LETTER

Low rates of p24 antigen detection using a fourth-generation point of care HIV test

INTRODUCTION

Over one-quarter of people living with HIV infection in the UK are unaware of their HIV infection.[1] HIV point-of-care testing (POCT) can greatly improve the uptake and acceptability of HIV testing across hospital and community settings[2 3] and, until now, has been carried out using a third-generation antibody assay. As such, cases of suspected PHI are referred for fourth-generation combination testing.

Identification of PHI is important, as identification during this hyperinfectiousness period may reduce onward HIV transmission events,[4–6] and early intervention with antiretroviral therapy may enhance the long-term clinical outcome.[7–10]

A significant advance in HIV POCT has been the development of the Determine HIV-1/2 Ag/Ab Combo assay (Inverness Medical, now renamed Alere). This is the first rapid fourth-generation assay for simultaneous detection of HIV p24 antigen and antibodies to HIV-1 and HIV-2. However, this assay has been introduced into routine care in the absence of a formal evaluation of its performance and, in particular, its ability to detect PHI.

We investigated the ability of the Determine assay to detect p24 antigen in samples identified as p24-positive using standard of care fourth-generation assays.

METHODS

Stored serum samples positive for HIV p24 antigen following standard laboratory testing conducted on-site (VIDAS HIV Duo Ultra HIV5, VIDAS HIV Duo Quick HIV6 p24 assay, Biomerieux, Marcy l'Etoile, France) or at a reference laboratory (Biorad EIA, Richmond, California) from 36 confirmed HIV-infected individuals were evaluated. All p24 antigen-positive results were confirmed with neutralisation. Twenty-six of the 36 samples (72.2%) were HIV-antibody-negative and 10 (27.7%) HIV-antibody-positive using a combination of on-site (Architect HIV Ag/Ab Combo, Abbott, Delkenheim, Germany; Bispot Immunocomb HIV-1/HIV-2 antibody assay, Sterilab, Malmo, Sweden; Vironostika HIV Ag/Ab EIA) and reference laboratory testing (Integral Ag/Ab EIA; Abbott Murex Combined EIA; in-house HIV-1 GACPAT and HIV-2 GACPAT).

Sequential samples from two individuals with confirmed PHI were also evaluated.

Ethical approval was not required for this study, as samples were anonymised by removal of all patient identifiers; a case note review was not possible. The only information retained for samples was HIV antibody and p24 antigen status.

Table 1 Evaluation of the fourth-generation determine HIV-1/2 Ag/Ab combo assay for identification of primary HIV infection

Standard serological test results	Determine point-of-care testing results				
	No	p24 Ag-positive/ antibody-negative	p24 Ag-positive/ antibody-positive	p24 Ag-negative/ antibody-positive	p24 Ag-negative/ antibody-negative
HIV p24 Ag-positive/ Ab-negative	26	14	2	1	9
HIV p24 Ag-positive/ Ab-positive	10	1	1	7	1

Samples were tested using the fourth-generation Determine HIV-1/2 Ag/Ab Combo POCT assay according to the manufacturers' instructions. Quality-control samples obtained from the Health Protection Agency for HIV-1 antibodies, HIV-2 antibodies, HIV p24 antigen together with an HIV antibody-negative sample were also tested. The Determine assay gave correct results, concordant with standard laboratory testing, with all four quality-control samples.

Exact 95% CIs were calculated using the binomial distribution.

RESULTS

The Determine assay detected p24 antigen in 18 of 36 (50%; 95% CI 34% to 66%) samples identified as p24 antigen-positive by standard testing. Specifically, it detected p24 antigen in 16 of 26 (62%, 95% CI 41% to 80%) p24 antigen-positive/antibody-negative samples and in two of 10 (20%, 95% CI 3% to 56%) p24 antigen-positive/antibody-positive samples. The Determine assay failed to detect HIV infection (either p24 antigen or HIV antibody) in 10 of 36 (28%) cases, 9 of which were p24 antigen-positive/HIV antibody-negative (ie, PHI) by standard testing (table 1).

