3091

Rapid HIV-1 Diagnostic Algorithms for Use in HIV Infection Screening

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Abstract:

Background:
Recent world events underscore the need for Rapid HIV screening techniques, because of both acute demands for blood products that exceed the screened supply and exposures to blood of unknown HIV status during rescue efforts. Clinics that support prevention and counseling also frequently lack the testing capacity to quickly provide HIV screening results. Existing HIV serodiagnostic techniques (EIA/Western blot) are too cumbersome to rapidly screen for HIV infection.

Methods:
We compared the performance of an algorithm using three newer, unlicensed HIV Rapid Test devices—Hema-Strip (H)(ChemBio Diagnostic Systems), Multispot (M)(Bio-Rad Laboratories), and OraQuick (O)(OraSure Technologies)--with results of conventional EIA/Western blot. These 3 devices were selected based on their previously demonstrated high sensitivity, specificity, and ease of use. We conducted a retrospective, masked study of 440 archived serum specimens (416 HIV-1 negative and 24 HIV-1 positive as determined by EIA/Western blot). All sera were screened in parallel with three combinations of two Rapid devices used together (MO, MH, OH). Concordantly nonreactive samples were coded as nonreactive while concordantly reactive or discordant samples were tested with the third device. Final results were based on "best of three" Rapid Test results for all three combinations (MO-H, MH-O, OH-M).

Results:
All three Rapid Test combinations yielded 100% sensitivity and specificity compared with EIA/Western blot. Thirteen samples with discordant results were correctly resolved by the algorithm design (best of three).

Conclusions:
The accuracy of combinations of HIV Rapid Tests used in a parallel algorithm is comparable to that of EIA/Western blot. These Rapid devices could be used in civil-military emergencies or in prevention and counseling clinics to provide rapid and accurate HIV diagnosis.

Introduction:

The need to have accurate Rapid HIV diagnostic tests is called to attention by situations such as civil-military emergencies that deplete blood bank supplies and require emergency use of unscreened blood, providers that have been exposed to blood during routine patient care, and walk-in clinics serving resource-poor communities. Standard diagnostic testing (Enzyme Immunoassay method [EIA] followed by a Western blot Test to confirm HIV positivity) is ineffective and cumbersome when accurate HIV results are needed within minutes. The Department of Molecular Diagnostics and Pathogenesis (DMDP), Division of Retrovirology, Walter Reed Army Institute of Research (WRAIR), Maryland, United States, has the mission to evaluate and assure quality of HIV diagnostic devices for the United States Army. DMDP has the task to fill a current void in quickly determining HIV status because of the inability to deploy standard HIV Testing. The typical standard algorithm, screens blood by performing a single EIA test. Reactive EIA samples are then typically confirmed in duplicate parallel testing also with an EIA method. Those still reactive are confirmed with a Western blot test. A single Rapid Test is therefore inadequate as a sole screening device and cannot duplicate the robust standard algorithms. The goal is to provide accurate diagnostic algorithms based solely on HIV Rapid Testing that mimic current standard algorithms (parallel and serial testing). With diagnostic algorithms based solely on HIV Rapid Tests, physicians exposed to blood in fixed medical treatment facilities, deployable/walk-in/field research clinics, emergency care workers, and soldiers on the battlefield are a few examples of those who will benefit from having quick but accurate ways to make an HIV diagnosis and prevent infection. Finally, there is no other technology currently or in the near future that can produce HIV results in the expedient manner that HIV Rapid devices provide.

Methods:

An extensive descriptive testing of several HIV Rapid Tests in DMDP, WRAIR, led to down selection of the following three Rapid Tests for use in this algorithm testing:

