

Factors associated with a low HIV reservoir in patients with prolonged suppressive antiretroviral therapy

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Background: The relevance of a low level HIV reservoir in patients with prolonged therapy is not well understood. Our objective is to determine factors that influence the establishment of small reservoirs in long-term treated patients (excluding treatment since acute infection) to a level similar to HIV Elite controllers (< 100 HIV Total DNA copies/10⁶PBMCs).

Methods: Cross-sectional study involving patients receiving highly active antiretroviral therapy (HAART) with plasma HIV RNA < 50 copies/ml for whom total DNA measurement were performed. Patients treated since early acute infection or receiving cancer chemotherapeutic/ immunosuppressive agents were excluded from the study.

Results: Overall, 246 patients receiving HAART with undetectable viremia were involved in the study. The median HIV DNA was 372 copies/10⁶PBMCs. Fifty eight patients had a low HIV DNA level < 100 copies/10⁶ PBMCs. A low proviral DNA was associated with an ultrasensitive Viral Load < 1copy/mL ($p < 0.0001$), a lower HIV RNA zenith ($p < 0.0001$), a higher CD4 T cells nadir ($p = 0.023$), lower current CD8 T cells counts ($p = 0.010$) and a higher current CD4/CD8 ratio ($p = 0.003$). In addition, such a low reservoir was also associated with a higher time spent with undetectable HIV-1 RNA ($p = 0.018$). Other factors such as length of time on HAART and duration of HIV-1 infection were not associated with levels of HIV-1 DNA.

Conclusions: The obtention of a low HIV DNA level, reflecting a limited pool of infected cells is associated with a high CD4 nadir and a low HIV RNA zenith, reinforcing the need to institute antiretroviral treatment early during chronic infection to control HIV reservoir. In addition, the fact that low reservoirs are associated with a higher time spent with undetectable viremia is consistent with previous findings showing that the pool of infected cells decreases with time under HAART. Our results reinforce the idea that a small reservoir may be related to stronger control of residual viremia that in turn keeps the immune activation system to a low activation status. This study helps to define factors associated with low proviral DNA setpoints after long-term treatment and should be useful to identify future candidates for strategies aiming at eradicating HIV.