HIV antibody results obtained with the Determine assay were concordant with standard laboratory testing in 31 of 36 samples (86.1%). Among the five samples with discordant results, two were antibody-negative in the Determine assay but positive on standard testing, and three were antibody-positive in the Determine assay and negative on standard testing.

Sequential samples from two individuals with confirmed PHI were evaluated. In the first case, standard fourth-generation testing identified p24 antigen only at baseline and HIV antibody only at day 35. The Determine assay failed to detect either antigen or antibody at baseline but detected HIV antibody at day 35. Thus, at baseline, the patient would have been given a negative HIV POCT result. In the second case, both Determine and standard laboratory testing detected p24 antigen only at baseline and day 2.

CONCLUSIONS

In this evaluation, the sensitivity of the fourth-generation Determine assay, for p24 antigen detection, was 50%. As such, only 16 of 26 (62%) cases were identified as PHI and 10 falsely identified as HIV-negative. This suggests that a relatively high proportion of PHI cases may be missed with significant public health consequences. This is not unexpected for a rapid lateral flow device, which would be unlikely to reach the high level of sensitivity associated with standard fourth-generation assays; however, larger numbers are required to confirm these findings.

In light of its variable ability to detect p24 antigen, further clinic-based evaluations are indicated to define the role of the fourth-generation POCT in the clinical setting. Such studies are planned, but none are currently recruiting. We recommend that standard fourth-generation assays still be indicated in individuals with suspected PHI and that providers inform users of the test limitations.

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REFERENCES

1. **Health Protection Agency**. HIV in the United Kingdom: 2008 report, 2008. http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1227515299695.
2. **Appiah LT,** Havers F, Gibson J, *et al*. Efficacy and acceptability of rapid, point-of-care HIV testing in two clinical settings in Ghana. *AIDS Patient Care STDS* 2009;**23**:365–9.
3. **Knapp H,** Anaya HD, Feld JE. Expanding HIV rapid testing via point-of-care paraprofessionals. *Int J STD AIDS* 2008;**19**:629–32.

4. **Hollingsworth TD,** Anderson RM, Fraser C. HIV-1 transmission, by stage of infection. *J Infect Dis* 2008;**198**:687—93.
5. **Pilcher CD,** Joaki G, Hoffman IF, *et al*. Amplified transmission of HIV-1: comparison of HIV-1 concentrations in semen and blood during acute and chronic infection. *AIDS* 2007;**21**:1723—30.
6. **Pilcher CD,** Tien HC, Eron JJ Jr, *et al*. Brief but efficient: acute HIV infection and the sexual transmission of HIV. Quest Study; Duke-UNC-Emory Acute HIV Consortium. *J Infect Dis* 2004;**189**:1785—92.
7. **Volberding P,** Demeter L, Bosch RJ, *et al*; the ACTG 371 Team. Antiretroviral therapy in acute and recent HIV infection: a prospective multicenter stratified trial of intentionally interrupted treatment. *AIDS* 2009;**23**:1987—95.
8. **Barbour JD,** Ndhlovu LC, Xuan Tan Q, *et al*. High CD8+ T cell activation marks a less differentiated HIV-1 specific CD8+ T cell response that is not altered by suppression of viral replication. *PLoS One* 2009;**4**:e4408.
9. **Apuzzo LG,** Vaida F, Gallant JE, *et al*. Tolerability and efficacy of PI versus NNRTI-based regimens in subjects receiving HAART during acute or early HIV infection. *AIDS* 2009;**50**:267—75.
10. **Hecht FM,** Wang L, Collier A, *et al*; AIEDRP Network. A multicenter observational study of the potential benefits of initiating combination antiretroviral therapy during acute HIV infection. *J Infect Dis* 2006;**194**:725—33.

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