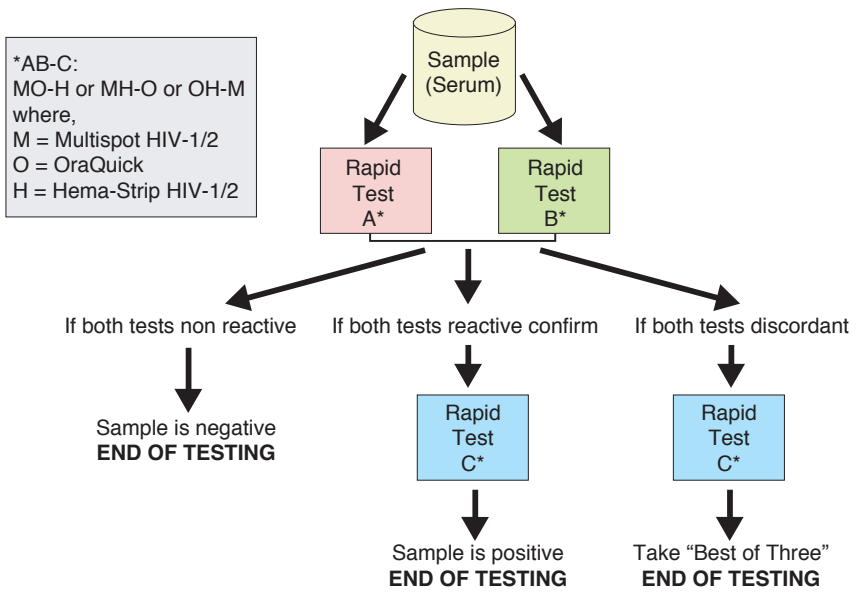
1) Multispot® HIV-1/2 (M), Bio-Rad Laboratories Inc., Hercules, CA.
2) OraQuick® HIV-1, (O), OraSure Technologies, Bethlehem, PA.
3) Hema-Strip® HIV-1/2 (H), ChemBio Diagnostic Systems (Saliva Diagnostic Systems), Medford, NY.

Samples:
Testing was performed on a pedigreed serum panel of 440 samples drawn from the U.S. population. This panel consisted of 416 EIA negative and 24 EIA/Western blot reactive specimens. Operators were blinded.

Testing:
Testing was performed on a parallel study design. Two Rapid Tests from different manufacturers were used in the initial screen. Concordant non-reactive testing was coded as HIV negative. Concordant reactive and discordant tests were subjected to a confirmatory test, which acted as the discriminator. For samples that were concordant reactive, if the confirmatory test was also reactive, the sample was coded as HIV negative. Final reactivity was "best of three" for those samples that were initially discordant (Table 1).

TABLE 1

Design of HIV-1 Diagnostic Algorithm Using 3 Rapid Tests in Parallel Mode



Results:

Accuracy was 100%. There were 0 false positives and 0 false negative final interpretation determinations with any two test combinations used up front (MO, MH, OH) to screen and the third test used as a confirmatory test (H, O, M respectively). Thirteen samples with discordant results were correctly resolved by the algorithm design (best of three). Multispot had no false results, OraQuick had one false negative result and Hema-Strip had two false positive and ten false negative results likely accruing to test manufacturing issues (Table 2). This small-scale parallel algorithm study will be confirmed with a larger panel of serum specimens with a higher sero-prevalence. This initiative, the confirmation of the small-scale parallel algorithm with a larger panel, is in accordance with DMDPs quest to provide HIV diagnostic algorithms the accuracy of which is equal to that of standard algorithms, and that can be used in settings where traditional testing is not feasible.

TABLE 2

Parallel HIV-1 Diagnosic Algorithm Results Using Rapid Tests

Panel n=440, 416 Negatives, 24 Positives Serum Samples

1st Algorithm	Quantity	Oraquick	Hemastrip	Multispot	Rapid Algorithm Final Interpretation	EIA/Wb Result	Correct?
	415	N	N		N	N	Yes
	24	R	R	R	R	R	Yes
	1	N	*R*	N	N	N	Yes
	440						
2nd Algorithm		**Multispot**	**Oraquick**	**Hemastrip**			
	416	N	N		N	N	Yes
	20	R	R	R	R	R	Yes
	3	R	R	*N*	R	R	Yes
	1	R	*N*	R	R	R	Yes
	440						
3rd Algorithm		**Hemastrip**	**Multispot**	**Oraquick**			
	413	N	N		N	N	Yes
	17	R	R	R	R	R	Yes
	7	*N*	R	R	R	R	Yes
	1	*R*	N	N	N	N	Yes
	2	No Sample					N/A
	440						

N = Non-Reactive, R = Reactive

Conclusions:

1. The accuracy of combinations of different HIV Rapid Tests used in a parallel algorithm is comparable to that of EIA/Western blot.
2. All three combinations, MO, MH, OH up front to screen and the third test used as a confirmatory/ discriminatory test (H, O, M respectively) showed equal sensitivity and specificity.
3. These Rapid devices could be used in civil-military emergencies or in prevention and counseling clinics to provide rapid and accurate HIV diagnosis since they are deployable, durable and have similar sample requirements.