Journal of Associated Medical Sciences 2020; 53 (1): 37-41

JAMS
Journal of Associated Medical Sciences

Thai-Journal Citation Index Centre (TCI) & ASEAN Citation Index (ACI)

Journal of Associated Medical Sciences

Journal homepage: https://www.tci-thaijo.org/index.php/bulletinAMS/index

Performance of the Determine HIV-1/2 Combo rapid test for detection of acute/early HIV-1 infection

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ARTICLE INFO

Article history:
Received 18 July 2019
Accepted as revised 2 December 2019
Available online 6 December 2019

Keywords:
HIV, acute infection, Determine HIV Combo

ABSTRACT

Background: New guideline from CDC for HIV testing recommended the 4th generation assay as the primary screening test to avoid late diagnosis and to shorten the window period. The first point-of-care HIV assay named Determine HIV Combo was used in high prevalence setting. The capacity of this assay detects HIV infection more rapid than IgM/IgG laboratory-based assays. Sensitivity of HIV-1 p24 antigen (Ag) detection was lower than those of laboratory-based 4th generation assays. However, the capacity to detect acute/early HIV-1 infection in high risk subjects is needed to evaluate.

Objectives: To evaluate the performance of Determine HIV Combo in seroconversion plasma specimens of acute/early HIV-1 patient.

Materials and methods: Twelve seroconversion plasma specimens from 5 acute/early patients were diagnosed by Elecsys HIV Ag, 4th generation ECLIA (Elecsys HIV Combi PT) and supplemented by NAAT (viral load) to evaluate the performance of Determine HIV Combo sensitivity. McNemar's exact test was applied to compare the difference in reactivity during acute/early infection between tests. Specificity was evaluated with 96 HIV-1 negative plasma specimens.

Results: Seroconversion sensitivity of Determine HIV Combo was 91.67% (11/12, p=0.32) compared to 4th generation ECLIA and Elecsys HIV Ag results. There were 3 discordant results with 3rd generation HIV POCT (p=0.14). The reactivity of HIV p24 Ag detection which compared to Elecsys HIV Ag, were 41.67% (5/12, p=0.0021). Determine HIV Combo had 8.33% (1/12) false negative result and 100% specificity. The first positive HIV p24 Ag and antibody results from Determine HIV Combo were found on 14 days and 21 days, respectively.

Conclusion: Determine HIV Combo provides poorer antigen sensitivity compared to HIV Ag and viral load performance, p24 Ag. However, Determine HIV Combo can detect acute/early HIV-1 infection at more than 13 days after sexual exposure. It can improve HIV rapid test to decrease the window period, expand access to HIV testing and prevent HIV transmission.

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doi: 10.14456/jams.2020.5
E-ISSN: 2539-6056

Introduction

The 4th generation or Combo HIV-1/2 antigen/antibody (Ag/Ab) immunoassays was used as the primary screening test in the algorithm recommended by the Centers for Disease Control[1] and combination assays to detect HIV-1 p24 antigen has affected to reduce diagnostic window period and improve detection of HIV-1 infections when compare to the 3rd generation (Ab only) assays.[2-4] Early diagnosis and early treatment of acute HIV infection by HIV combo tests were accepted to diagnose HIV-infected individuals for early antiretroviral treatment, which can reduce transmission, improve quality of life and health outcomes for infected persons and their partners.[5] USA FDA approved seven HIV Ag/Ab assays for use in the U.S. and one of those is Determine HIV Combo rapid test which using fingerstick blood, venous whole blood, serum and plasma. The results can be read in 20 minutes. It was commonly used in non-laboratory settings and can differentiate HIV-1 p24 Ag from HIV-1/2 Ab reactivity. Recently, Thailand-FDA has approved another new Alere HIV Combo assay in August, 2018.[6] Increasing early HIV diagnosis and connecting to care in HIV care units is a strategy to reduce HIV transmission and target the next set of goals to end AIDS by 2030 (95-95-95 for treatment: 95% of people living with HIV knowing their HIV status; 95% of people who know their status on treatment; and 95% of people on treatment with suppressed viral loads). However, the potential of Determine HIV Combo for detection of acute/early HIV infection is needed for further evaluation.

