MINI REVIEW

Short note on infecfion with HIV over time

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ABSTRACT

Review recently published research in the following three areas: long term nonprogression/viral control; determinants of viral load set point/disease progression; and potential Antiretroviral Therapy (ART) effects in early HIV infection.

With some HIV positive people being able to maintain high CD4 cell counts and/or suppressed viral loads in the absence of ART, the natural course of untreated HIV infection varies greatly. Although similar, the underlying mechanistic mechanisms that result in viral control and long term nonprogression are probably different. The identification of host factors that are causally connected to these traits through concerted ongoing research efforts should present prospects for the creation of novel therapeutic or preventive approaches. Although there is growing evidence that starting ART during primary infection may stop the immunological decline that would otherwise be seen in HIV infection left untreated, current studies have not focused on the longer term therapeutic advantages of starting ART at this very early stage.

It may be possible to find new targets for treatment and prevention of HIV infection by having a better understanding of the relative effects of viral, host, and environmental variables on the natural course of HIV infection.

Keywords: Antiretroviral Therapy (ART); HIV infection; Therapeutic advantages; Determinants; Immunological decline

INTRODUCTION

Early on in the HIV epidemic, understanding of the natural history of HIV grew quickly. However, the widespread use of effective Antiretroviral Therapy (ART) caused a change in the scientific community's attention from investigations into the natural course of infection to those into infections that have been treated. Nevertheless, there have been significant advancements in our understanding of natural history in recent years. We will concentrate on three topics in this review that are important to treating clinicians: long term viral control and nonprogression; determinants of viral load set point and disease progression; and potential effects of ART in early HIV infection.

Untreated HIV infection has a diverse natural history. There has been a lot of interest in finding subgroups of HIV positive people who have different disease progression patterns over the past ten years. It is envisaged that the knowledge gained from the identification of such people would help in the development of vaccinations and new therapeutic strategies.

Long Term Nonprogressors (LTNP) are those who have a high CD4 cell count and remain asymptomatic for a long time off ART (see reviews by Poropatich and Sullivan and Gaardbo, et al. Although it is frequently stated that 1%-5% of HIV positive people are LTNP, these estimates are complicated by the lack of a standardised definition of an LTNP, leading to a wide range in the definitions used (and the manner in which they are applied, particularly in the presence of variable follow-up and irregularly measured CD4 cell counts).

In a military cohort, Okulicz, et al. reported prevalence of 5.02% using a similar definition but with only 7 years of follow up. Only 0.4% of patients in the French Hospital's HIV database, in contrast, had LTNP status identified. Mandalia, et al., detected asymptomatic HIV positive people who had been infected for more than 7 years in a UK research. These people were ART-naive. Only 50 of the 312 patients in this group maintained stable CD4 cell counts, and only 13 of them regularly had CD4 cell counts within the normal range. As a result, LTNP made up only 0.2% of patients receiving care, a far smaller percentage than that reported by Okulicz, et al., probably as a result of the requirement that people have stable CD4 cell counts.

DESCRIPTION

Recently, attention has switched to finding people who can suppress HIV replication to the point that viral load levels are undetectable even in the absence of ART. They are often referred to as viral controllers or elite controllers. Elite controllers were those patients with at least three longitudinal undetectable HIV RNA readings who had been ART-naive for more than 12 months in the military cohort published by Okulicz, et al. People were allowed to occasionally have HIV RNA levels up to 1000 copies/ml, provided that these occurrences constituted a small minority of all determinations.

These elite controllers were separated from viremic controllers, who tended to have viral loads between 1000 and 2000 copies/ml as their predominant viral loads. Of the 4586 people studied, 0.6% was elite controllers and 3.3% were viremic controllers. In elite controllers and viremic controllers, respectively, viral control was achieved a median of one year after seroconversion, persisted for 846 and 1085 days, and was linked to a lower risk of clinical progression. It's interesting to note that whereas elite controllers CD4 cell counts initially increased before stabilising, viremic controllers typically experienced CD4 cell loss. The elite controller's status is established quickly following primary infection in the national agency for AIDS research PRIMO cohort.

These studies show that ART can stop immune system deterioration that would otherwise occur in the absence of treatment, but they do not address whether patients who start ART during primary infection experience any long-term clinical benefit (in terms of decreased morbidity or mortality) from this treatment. As a result, they do not address whether allowing CD4 cell counts to decline will have any noticeable negative effects over the short or long term. Unfortunately, in order to gather such data, clinical endpoint studies with much bigger sample numbers are the only ones that can be used. This query is the focus of the ongoing Strategic Timing of Anti-Retroviral Treatment (START) study.

CONCLUSION

Untreated HIV infection can have a variety of clinical, immunological, and virological outcomes, but few people who are followed for more than 8 to 10 years show no signs of disease progression. The varying natural course of HIV infection may be influenced by a variety of viral traits, host defense

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mechanisms (possibly explained by varying host genetics), and environmental factors. The relative importance of these factors is beginning to be clearer. This field of study has the potential to uncover brand new targets for treatment and prevention of HIV infection.