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ORIGINAL PAPER

Comparisons of New HIV Rapid Test Kit Performance

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Abstract
The development of rapid point-of-care tests for HIV infection has greatly reduced the problem of failure to return for test results. Test manufacturers are now developing test kits that can test for two or even three diseases at the same time, multiple-disease test kits. This study reports on the sensitivity and specificity of HIV tests when included on multi-disease test kits. 1029 participants were recruited from 2011 to 2014. HIV test kit sensitivities ranged from 91.1 to 100%, and the HIV test kit specificities from 99.5 to 100%. The two HIV kits which used oral fluid instead of blood performed well.

Keywords HIV testing · Point-of-care tests · Rapid tests

Resumen
El desarrollo de pruebas rápidas en el punto de atención (POC) para la infección del VIH ha reducido enormemente el problema de la falta de retorno por los resultados de las pruebas por parte del paciente. Los fabricantes de pruebas ya están desarrollando kits que pueden probar dos o incluso tres enfermedades al mismo tiempo, los llamados kits de prueba de enfermedades múltiples. Este estudio informa sobre la sensibilidad y especificidad de las pruebas de VIH cuando se incluyen en kits de pruebas de enfermedades múltiples. 1029 participantes fueron reclutados entre 2011 y 2014. Las sensibilidades del kit de prueba de VIH oscilaron entre 91.1% y 100%, en tanto que las especificidades estuvieron entre 99.5% y 100%. Los dos kits de VIH que usan fluido oral en lugar de sangre funcionaron bien.

Introduction

There have been several rapid-test kits used for point-of-care (POC) screening of antibodies to human immunodeficiency virus (HIV) and other sexually transmitted infections (STIs) that have been approved by the Food and Drug Administration (FDA) [1]. There are also some POC test kits for detection of antibodies to Hepatitis C virus (HCV) [2]. These devices have led to reductions in the time from specimen collection to test results [3]. This has resulted in much lower loss to follow-up of individuals who provide a specimen, but never return to receive their test results [4]. A further benefit of rapid tests is that they facilitate those who are positive to become involved in treatment sooner [5], resulting in fewer inpatient and outpatient hospital visits.

Of great clinical importance is the use of HIV rapid testing in the development and application of four different HIV testing algorithms, which are used to reduce time to HIV diagnosis (i.e. only one visit is necessary) while still ensuring a correct HIV diagnosis [6]. The first algorithm requires only a single rapid test and if the single HIV rapid test was positive, then the patient is referred to laboratory testing. The second and third algorithms require two different rapid tests that are done on kits from two different companies. There are different decisions that are made depending upon whether the two test kits agree or disagree, and for the third

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algorithm, whether one of the tests is done on oral fluid. The fourth algorithm uses at least two test kits, and if they are discrepant, then a third test using a kit from a third test manufacturer could be used as a tie-breaker [6].

The rapid-test kits that have already been approved by the FDA have been single-disease kits. However, test manufacturers have recently developed multiple-disease rapid tests that combine tests for various conditions into one device [7]. Some of these multiple-disease kits have been approved by other countries. Multiple-disease testing affords higher user convenience for optimized patient management. Additional advantages of multiple-disease testing include increased uptake of testing for other infections, such as syphilis and hepatitis, that may co-occur with HIV. The development of these new kits requires evaluation of their characteristics and how potential patients will respond to them.

The primary objective of the study was to compare the performance characteristics of rapid-test kits for HIV from several different manufacturers on both whole blood and oral fluid.

Methods

Materials

The following kits were evaluated in this study: Dual Path Platform (DPP®) HIV 1/2 Screen Assay Oral Test (HIV 1/2 Screen Oral), DPP® HIV-HCV Screen Assay Oral Test (HIV-HCV Screen Oral), Determine HIV 1/2 Ag/Ab Combo (HIV 1/2 Combo), DPP® HIV 1/2 Screen Assay Blood Test (HIV 1/2 Screen Blood), DPP® HIV-HCV Screen Assay Blood Test (HIV-HCV Screen Blood), DPP® HIV-Syphilis Screen Assay Blood Test (HIV-Syphilis Screen Blood), DPP® HIV-HCV-Syphilis Screen Assay Blood Test (HIV-HCV-Syphilis Blood), Multiplo Rapid HIV/HCV Antibody Test (HIV/HCV Ab), Multiplo Rapid HIV/HCV/HBV Antibody Test (HIV/HCV/HBV), INSTI™ HIV-1 Antibody Test (HIV-1). The DPP® test kits were manufactured by CHEMBIO Diagnostic Systems, Inc., Medford, NY. The Multiplo kits were manufactured by MedMira Inc., Halifax, NS, Canada. The INSTI™ kits were manufactured by bioLytical laboratories, Richmond, BC, Canada. For tests with combinations of HIV with another disease, this paper only reports on the HIV results.

