Expert Review of Molecular Diagnostics

ISSN: 1473-7159 (Print) 1744-8352 (Online) Journal homepage: informahealthcare.com/journals/iero20

Oral fluid-based rapid HIV testing: issues, challenges and research directions

Nitika Pant Pai

To cite this article: Nitika Pant Pai (2007) Oral fluid-based rapid HIV testing: issues, challenges and research directions, Expert Review of Molecular Diagnostics, 7:4, 325-328, DOI: 10.1586/14737159.7.4.325

To link to this article: https://doi.org/10.1586/14737159.7.4.325

Nitika Pant Pai
McGill University Health Centre, Division of Infectious Diseases & Immunodeficiency Service, Montreal Chest Institute, 3650 St Urbain Street, Montreal, Quebec, H2X 2P4, Canada
Tel.: +1 514 889 9604
nitika.pai@mail.mcgill.ca

Oral fluid–based rapid HIV testing: issues, challenges and research directions

'… it is hoped that detection of (HIV-infected) individuals with high-quality, rapid, accurate point-of-care oral HIV tests will enable provision of early, timely and highly effective ART or expedite triage to care and prevention.'

Expert Rev. Mol. Diagn. 7(4), 325–328 (2007)

Global efforts to scale-up HIV testing

The HIV pandemic continues to take a heavy toll on developing countries, where the Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates suggest that less than one in ten people are aware of their HIV serostatus [1,2]. In an effort to scale-up detection of HIV and enhance prevention and treatment programs, agencies such as the UNAIDS and WHO suggest a shift from the current client-initiated HIV testing approach to a provider-initiated testing and counseling (PITC) [1]. With the PITC approach, healthcare professionals actively encourage clients to get tested for HIV, thereby enabling treatment, care and prevention services to be provided. It is hoped that PITC will help in the detection of individuals with undiagnosed HIV and improve the uptake of antiretroviral treatment (ART) services now available in many resource constrained settings [1,2].

'To expedite screening and accurately diagnose HIV infection, rapid point-of-care HIV tests have been a breakthrough of sorts.'

By contrast, in resource-rich settings, such as the USA, the Centers for Disease Control and Prevention (CDC) estimates that approximately 250,000–312,000 individuals are unaware of and living with undiagnosed HIV infection [3]. In addition, approximately 40% of adults chose to get tested only in the late stages of infection, which increases morbidity as well as healthcare costs [3]. The CDC recently published revised guidelines on testing in order to increase early detection in undiagnosed individuals and patients who present late, establish linkages to treatment and care, and reduce the stigma associated with HIV testing [3]. These guidelines recommend routine opt-out testing of all individuals (i.e., adolescents, pregnant women and adults between 13–64 years of age), and does not require pretest counseling or informed consent [3]. Thus, agencies such as the UNAIDS, WHO and CDC are making concerted efforts to scale-up HIV testing and make testing accessible and user-friendly.

Rapid point-of-care HIV tests & use of nonconventional specimens

To expedite screening and accurately diagnose HIV infection, rapid point-of-care HIV tests have been a breakthrough of sorts. Although, the majority of these rapid tests utilize whole blood, plasma and finger stick blood specimens, a few tests employ nonconventional specimens, such as saliva, oral mucosal fluid and urine [4,5]. Oral fluid-based rapid tests have potential advantages over blood-based rapid tests because of their convenience, noninvasiveness, ease of specimen collection, cultural acceptance, high accuracy and rapidity [4,6–8].

  ISSN 1473-7159

Although salivary and oral fluid-based tests have been in development for the past 20 years, it is only recently that oral fluid-based, rapid point-of-care tests have increased in popularity [5]. Oral fluid tests are based on a salivary component, the oral mucosal transudate or crevicular fluid, an interstitial transudate rich in IgG antibodies, used for diagnosing HIV infection [4,5,9]. Currently, only two commercial oral fluid-based rapid tests exist, with variants sold under different names [4,6,8,10]:

- OraQuick® Advance (OraSure Technologies Inc., PA, USA; a US FDA-approved, Clinical Laboratory Improvement Amendments-waived test) and OraQuick RAPID HIV1/2 test (available in developing countries)
- Calypte Vanguard HIV® (Calypte Biomedical Corp., OR, USA) and Calypte Aware® HIV1/2 is awaiting FDA approval

All these rapid point-of-care tests utilize oral mucosal fluid, and test results are available in less than 30 min [5,11,12].