Materials and methods

Study designs

HIV-1 specimens

Plasma HIV diagnosis testing in high risk population (men who have sex with men: MSM, transgender: TG and Female sex worker: FSW) was performed. The samples were recruited from Reach-Recruit-Test-Treat- Retain (RRTTR) program, AIDS ZERO Plan of Thailand at District drop in center (DIC) and three mobile HIV-testing services including Bangkok, Chon Buri, and Phuket Province during January-June 2015. All participants were asked for given writing or verbal consent received counseling before HIV testing. The study was approved by the Department of Diseases Control, Ministry of Public Health, Thailand. Among 529 participants, five acute/early HIV-1 infection was characterized including four MSM and one FSW. Twelve serial EDTA plasma specimens with HIV Ag positive were studied by Elecsys HIV Ag which were used to evaluate the performance of Determine HIV Combo assay for its seroconversion sensitivity. Specificity of this assay was compared to 96 HIV-1 negative plasma specimens tested by Elecsys HIV Combi PT (4th generation assay).

HIV assays

The 4th generation rapid test, Determine HIV Combo assay (Determine HIV-1/2 Ag/Ab Combo, Alere Inc., Japan) was tested in 12 acute/early HIV-1 seroconversion plasma specimen to compare sensitivity with 4th generation assay (Elecsys HIV Combi PT, Roche Diagnostics GMBH, Germany) and HIV Ag assay (Elecsys HIV Ag, Roche diagnostics, GMBH, Germany). Days after sexual exposure and temporal trend of laboratory tests were compared with 3rd generation HIV POCTs, including Alere Determine HIV -1/2 (Inverness Medical Japan Co., Ltd., Japan), DoubleCheckGold Ultra HIV1&2 (Organics Ltd., Israel) and SD Bioline HIV-1/2 (Standard Diagnostics, Inc. Korea). Nucleic Acid Amplification Test (NAAT) viral load (Cobas AmpliPrep/ CobasTagMan HIV-1 test, version 2.0, Roche Molecular Systems, Inc., USA) was used to confirm acute/early infection at the first visit. All tests were performed by the protocol recommended by manufacturers.

Analysis of assay performance in acute/early HIV-1 infection

Seroconversion sensitivity of Determine HIV Combo assay was calculated from the positive test results versus the days before the 4th generation assay (Elecsys HIV Combi PT), HIV Ag assay (Elecsys HIV Ag) and/or NAAT viral load test (Cobas AmpliPrep/ CobasTagMan HIV-1 test) became positive in 12 plasma specimens of seroconverts. McNemar's exact test was used to compare the difference in reactivity during acute/early infection between tests. Specificity was calculated by the results of 96 HIV-1 negative specimens.

Results

Reactivity of the Determine HIV Combo was analyzed and compared to 4th generation assays in 12 seroconversion specimens. The sensitivity of Determine HIV Combo was 91.67% (11/12), compared to 4th generation ECLIA, Elecsys HIV Combi PT and Elecsys HIV Ag (p=0.32). Of the 12 seroconversion acute/early HIV-1 specimens tested, Determine HIV Combo gave 41.67% (5/12) reactive for p24 Ag (Ag+/Ab+, Ag+/Ab-), whereas 25% (3/12) were reactive for p24 Ag only. Of 66.67% (8/12) were found HIV Ab band, and 6 of them (50%) were reactive for antibody only. There was one non-reactive in both Ag and Ab by Determine HIV Combo. There were 3 specimens showing discordant results with 3rd generation HIV POCT. The HIV p24 Ag reactivity of Determine HIV Combo compared to Elecsys HIV Ag, was 41.67% (5/12, p=0.0021). The specificity of Determine HIV Combo compared with 4th generation ECLIA, Elecsys HIV Combi PT was 100% (Fig. 1). Determine HIV Combo detected the first Ag p24 and antibody positive results after sexual exposure at 14 days and 21 days, respectively (Table 1). HIV viral load of all participants at the first visit were 117,800 - >10,000,000 copies/ml.