Participants

Data for this study were collected from 26 May 2011 to 25 June 2014 from 1029 participants who were recruited at the Center for Behavioral Research and Services (CBRS), which is an off-campus research center of California State University, Long Beach (CSULB). In addition to conducting research, CBRS provides free HIV and STI testing to the community. Participants were compensated $20 at baseline and $50 when they came back for the results of the laboratory tests. Most participants were recruited when they came in to receive the free HIV/STI testing. Some participants responded to flyers distributed to the HIV Planning Group of the City of Long Beach. Eligible participants were: 15 years of age and older, had not participated previously, and reported being in a behavioral risk group. The IRB approved allowing 15-year old participants into the study, which is consistent with California state law. Behavioral risk groups were defined as follows: [1] Persons Who Inject Drugs (PWIDs) with verified track marks (i.e. visible signs of injection) [8]; [2] women who reported at least 2 male partners in the last 2 years or engaging in anal intercourse, sex trading, or sex with a man who has sex with men (MSM), a PWID or an HIV-positive man; [3] MSM and men who have sex with men and women (MSMW); and [4] transgender individuals. Both transgender men and transgender women were included in the sample although most of the transgender participants were transgender women. The definitions of these risk groups were based on guidelines from the Los Angeles County Department of Public Health (LACDPH). Participants were not excluded based on prior infection history.

Procedures

When an eligible participant agreed to participate, they gave written informed consent under a protocol approved by the CSULB Institutional Review Board (IRB).

All testing was provided free of charge. A California State licensed phlebotomist drew a venous blood sample by standard laboratory practices for the POC tests, as well as the reference confirmatory tests [9]. Only one blood draw was necessary to perform all of the blood tests. The participant had their blood drawn and then waited in the phlebotomy laboratory for the test results. The entire procedure was completed in 1 day with the client receiving the results of their POC tests at the initial visit. Every test that had been provided by the manufacturers was completed on the whole blood specimen or the oral fluid specimen of each participant. However, there was variation in sample size by test because all experimental test kits were not always available. Reference results were performed and were available 2 weeks after the initial visit, when the participant returned for the reference results. The effect of this meant that the phlebotomists were blind to the reference results during the initial POC session. The test kits were stored in a temperature-controlled setting with the temperature being both monitored and recorded. The temperature was set to the manufacturer's recommendations. The test procedures were based on the manufacturer's venipuncture whole-blood or oral fluid instructions. The

phlebotomists were trained in person onsite in Long Beach by Chembio staff for the Chembio tests, via videoconference by MedMira staff on the MedMira tests, and in person onsite in Long Beach by bioLytical staff on the INSTI test.

Statistical Methods

Sensitivity and specificity of the test kit performances were simple proportions, with exact binomial confidence intervals being constructed by inverting the equal-tailed test based on the binomial distribution [10]. All analyses were done using SAS 9.4(TS1M2) on a virtual windows server 2008 R2.

Results

The participants were evenly divided between men and women. The largest group (39%) was Black (not of Hispanic origin), followed by White (not of Hispanic origin) at 29%, then Hispanic/Latino at 20%. Most (65%) of the participants had graduated from high school, although the second largest group (25%) had less than a high school education. There was a large proportion (35%) who were either college graduates or who had some college education. Most participants were not homeless, although a large proportion self-reported they were homeless (42%). Mean age was 40.16 years (SD = 17.62).

Table 1 shows the sensitivities and specificities with exact confidence intervals of the experimental POC tests used in this study. The highest sensitivities were for the Chembio HIV 1/2 blood, and the Chembio HIV/HCV/Syphilis on the HIV antibody only. The lowest sensitivity was on the MedMira HIV/HCV on the HIV antibody only. The two oral tests, Chembio HIV 1/2 Oral and Chembio HIV/HCV Oral—HIV Ab, performed well at 97.2 and 97.9% sensitivity. The sensitivities and specificities only differed slightly between tests and confidence intervals overlap. Therefore, any differences between tests on these performance characteristics may not be statistically significant.

