Using quantitative HIV RNA viral load to diagnose HIV infection

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BACKGROUND AND OBJECTIVES

The third generation enzyme immunoassays (EIA) currently used in Canada as the initial screen for HIV antibodies have an estimated diagnostic window period of 4-6 weeks. However, the Canadian case definition for HIV is based on a positive confirmatory Western Blot (WB) which is less sensitive than EIA. Early diagnosis of HIV infection optimizes individual patient management and clinical outcomes. Moreover, acute HIV seroconverters usually have a very high viral load, which is an important determinant of infectivity. Another challenge using serology as the diagnostic criterion is the recognition of vertical transmission because of transplacental maternal antibodies in infants. While quantitative HIV RNA viral load (QVL) is only licensed for the clinical monitoring of HIV infected patients, it has also been shown to be sensitive and specific in previous studies as a diagnostic test. We examined the performance of QVL as a HIV diagnostic test in two populations:

1) infants born to HIV infected mothers, and
2) patients with reactive EIA and negative/indeterminate (neg/ind) WB.

METHODS

Provincial Public Health Laboratory (ProvLab) performs all diagnostic HIV serology tests for the province of Alberta using an algorithm that includes two EIA assays and WB for patients with a positive EIA screen (Figure 1). Each clinician is phoned by the virologist to discuss the WB result of a patient and to obtain HIV risk history, reason for testing and presenting symptoms. QVL is recommended when there is a high suspicion for acute seroconversion or if the QVL is deemed to be useful in the clinical management and/or counselling. QVL was performed by both regular and ultrasensitive Roche Cobas® Amplicor® HIV-1 Monitor (v1.0 and v1.5). The ProvLab database contains data of diagnostic HIV serology for Northern Alberta from Feb 1998 to Feb 2002 and for the whole province from Mar 2002 to present. Information on two specific patient population groups was extracted from the database:

1) All infants born to HIV infected mothers from 1998 to 2006 who had QVL testing prior to 18 months of age, and
2) All persons with reactive HIV antibodies by EIA and neg/ind by WB from 1998 to 2005 who also had QVL performed within 150 days of their neg/ind WB. This population was further categorized as:

a) patients with risk history and/or clinical symptoms suggestive of acute HIV seroconversion
b) patients with no risk factors for HIV infection and suspected to have false reactive result by the screening EIA

Sensitivity and specificity of QVL was determined using serological diagnosis as a gold standard, and 95% confidence intervals were calculated using binomial distribution.

RESULTS AND DISCUSSION

The number of HIV screening EIA performed per year from Feb 1998 to 2005 and the percentage of indeterminate and positive EIA results are shown in Figure 2 and the percentage of EIA positive specimens that were confirmed as WB positive is shown in Figure 3.

For the study period, 130 patients had QVL performed < 150 days of their negative/indeterminate (neg/ind) WB (Table 1). Fifty-five patients had at least one detectable QVL; 46 were subsequently confirmed to be HIV infected by positive WB, 8 had multiple detectable QVL supporting an HIV diagnosis and one patient had only one specimen submitted for QVL and no follow-up serology. One of the patients who had a follow-up positive WB had a very low viral load set point with the first viral load tested as <50 copies/ml and a second viral load tested as 85 copies/ml. Overall, the median first detectable viral was 87,000 copies/ml (range: 85 to 2.3E7 copies/ml).

For the diagnosis of vertical transmission, QVL was performed on 176 HIV-exposed infants. Six infants had a detectable QVL with the median age of first detectable WB at 2 months and the median first detectable viral load at 4.3E5 copies/ml (280 to 1.7E6). For the 170 infants (male=96, 56.4%) with undetectable QVL, 131 (77.1%) had negative follow-up serology while the remainder either had no follow-up serology or had not reached 18 months of age. A total of 535 QVL test were performed for the 170 infants with undetectable QVL; 143 infants had 2 or more tests (median=3, range 1-6) with most of the specimens submitted at less than 6 months of age.

CONCLUSION

QVL is sensitive and specific for the diagnosis of HIV in HIV-exposed infants and suspect acute seroconverters. Our data support the use of QVL as a diagnostic test for HIV.

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