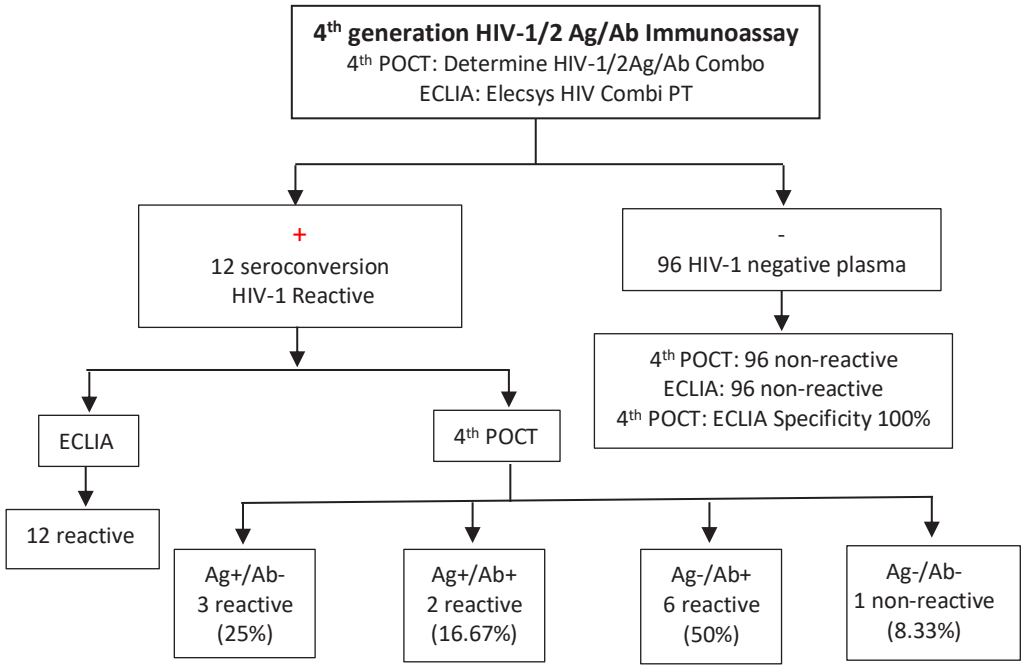

Figure 1. *Laboratory HIV testing algorithm for seroconversion plasma specimens in this study. POCT: Point of care Testing, ECLIA; Electrochemiluminescence Immunoassay, Ag: antigen, Ab: antibody.*

Table 1 Days after exposure and temporal trend of HIV testing in 12 seroconversion specimens.

No.	Risk group	Days after sexual exposure	4th generation			3rd generation POCT			Elecsys HIV Ag (S/CO) Positive>0.9	HIV RNA (copies/ml)
			Determine HIV Combo		Elecsys HIV Combi PT (S/CO) Positive>1	Alere Determine HIV-1/2 Ab	Double CheckGold Ultra HIV1&2	SD Bioline HIV-1/2		
			Ag	Ab						
1	MSM	14	+	-	+(111.3)	-	-	-	+* wp (4.9)	>10,000,000
2		19	+(pale)	-	+(338.4)	-	-	-	+(11.9)	Not done
3		21	-	+(pale)	+(443.2)	+(pale)	+(pale)	+(Pale)	+ (8.3)	Not done
4	MSM	22	+	+	+(504.4)	+	+(pale)	+(pale)	+*(8.7)	474,000
5		32	-	+	+(646.8)	+	+	+	+(11.1)	Not done
6	MSM	22	-	+	+(431.2)	+	+	+	+*(9.6)	291,000
7		27	-	+	+(332.2)	+	+	+	+wp(5.8)	Not done
8		35	-	+	+(713.8)	+	+	+	+wp(3.8)	Not done
9	MSM	25	+	+	+(89.4)	+ (pale)	+ (pale)	+(pale)	+*(7.3)	380,000
10		33	-	+	+(423.0)	+	+	+	+wp(5.4)	Not done
11	FSW	13	-	-	+(59.9)	-	-	-	+*(5.7)	117,800
12		16	+(pale)	-	+(89.8)	-	-	-	+(9.1)	7,480,000