Since the emergence of salivary and oral fluid tests nearly two decades ago, over 60 studies on conventional and rapid point-of-care oral fluid tests have been conducted in various settings worldwide (>90 studies if salivary tests are also counted). These studies have evaluated various outcomes, such as diagnostic accuracy, client preference, acceptability, uptake and cost- and time-effectiveness [13–17]. It is now an established fact that diagnostic accuracy of oral rapid point-of-care tests is high and that their test results are consistent across developed and developing countries [7,13,18]. However, although accuracy is very high, oral fluid test results are considered preliminary. Therefore, the results of oral fluid tests require confirmatory testing with conventional tests, such as ELISA and/or western blot [12]. The growing use of oral fluid HIV testing has raised certain issues and challenges, and these are discussed later.

'… diagnostic accuracy of oral rapid point-of-care tests is high and … their test results are consistent across developed and developing countries. However, … oral fluid test results are considered preliminary.'

Concerns regarding nonreactive, false-positive & false-negative test results

As with any rapid point-of-care test, there is a possibility of false-positive, false-negative or nonreactive results with oral fluid tests. For example, in 2005, there were reports of false-positive results with the oral OraQuick test from selected clinics in New York city and San Francisco in the USA [18]. However, subsequent investigations by the CDC were unable to clarify whether the quality of kits or inadequate quality control was responsible for the false-positive results [7,18]. By contrast, more recently, a study from India showed 100% sensitivity and specificity of the oral fluid-based OraQuick RAPID HIV1/2 test, demonstrating excellent performance of oral fluid testing even in a rural setting in India [13]. Thus, it is unclear why some studies report higher than usual rates of false-positive results.

False-negative test results may occur if testing is performed after ART is initiated or in acute HIV infection, where seroconversion has not occurred [15]. A nonreactive result in a recently exposed individual is another possibility; therefore, repeat testing of such high-risk individuals is recommended. Also, certain medical conditions may produce nonreactive results, such as IgG gammopathy, multiparity, rheumatoid arthritis, hepatitis, multiple myeloma, syphilis and lupus. Furthermore, certain substances may interfere with test performance, such as heparin, bacterial contamination, sodium citrate and elevated bilirubin [19].

To reduce erroneous results, quality assurance and quality control procedures laid down by the CDC should be met [101]. These include maintaining kits at the recommended temperature, maintaining temperature logs, running controls at regular intervals and performing external and internal control checks [19]. In addition, healthcare professionals must avoid using kits beyond the expiration date and discard poorly performing lots of kits. Overall, users of oral fluid tests must anticipate errors in test performance and carefully follow manufacturers' instructions and the CDC recommended guidelines on rapid HIV testing [101]. Furthermore, even if accuracy is high, predictive values of any test depend on disease prevalence and can vary across populations. This often ignored fact must be kept in mind while interpreting results of any test in any setting.

Cultural acceptance of oral fluid HIV testing

It is well known that blood specimen collection is a sensitive issue in some countries and racial/ethnic groups. For example, rural Indians do not like to give blood specimens because they perceive it will further worsen their health or make them weaker. A recent study in rural India found high preference for oral fluid vis-à-vis blood-based finger stick HIV testing [13]. This study suggests that, in certain settings, non-invasive specimens, such as oral fluids and urine, should be further studied owing to their potentially higher acceptance and greater feasibility even for large-scale population surveys.

Populations where oral fluid HIV testing can have an impact

Because oral fluid HIV tests are accurate, feasible, noninvasive and culturally acceptable, they have the potential to make an impact in several high-risk, vulnerable populations. For example, oral fluid tests can be used in the labor room and emergency room settings in both developed and developing countries to expedite provision of interventions that can reduce mother-to-child HIV transmission [20]. They may also be helpful in testing marginalized populations, (i.e., sex workers, immigrants, intravenous drug users, and the homeless and incarcerated) living with undiagnosed HIV infection [21,22]. Targeted testing in these populations can help detect HIV early and reduce high-risk sexual practices/behavior, preventing further HIV transmission. Healthcare workers in developing countries are at risk of contracting HIV due to occupational exposure [16]. In such occupational settings, oral fluid rapid tests can greatly help in providing cost- and time-effective postexposure prophylaxis [16].