Discussion

In the current paper, we report on the characteristics of single HIV-only test kits, HIV and syphilis test kits, HCV and HIV kits, and one kit, by Chembio, that is a three-infection multiple-disease test: HIV, HCV, and syphilis. The three-infection test kit in our study had 100% sensitivity and 99.9% specificity for detection of antibodies to HIV, which demonstrates that the HIV portion of the test kit performed very well. A second three-infection kit, by MedMira included HIV, HCV, and HBV. The HIV portion of this kit had average sensitivity when compared to the other tests in this study, but the specificity was 100%. We have been unable to find any other reports in the literature on the performance of the three-infection test kits.

Two of our test kits were designed to be used with oral fluid. These kits tested for HIV only or HIV with HCV. The Chembio HIV 1/2 Oral had lower sensitivity at 97.2% than the comparable Chembio HIV 1/2 Blood at 100%, but the specificities of the two kits were identical at 99.7%. The Chembio HIV/HCV Oral—HIV Ab sensitivity at 97.9% was almost equal to the Chembio HIV/HCV Blood—HIV Ab at 98.0%. The specificity of the oral kit at 99.5% was only slightly higher than the blood kit at 99.4%. One of the issues that has been raised about oral fluid HIV tests is that they may have lower sensitivity and lower positive predictive value than tests performed on blood [11–14]. Furthermore, some client populations perceive blood testing to be more accurate than oral fluid testing [15, 16]. Among the test kits that were evaluated in the current study, the test kits for oral fluid testing ranked 3rd and 4th for sensitivity among the 10 kits evaluated. This would suggest that oral fluid testing was not inferior to blood testing in our study. This finding is especially important given the rapid test algorithm 3, which specifically uses HIV oral fluid testing.

The use of POC testing for HIV infection has been shown to be effective in a variety of settings in the US

Table 1 Experimental point-of-care tests compared to laboratory reference test for human immunodeficiency virus

Test name	Sensitivity (%)	Exact 95% CI	Specificity (%)	Exact 95% CI
bioLytical HIV-1	95.5	87.3–99.1	100	99.6–100
MedMira HIV/HCV—HIV	91.1	80.4–97.0	100	99.6–100
MedMira HIV/HCV/HBV—HIV	94.0	83.5–98.8	100	99.5–100
Chembio HIV 1/2 Blood	100	91.6–100	99.7	99.0–99.9
Chembio HIV/HCV Blood—HIV Ab	98.0	89.6–99.9	99.4	98.6–99.8
Chembio HIV/Syphilis—HIV Ab	97.0	89.5–99.6	99.8	99.2–99.9
Chembio HIV/HCV/Syphilis—HIV Ab	100	94.0–100	99.9	99.4–100
Determine HIV-1/2—HIV Ab	94.6	84.9–98.9	99.9	99.2–100
Chembio HIV ½ Oral	97.2	85.5–99.9	99.7	98.9–99.9
Chembio HIV/HCV Oral—HIV Ab	97.9	88.2–99.9	99.5	98.9–99.9

including drug treatment programs [3, 17], family planning clinics [18], and mobile van clinics [4] among others. There are major advantages of using rapid tests instead of the standard tests, and the manufacturers have responded to this by manufacturing POC test kits that test for more than one infection from a single fingerstick or venipuncture. It would seem to be a very efficient way of testing in busy clinics and has been advocated for use in substance abuse treatment programs. Our results support the use of multiple-disease test kits as sensitive and specific rapid tests for HIV in these settings.

Limitations

The major limitation is that our results are generalizable only to US high-risk populations.

Conclusions

The contributions to new knowledge that this paper contains include: 1. The first report of triple-infection test kits, 2. Data indicating that the oral fluid test kits performed acceptably. This study is the first to report on the sensitivity and specificity of the HIV-test portion of triple-infection test kits. Multiple-disease test kits offer the convenience of obtaining results from a single specimen thus improving the ability to gain information to provide appropriate education and follow-up for patients. The knowledge gained from this study can assist health care providers and testing sites in developing protocols for their use among high-risk clients. Second, the data from this study indicate that the oral fluid test kits performed acceptably, and this method is a valid option for testing. As previous studies have reported, some patients have been skeptical about the reliability of oral fluid tests [11] and some studies have found that oral fluid tests do not perform as well as blood tests [12]. Oral fluid testing provides a safer means of collecting specimens for testing, as the collection of blood increases the safety risk of possible exposure [19]. In addition, patients who may fear the pain of blood draws may choose this option more frequently, thus increasing overall testing participation [15, 20].

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Compliance with Ethical Standards

Conflicts of interest All authors declare that they have no conflicts of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study under a protocol and using an Informed Consent Form approved by the California State University, Long Beach, Institutional Review Board.

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