+ (pale): reactive with pale color of band, wp= weakly positive, + : Elecsys HIV Ag positive (specimen no.1,4,6,9 and 11) confirmed HIV Ag positive by HIV Ag neutralization test.*

Discussion

Determine HIV combo is 4th generation rapid test device capable of determining 26 HIV-1 p24 antigen and both of IgM & IgG HIV-1/2 antibodies in serum, plasma and whole blood. Sensitivity and specificity of Determine HIV Combo according to this study were 91.67% and 100%, respectively compared to 4th generation ECLIA, Elecsys HIV Combi PT. The sensitivity shown in package insert are 99.9% and 100%, using all types of specimens for low risk subjects and ranges from 98.9% (serum) to 99.7% (whole blood) for high risk subjects.[7] Previously report and our finding indicated that antibody sensitivity is comparable to package insert for high risk subjects, but the antigen component is not detected in most acute/early HIV-1 infections revealed by laboratory 4th generation assays.[8-9] Like in our cases, performance of Determine HIV Combo was evaluated on seroconversion plasma specimens from patients with laboratory algorithm defined acute/early HIV-1 infection. Determine HIV Combo failed to detect early HIV-1 infection in 8.33% (1/12). The studies of Faraoni and Cohen also showed that Determine HIV Combo (detecting both IgM & IgG antibodies and p24 antigen) had been found to be less accurate in identifying the acute phase of HIV infection.[10-11] Result from the present study evidenced that time to reactivity for Determine HIV Combo is 7 days earlier than 3rd generation assays (POCT) in one MSM subject (Table 1). This was the same as studies of CDC that compared all US FDA-approved tests in the same plasma specimens collected from individuals during seroconversion. It showed that Determine HIV Combo can detect HIV infection 1-2 weeks before other 3rd generation rapid tests, and 3-4 days after 4th generation assays.[12] The previous data from Delaney and colleagues studied on plasma specimens showed that the median time to reactivity of Determine HIV Combo is 2.3-3.5 days faster than laboratory-based 3rd generation assays.[13] We found 3 plasma specimens which were detected by Determine HIV Combo, meanwhile 3rd generation assays (POCT) could not detect. There were 2 cases of acute HIV-1 infections which had high viral load and HIV Ag positive. One (MSM) of two subjects had viral load >10,000,000 copies/ml and a positive Determine HIV Combo result at 14 days after sexual exposure. In contrast, the other (FSW) failed to diagnosis with Determine HIV Combo and had HIV viral load 117,800 copies/mL at 13 days after sexual exposure. While 3 days later, HIV viral load reached to 7,480,000 copies/mL and Determine HIV Combo was positive Ag band (Table 1). This revealed that early diagnosis of HIV infected cases and early treatment can decrease the spread of HIV to their partners. Our finding revealed performance of the Determine HIV Combo test can be detected the infection 14 days after sexual exposure, which is 7 days faster than 3rd generation POCT. (Table 1) Thus, active HIV case finding in high risk, hard to reach populations, such as MSM and FSW, need non-laboratory based HIV testing in field, non-instrument based and rapid turnaround time.[14] The 4th generation POCT assay seems to be appropriated for the first HIV screening test after sexual exposure more than 13 days. Therefore, when less than 14 days, when reporting negative results by Determine HIV Combo, high risk population who have sexual risk behavior should be performed supplement tests such as HIV Ag assay, laboratory-based 4th generation HIV tests and/or HIV RNA assay because they can migrate and spread transmission to others.

Conflicts of interests

No conflict of interest

Acknowledgements

We thank the owner of plasma specimens, NGO staffs and HIV care center.

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