control of virus replication in some compartments and consequently decrease the residual level of viral load. The clinical relevance of having a viral load below 1 copy/ml has now to be studied for example on systemic inflammatory or immune activation markers.

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Introduction

All guidelines for the use of antiretroviral agents in HIV-1-infected patients recommend currently to achieve plasma virological suppression (HIV-1 viral load <50 copies/ml) under treatment. However, virological suppression in plasma does not preclude HIV-1 to persist in some reservoirs such as latently infected CD4+ T cells, central memory and transitional memory CD4(+) T cells as the major cellular reservoirs for HIV [1]. Moreover, it has been shown that low level, persistent viremia under suppressive antiretroviral therapy (ART) (stavudine/lamivudine/lopinavir) appears to arise from at least two cell compartments; one in which viral replication declines with time and another in which replication remains stable for at least 7 years [2]. Recent studies have shown that in treated patients, a viral load of 40–49 copies/ml is an independent predictor of viral load rebound above 50 and 400 copies/ml during 12 months of follow-up, suggesting that current guidelines recommending viral load suppression to below 50 copies/ml may not be the optimum goal of ART [3]. In a previous study, the use of non-nucleoside reverse transcriptase inhibitor (NNRTI) vs. protease inhibitor (mainly unboosted) seemed to be associated with a viral load below 2.5 copies/ml, without differentiating nevirapine (NVP) from efavirenz (EFV) [4]. In another study, the use of NVP was associated with a higher percentage of patients with a viral load below 2.5 copies/ml compared with the use of EFV or boosted lopinavir [5]. However, in the latter studies, nucleoside reverse transcriptase inhibitor (NRTI) backbone varied and could have a potential impact on the level of residual viremia. In the present study we compared residual viremia in patients taking a NVP or EFV-containing regimen with the same NRTI backbone using an ultrasensitive HIV-1 RNA quantification assay.

Methods

Patients studied were followed in two public hospitals (Pitié-Salpêtrière and Saint-Antoine Hospitals) and all of them were screened to be involved in the study since they achieved virological suppression (viral load <50 copies/ml) for at least 6 months with a regimen including tenofovir (TDF) and emtricitabine (FTC) and EFV or NVP. One hundred and sixty-five HIV-1 (165) patients included in the study, according to the inclusion criteria. Characteristics of the population for both groups and differences between groups are reported in Table 1. Patients in the NVP group had more frequently a viral load below 1 copy/ml than patients in the EFV group (81.3 vs. 55.6%, P < 0.001). In the univariate analysis, factors associated with a plasma viral load below 1 copy/ml were the use of NVP (P = 0.0006) and time of viral suppression under antiretroviral treatment (P = 0.0003). In the multivariate analysis, only NVP vs. EFV [P = 0.005, odds ratio (OR) = 2.85 (1.4–6.1)] and time of viral suppression under antiretroviral treatment [P = 0.005, OR = 2.07 (1.3–3.5)] were independently associated with a plasma viral load below 1 copy/ml. The median time under this NRTI-containing regimen was longer in the NVP group compared with the EFV group (3.4 vs. 2.8 years, P = 0.086). Adjustment for this latter variable did not change the results: NVP vs. EFV [P = 0.005, OR = 2.91 (1.4–6.1)] and time of viral suppression under antiretroviral treatment [P = 0.004, OR = 2.32 (1.3–4.1)].

Discussion

These results showed that the deeper virological control observed with NVP vs. EFV is linked to the type of NNRTI intake since associated NRTIs (TDF/FTC) were the same in both groups. Beyond the use of NVP (vs. EFV), the time spent below 50 copies/ml whatever the treatment regimen was independently associated with a residual viremia below 1 copy/ml. Another recent study showed a similar result with a proportion of patients with undetectable viral load positively correlated with the...
duration that the viral load was undetectable [7]. Although some characteristics of the studied patients were different, none of those variables was independently associated with having plasma HIV-1 RNA below 1 copy/ml. Indeed, the median time with viral load below 50 copies/ml under NNRTI-containing regimen was longer in the NVP group compared with the EFV group (2.8 vs. 2.3 years, P = 0.034). However, adjustment on the treatment duration of TDF/FTC and NNRTI did not change the results of the final multivariate model.

Other studies have suggested that the use of NNRTI-based regimen, and especially NVP, was associated with viral suppression below 2.5 copies/ml [5]. However, in those studies, patients received various NNRTI backbone that could interfere with this result. Thus, taken together with our results, there are convergent data showing the stronger ability of NVP than EFV to better control residual viremia, in patients presenting low-level viremia. It is well known that NVP has a good penetration in anatomic compartments [8,9]. Therefore, this could explain a deep control of virus replication in some patients. In fact, NVP does not completely decrease the residual level of viral load [9–11]. It is still not clear if the origin of residual low-level viremia is the release of viruses from reservoirs or ongoing replication or both [12]. However, our data argue in favor of residual viral replication as one of the origins of persistent viremia below 50 copies/ml under treatment. The clinical relevance of having a viral load below 1 copy/ml has yet to be shown and other investigations have to be conducted to explore, for example, the relationship between the level of residual viremia and systemic inflammatory or immune activation markers.

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References


