Sensitivity of the INSTI™ HIV-1 Antibody Point-of-Care Test for detection of acute HIV Infection

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BACKGROUND

The sensitivity and specificity of Point-of-Care (POC) HIV tests for detection of established HIV infection is similar to 3rd generation enzyme immunoassay (EIA) screening tests used in laboratories. However, recent reports have demonstrated that POC HIV tests vary in their ability to detect individuals with early HIV infection.[1,2] This is attributed to differences in the window period between test products.[3,4]

The INSTI™ HIV-1 antibody test is currently the only licensed POC HIV test in Canada. In BC this test is in use in a small number of primary care clinics and demonstration sites. According to the product monograph, using sero-conversion panels the INSTI™ HIV-1 Antibody Test detected HIV infection at the same time or up to 8 days after a 3rd generation EIA test such as the one used by PHSA Laboratories. Using the PHSA Laboratory or standard test protocol which uses 3rd generation EIA, we have identified individuals with acute HIV infection (i.e., who have a reactive 3rd generation EIA, indeterminate or non-reactive western blot, and are p24 antigen positive). In this study, we wanted to assess the real-world performance of the INSTI™ HIV-1 antibody test in individuals identified with acute HIV infection using the standard HIV test protocol.

OBJECTIVE

The study objective was to assess the sensitivity of the INSTI™ HIV-1 Antibody Test in comparison to the current standard HIV test protocol in the PHSA Laboratories (i.e., screening by 3rd generation EIA) to detect acute infections. Testing involved the use of residual sera from confirmed HIV positive individuals with test results suggestive of acute HIV infection as indicated by identification of p24 antigen (which is typically present for approximately 2 to 5 weeks after HIV infection).

METHODS

All specimens with a reactive HIV result in the PHSA Laboratory database (between February 22, 2006 and October 31, 2008) which were positive for p24 antigen (Biomeriéux Vironostika HIV-1 Antigen) with confirmation by a p24 neutralization assay or HIV nucleic acid testing , with a reactive or non-reactive 3rd generation EIA test (Siemens ADVIA™ Centaur HIV-1/O/2) and non-reactive or indeterminate Western Blot (BioRad Genetic Systems HIV-1 Western Blot) result were identified.

Specimens were excluded if: there were insufficient sera for testing; the initial reactive result was not confirmed by follow-up western blot, PCR, or physician reported viral load result; or individuals were known to have advanced HIV disease at diagnosis based on receipt of an AIDS case report within 6 months of a reactive result. The INSTI™ HIV-1 antibody test was performed on all included specimens. Sensitivity was calculated as the proportion of specimens having a reactive INSTI result (i.e., where reactivity under the current standard

test protocol was assumed to be the "gold standard"). If the initial INSTI™ HIV-1 antibody test was non-reactive or indeterminate on the initial specimen, the test was repeated on follow-up specimens from the same individual (where available). Exact 95% binomial confidence intervals were calculated for proportions. UBC ethics approval was obtained for this study.

RESULTS

There were 61 eligible specimens, of which 8 were excluded (4 due to insufficient sera, 2 whose initial reactive result was not confirmed, and 2 due to an AIDS case report received within 6 months of a reactive result). Specimens from 53 individuals were available for analysis.

Among the 53 individuals two groups emerged based on the result of the 3rd generation EIA screening test (Table 1). In group 1 (n=4), the initial 3rd generation EIA test and WB were non-reactive and a positive p24 antigen test alone indicated acute HIV infection (these likely were specimens where the requisition indicated a request to test for p24 antigen, for example, due to seroconversion symptoms). In group 2 (n=49), the initial 3rd generation EIA screening test was reactive, and the WB results was non-reactive (13), non-specific (2), or indeterminate (34).

The performance of the INSTI™ HIV-1 antibody test in these two groups is presented in the table below. All individuals in group 1 had a non-reactive INSTI™ HIV-1 antibody test on the initial specimen, with reactive results on follow-up specimens. In group 2, the INSTI™ HIV-1 antibody test was reactive on the majority of initial specimens with reactive results on subsequent follow-up specimens for specimens having an initial non-reactive or indeterminate result. The estimated sensitivity of the INSTI™ HIV-1 antibody test for detection of acute HIV infection compared to the standard test protocol was 69.4% [95% CI 54.6-81.8%].