Although a few studies have evaluated the cost–effectiveness of oral fluid testing in comparison with conventional tests, the cost of the tests is a concern for its widespread use in developing countries [23]. In an effort to scale-up prevention and treatment linkages, the costs of these oral fluid tests must be kept affordable for people in developing countries that bear the brunt of the HIV epidemic and need them the most.

Future research directions

Although oral fluid HIV tests are highly accurate, the actual clinical and public health impact of the use of these tests in improving patient care and treatment outcomes are yet to be fully determined. Therefore, large-scale, pragmatic studies are needed in real-life settings, especially in high-risk, vulnerable populations. These studies should not focus on accuracy, but focus on applicability and impact on long-term patient outcomes. For example, will the introduction of routine oral fluid-based rapid testing in a labor ward in India or Africa actually help expedite the delivery of interventions to reduce perinatal HIV transmission? There is also a need to determine whether innovative approaches using oral fluid rapid tests can help in preventing transmission of HIV by modification of risk behavior. For example, will the easy availability of rapid oral fluid tests enhance voluntary testing among commercial sex workers and their clients?

'Although a few studies have evaluated the cost–effectiveness of oral fluid testing in comparison with conventional tests, the cost of the tests is a concern for its widespread use in developing countries.'

In developed countries, there is a steadily growing demand for home-based HIV tests (along the lines of home-based pregnancy testing). Oral fluid tests are ideally suited for home-based self-testing because of their high accuracy, simplicity and ease of use. The FDA is considering the possibility of approving over-the-counter tests for HIV, but concerns remain about the lack of adequate pre- and post-test counseling. Data are lacking on the feasibility of home-based HIV self-testing and diagnostic trials are needed to evaluate them for home-based use.

In conclusion, given the large numbers of individuals living with undetected HIV infection worldwide, it is hoped that detection of such individuals with high-quality, rapid, accurate point-of-care oral HIV tests will enable provision of early, timely and highly effective ART or expedite triage to care and prevention. However, throughout the testing process, ensuring privacy and confidentiality of test results, ensuring quality control and following quality assurance procedures at all times will help generate high-quality test results, leading to increased confidence in test results and encourage more individuals to come forward for HIV testing. Thus, rapid oral fluid-based point-of-care HIV tests can produce substantial cost savings and reduce the global burden of HIV infection.

Conflict of interest

None

Acknowledgements

Nitika Pant Pai is supported by a fellowship from the Canadian HIV Trials Network.

References

1 Bass E. WHO and UNAIDS set controversial course for HIV testing. *Lancet* 6(12), 760 (2006).

2 De Cock KM, Bunnell R, Mermin J. Unfinished business – expanding HIV testing in developing countries. *N. Engl. J. Med.* 354, 440–442 (2006).

3 Centers for Disease Control and Prevention. Revised Recommendations for HIV Testing of Adults, Adolescents, and Pregnant Women in Health-Care Settings. *Morb. Mortal. Wkly Rep.* RR14, 1–17 (2006).

4 Gottfried TD, Mink RW, Phanuphak P. Calypte AWARE HIV-1/2 OMT antibody test using oral fluid: special challenges of rapid HIV testing in the developing world. *Expert Rev. Mol. Diagn.* 6, 139–144 (2006).

5 Jones JP. In the culture of now. The arrival of the OraQuick rapid HIV test. *Posit. Aware* 15, 35–36 (2004).

6 Branson BM. FDA approves OraQuick for use in saliva. On March 25, the FDA approved the first rapid test for HIV in oral fluids. *AIDS Clin. Care* 16, 39 (2004).

7 Delaney KP, Branson BM, Uniyal A *et al.* Performance of an oral fluid rapid HIV-1/2 test: experience from four CDC studies. *AIDS* 20, 1655–1660 (2006).

8 Greenwald JL, Burstein GR, Pincus J, Branson B. A rapid review of rapid HIV antibody tests. *Curr. Infect. Dis. Rep.* 8, 125–131 (2006).

