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Viral load versus p24 antigenaemia in human immunodeficiency virus infected patients

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Monitoring human immunodeficiency virus type-1 (HIV-1) RNA levels is important in the management of patients with HIV-1 infection, and its use is well accepted.[1,2] During the past three years, its incorporation in the attendance routine has been strengthened in our medical scene. There is no need to emphasise the improvements in its technical fulfilment as well as in the sensitivity of quantitation methods,[3] while there is a widespread tendency to limit or even omit p24 antigen detection and quantitation. However, not every healthcare facility has been able to switch from antigenaemia detection to viral load measurement.

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Here, we report the results of a comparative study of plasma viral load levels and serum p24 antigenaemia in 109 HIV-1-infected subjects, at different stages of infection, to establish whether or not they correlate. HIV-1-infected subjects were enrolled in this study between November 1997 and September 1998. The stage of HIV-1 infection was determined for each subject according to the Centers for Disease Control and Prevention (CDC) 1993 classification system.[4]

Plasma HIV-1 RNA levels were determined using a reverse transcription polymerase chain reaction (RT-PCR) assay (Amplicor HIV-1 Monitor test, Roche Molecular Diagnostic Systems, Inc., Brachburg, NJ, USA), giving 400 HIV-1 RNA copies/mL as the lower quantitation limit within the linear range.

p24 antigen was measured using a sandwich-type enzyme immunoassay (EIA) (Elavia Ag I, Sanofi Diagnostic Pasteur, France) with polyclonal antibodies selected for their ability to bind to various HIV-1 constitutive (internal and external) proteins. In order to improve the sensitivity of the test, serum samples were analysed in two forms — plain serum and serum treated with a mild acid solution (ICS) (Elavia Ag I Immune Complexes Dissociating Reagent, Sanofi Diagnostic Pasteur, France) to dissociate any antigen–antibody complexes — and the assay performed both qualitatively and quantitatively. The latter was achieved by means of a reference curve drawn from the results of five standards (dilutions of HIV-1 antigen, Sanofi Diagnostic Pasteur, France) included with each test run. Positive samples (HIV-1 antigen >30 pg/mL) were confirmed by blocking with HIV-positive serum included in the EIA kit (neutralised antigen).

In order to compare the results, we divided viral load levels into six ranges as follows: range 1 (<400 copies/mL); range 2 (400–10^4 copies/mL); range 3 (>10^4–3 x 10^4 copies/mL); range 4 (>3 x 10^4–5 x 10^4 copies/mL); range 5 (>5 x 10^4–5 x 10^5 copies/mL); and range 6 (>5 x 10^5 copies/mL). Viral load results were log-transformed and statistical analysis was performed using SAS/STAT.[5] Comparison between mean values for viral load and p24 antigenaemia was performed using a logistic regression model. $P < 0.05$ was considered significant statistically.

One hundred and nine HIV-1-positive patients (both male and female; median age [25th to 75th percentiles]: 33–47 years) were enrolled in the study and the split in CDC classification of HIV-1 status was as follows: CDC A, 26 patients; CDC B, 41 patients; and CDC C, 42 patients. According to the ranges of viral

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load, distribution of the patients was 14.7% in range 1, 19.3% in range 2, 12.8% in range 3, 8.3% in range 4, 27.5% in range 5, and 17.4% in range 6.

Two main observations arise from this study. In terms of the detection of p24 antigenaemia, 37.5% of the serum samples were positive after mild acid treatment (immunocomplex dissociation) but only 25.7% (28 samples) remained positive after neutralisation. Of the 28, only four (23.8%) were from patients with viral load levels ≤3 x 10^4 RNA copies/mL; the other 24 (76.2%) had values above 3 x 10^4 copies/mL.

Although conscious of the fact that p24 antigenaemia is not a suitable marker to monitor response to antiretroviral therapy, just over 40% of patients with viral load levels >3 x 10^4 RNA copies/mL have positive antigenaemia in our experience. This demonstrates that laboratories unable to switch to viral load quantitation to monitor HIV infection would have a sensitivity <40%, and supports a recent study by Steindl *et al.*,[6] which found positive antigenaemia in 44.9% HIV-infected patients at different stages (not depending on the viral load level) using conventional methods similar to that described here. The slightly improved sensitivity was obtained by use of a preliminary denaturation procedure.

The probability that a subject would have positive antigenaemia depends directly on the level of viral load, being greater than 40% for those >1 x 10^5 RNA copies/mL (Figure 1). However, there is evidence that the higher the viral load the greater the rate of p24 antigenaemia, for both neutralised p24 antigen ($P < 0.05$) and following dissociation of immunocomplexes ($P < 0.05$) In this way, the probability that rising viral load corresponds with rising antigenaemia is greater when the latter is measured by ICS (odds ratio [OR] = 3.32) than as free neutralised p24 antigen (OR = 2.39).

A previous study[7] has demonstrated that ICS is the most sensitive method of detecting antigenaemia; however, in our opinion, cohort studies are needed to confirm the correlation between the two parameters evaluated in the present study. Nowadays, the role of p24 antigenaemia detection appears to be restricted to that of a helpful serological marker of HIV seroconversion. In this context, and without the ability to determine viral load, this marker may find application despite only moderate correlation with viral load.

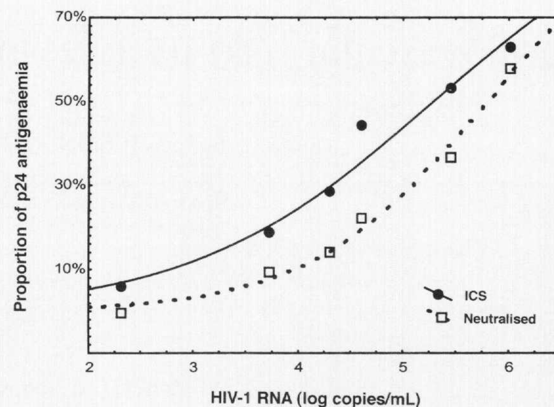

Fig. 1. Association between viral load and p24 antigenaemia (ICS and neutralised) in HIV-1-infected patients.

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