Table 1: Performance of INSTI™ HIV-1 antibody test on remnant sera from individuals with acute HIV infection detected through standard test protocols

Group	INSTI™ HIV-1 Antibody Test result on initial specimen	N (%)	95% Confidence Interval
1. Screening EIA non-reactive (n=4)	Reactive	0 (0%)	
	Indeterminate	0 (0%)	
	Non-reactive	4 (100%)*	
2. Screening EIA reactive (n=49)	Reactive	**34 (69.4%)**	[54.6 – 81.8%]
	Indeterminate	5 (10.2%)*	[3.4 – 22.2%]
	Non-reactive	10 (20.4%)*	[10.2 – 34.3%]

*A reactive INSTI result was obtained on follow-up specimens for each case with an indeterminate or non-reactive initial result (where sera were available for testing).

INTERPRETATION

No individuals who were p24 antigen positive but negative on a 3rd generation EIA test had a reactive POC test (group 1). These cases likely represent acute HIV infection prior to the development of an antibody response and therefore the non-reactive POC antibody test is not surprising.

Among individuals with an initial reactive 3rd generation EIA test (group 2), the sensitivity of the INSTI™ test for detection of acute HIV infection was 69.4% [95% CI 54.6-81.8%]. These findings are consistent with the reported performance of the INSTI™ HIV-1 antibody test on sero-conversion panels.

On the basis of this study an estimated 69% of individuals with results suggestive of acute HIV infection detected through the current standard test protocol would have a reactive test using the INSTI™ POC test. In clinical practice, an INSTI™ result which is indeterminate should lead to collection of a venipuncture specimen which is then tested under the standard test algorithm. Accordingly in practice the use of the INSTI™ HIV-1 antibody test as an initial screening test instead of a 3rd generation EIA test may lead to the detection of HIV in 80% of individuals with acute HIV infection, and a small number of acute HIV infections would not be diagnosed. The 10 individuals having a non-reactive INSTI™ HIV-1 antibody test in Group 2 represented 1% of the 982 new positive HIV tests in BC during the study period.

The confidence intervals for these estimates are wide due to the small number of specimens evaluated. Another limitation of this analysis is that individuals with advanced HIV disease may have similar patterns of HIV results (e.g., 3rd generation EIA reactive, p24 antigen positive, WB indeterminate). Due to incomplete AIDS reporting and reporting delay we may have misclassified some individuals with advanced HIV infection as acute.

This study did not assess the specificity of the INSTI™ HIV-1 antibody test by testing of specimens which are non-reactive under the standard testing protocol. Accordingly our design did not allow for the identification of individuals with acute HIV infection who may have had an initial positive INSTI™ HIV-1 Antibody Test at the same time as a negative standard 3rd generation EIA test, as has occasionally been identified with other POC HIV test products.[1,5] Sera was used for this study. As the INSTI™ HIV-1 POC test performs similarly on both sera and whole blood, it is expected these results are generalizable to the use of whole blood in clinic settings.

CONCLUSION

The performance of the INSTI™ HIV-1 antibody test appears consistent with the reported performance of the test on sero-conversion panels, and these findings confirm that in some individuals the window period of reactivity is longer for the INSTI™ HIV-1 antibody test compared to the 3rd generation EIA tests currently in use in BC.

These findings reinforce current BC guidelines that the most appropriate use of POC HIV testing is in clinical scenarios where rapid knowledge of an HIV result can guide subsequent interventions and in specific voluntary counselling and testing settings (e.g., in populations with a higher prevalence of HIV or where not returning for HIV test results is likely). In some settings where the expected HIV incidence is higher (e.g., clinics accessed by MSM) offering both a POC HIV test and a blood draw for standard HIV testing may be of benefit as has been implemented in some jurisdictions in the US.[6] A knowledge of relative window periods is required for all clinicians conducting HIV testing in BC, particularly as new HIV test technologies become widely available in the future (e.g., as 4th generation EIA screening tests which combine p24 antigen and antibody testing become increasingly adopted, as these tests have a shorter window period and greater sensitivity for acute HIV infection compared to 3rd generation EIA tests).

ACKNOWLEDGEMENTS

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For further information about the nature of the tests discussed in this update, and associated window periods, please refer to "Understanding the Window Periods of HIV tests", SHAKE Knowledge Corner 2009: 2(1). http://www.phsanewsletters.ca/bccdc/LandingPage.aspx?id=358925&p=1.

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