9 Donovan BJ, Rublein JC, Leone PA, Pilcher CD. HIV infection: point-of-care testing. *Ann. Pharmacother.* 38, 670–676 (2004).

10 Centers for Disease Control and Prevention. Approval of a new rapid test for HIV antibody. *Morb. Mortal. Wkly Rep.* 51, 1051–1052 (2002).

11 Burrage J Jr. HIV rapid tests: progress, perspective, and future directions. *Clin. J. Oncol. Nurs.* 7, 207–208 (2003).

12 Reynolds SJ, Muwonga J. OraQuick ADVANCE Rapid HIV-1/2 antibody test. *Expert Rev. Mol. Diagn.* 4, 587–591 (2004).

13 Pant Pai N, Joshi R, Dogra S *et al.* Evaluation of diagnostic accuracy, feasibility and client preference for rapid oral fluid-based diagnosis of HIV infection in rural India. *PLoS ONE* 2, e367 (2007).

14 Aaron E, Levine AB, Monahan K, Biondo CP. A rapid HIV testing program for labor and delivery in an inner-city teaching hospital. *AIDS Read* 16, 22–24 (2006).

15 O'Connell RJ, Merritt TM, Malia JA *et al.* Performance of the OraQuick rapid antibody test for diagnosis of human immunodeficiency virus type 1 infection in patients with various levels of exposure to highly active antiretroviral therapy. *J. Clin. Microbiol.* 41, 2153–2155 (2003).

16 Landrum ML, Wilson CH, Perri LP, Hannibal SL, O'Connell RJ. Usefulness of a rapid human immunodeficiency virus-1 antibody test for the management of occupational exposure to blood and body fluid. *Infect. Control Hosp. Epidemiol.* 26, 768–774 (2005).

17 Gallo D, George JR, Fitchen JH, Goldstein AS, Hindahl MS. Evaluation of a system using oral mucosal transudate for HIV-1 antibody screening and confirmatory testing. OraSure HIV Clinical Trials Group. *JAMA* 277, 254–258 (1997).

18 Jafa K, Patel P, Mackellar DA *et al.* Investigation of false positive results with an oral fluid rapid HIV-1/2 antibody test. *PLoS ONE* 2, e185 (2007).

19 OraQuick® ADVANCE rapid HIV1/2 antibody test, package insert. Orasure Technologies Inc., PA, USA.

20 Pai NP, Tulsky JP, Cohan D, Colford JM Jr, Reingold AL. Rapid point-of-care HIV testing in pregnant women: a systematic review and meta-analysis. *Trop. Med. Int. Health* 12, 162–173 (2007).

21 Bauserman RL, Ward MA, Eldred L, Swetz A. Increasing voluntary HIV testing by offering oral tests in incarcerated populations. *Am. J. Public Health* 91, 1226–1229 (2001).

22 Bucher JB, Thomas KM, Guzman D, Riley E, Dela Cruz N, Bangsberg DR. Community-based rapid HIV testing in homeless and marginally housed adults in San Francisco. *HIV Med.* 8, 28–31 (2007).

23 Doyle NM, Levison JE, Gardner MO. Rapid HIV versus enzyme-linked immunosorbent assay screening in a low-risk Mexican–American population presenting in labor: a cost–effectiveness analysis. *Am. J. Obstet. Gynecol.* 193, 1280–1285 (2005).

Website

101 Howerton D, Hearn TL, Onorato I, Branson B, Bock N, Kaplan J,Rayfield M; Centers for Disease Control and Prevention; US Department of Health and Human Services. Quality assurance guidelines for testing using the OraQuick Rapid HIV-1/2 Antibody test (Accessed June 2007) www.cdc.gov/hiv/topics/testing/resources/guidelines/qa_guide.htm

Affiliation

- *Nitika Pant Pai, MD, MPH, PhD*
Canadian HIV Trials Network Fellow, McGill University Health Centre, Division of Infectious Diseases and Immunodeficiency Service, Montreal Chest Institute, 3650 St Urbain Street, Montreal, Quebec, H2X 2P4, Canada
Tel.: +1 514 889 9604
nitika.pai@mail.mcgill.ca