

A Comparison of Viral Loads between HIV-1-infected Elite Suppressors and HAART-treated Individuals

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Abstract

Background: HIV-1-infected patients who control viremia without treatment, termed elite suppressors (ES), and patients on suppressive HAART-regimens both have viral loads below the clinical limit of detection, 50 RNA copies per ml of plasma (c/ml). In patients on HAART, viremia reaches a stable plateau of 3 RNA c/ml. Low-level viremia in ES has been detected but not quantified. We hypothesize viral loads in ES would be higher than in HAART-suppressed individuals.

Methods: Through the use of an ultrasensitive real-time PCR-based viral load assay with a limit of quantification of 1 c/ml, viral loads from 15 individuals on suppressive HAART were measured and compared with viral loads from 14 HAART-naïve ES. Two of the ES had repeated viral load measurements on archived plasma samples to determine if there were large fluctuations over time.

Results: The difference between the median viral loads of ES and HAART-treated individuals was not statistically significant ($p > 0.05$). However, ES displayed a greater range of viral loads than HAART-treated individuals ($p < 0.01$). More than half of the ES had undetectable viral loads whereas less than half of the HAART-treated individuals had undetectable viral loads. Using archived plasma samples, a longitudinal analysis showed that ES had more variable viral load dynamics than HAART-treated individuals.

Conclusions: We provide preliminary data on viral load dynamics in ES. Compared to patients on suppressive HAART, ES demonstrated a greater range of viral loads. In one ES followed over time, the viral loads ranged from 1 to 62 c/ml; however, in some ES we do not observe large viral load fluctuations over time. Both phenomena may reflect the varying degrees of ongoing replication occurring in the absence of antiretroviral therapy and/or the rate at which virus-producing cells are being cleared by the immune system.

Introduction

A subset of HIV-1-infected individuals termed elite suppressors (ES) maintain viral loads (VL) below the clinical limit of detection of 50 c/ml and normal CD4⁺ T cell counts without antiretroviral therapy. Similarly, HIV-infected individuals on suppressive highly-active antiretroviral therapy (HAART) maintain VL below 50 c/ml albeit through the use of antiretroviral therapy. Palmer and colleagues developed an ultrasensitive VL assay with single-copy sensitivity, termed the single-copy assay (SCA). Using the SCA, Maldarelli and colleagues have shown that individuals with suppression of viremia on HAART maintain a steady state VL below 50 c/ml, at a median of 3 c/ml. Here, we use the same assay to measure and compare VL in ES and HAART-treated individuals from archived plasma samples.

Methods

Patients: We studied 14 ES and 15 HAART-treated patients. Informed consent was obtained from each individual. All of the ES had undetectable VL as determined by the Johns Hopkins Hospital (AMPLICOR HIV-1 MONITOR Test, v1.5 Roche). Of the HAART-treated patients, 11 were on a non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimen while the remaining patients were on a protease inhibitor (PI)-based regimen. All HAART-treated patients had VL below 50 c/ml for at least 6 months as determined by the Johns Hopkins Hospital (AMPLICOR HIV-1 MONITOR Test, v1.5 Roche). **Viral load measurements:** Using an ultrasensitive real-time PCR-based viral load assay with a limit of quantification of 1 c/ml described by Palmer *et al.*, VL from 14 ES were measured and compared with VL from 15 individuals on suppressive HAART. In a longitudinal analysis, VL from 2 ES were measured over time using archived plasma samples.

Results

	Year of diagnosis	Last CD4+ T cell count (cells/ul)	SCA Viral Load (c/ml)	HLA-B
ES2	1986	399	0	5703.44
ES3	1991	728	2	5702.51
ES4	1996	783	0	08.44
ES5	1990	839	0	5703.58
ES6	1992	965	1	5703.15
ES7	1994	1362	87	5703.81
ES8	2003	602	48	5703.44
ES11	1993	721	25	35.63
ES14	2002	939	0	52.78
ES15	1996	927	0	5703.07
ES18	1998	1330	0	5703.42
ES19	1996	732	0	5703.07

Table 1. Clinical characteristics of ES. Year of HIV infection diagnosis, CD4⁺ T cell count, HIV RNA viral load, and HLA-B*57 status.

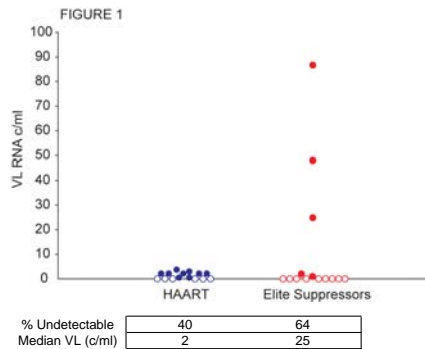


Figure 1. Single VL measurements in ES (red) and HAART-treated individuals (blue). Open circles represent undetectable VL (< 1 c/ml). The median VL were not statistically significant by an unpaired unequal variance t-test.

Results

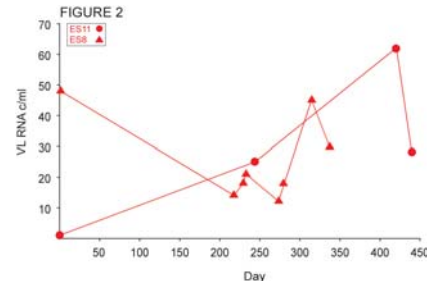


Figure 2. A longitudinal analysis of VL. VL from 4 separate blood draws in ES11 (circle). VL from 8 separate blood draws in ES8 (triangle).

Conclusions

In this preliminary study of viral load differences between ES and HAART patients, we found:

- (1) Evidence of greater variation in VL in our ES cohort than in our HAART patient cohort.
- (2) A greater proportion of undetectable VL in the ES cohort than in the HAART patient cohort.
- (3) No correlation between VL and CD4⁺ T cell count, HLA-B*57 allele status, or year of HIV-1 infection diagnosis in our ES cohort.

Based on these findings, we suggest that in ES with higher VL and greater fluctuations in VL dynamics, CTL-mediated killing of infected cells may not be as efficient as in those individuals with lower VL. Both phenomena may reflect the varying degrees of ongoing replication occurring in the absence of antiretroviral therapy and/or the rate at which virus-producing cells are being cleared by the immune system.

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