ORIGINAL RESEARCH ARTICLE

An evaluation of the performance of OraQuick® ADVANCE Rapid HIV-1/2 Test in a high-risk population attending genitourinary medicine clinics in East London, UK

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Summary: To date, no data have been published on the use of OraQuick® ADVANCE Rapid HIV-1/2 Test (OraQuick) in the UK. We report preliminary findings of an ongoing evaluation of OraQuick in UK genitourinary (GU) medicine clinics. A total of 820 samples from patients in high-risk groups for HIV were tested with OraQuick and results were compared with standard HIV antibody testing. HIV prevalence (enzyme immunoassay [EIA]) was 5.73%, sensitivity of OraQuick was 93.64% (95% CI 82.46–98.66%), specificity 99.87% (99.28–100%), positive predictive value 97.78% (88.27–99.94%) and negative predictive value 99.61% (98.87–99.92%). This includes three false-negatives considered to be due to observer error and now rectified by further training. This has increased test sensitivity to 100%. Our observed test performance of OraQuick compares well with EIA and with other rapid tests. We believe that simple, non-invasive antibody detection tests such as OraQuick can increase HIV testing and diagnosis in UK GU medicine and community settings.

Keywords: point-of-care, oral fluid, HIV, rapid, tests

INTRODUCTION

The advantages of rapid testing over conventional HIV testing are well recognized.[1,2] Rapid tests have already led to increased detection of previously undiagnosed HIV-infected individuals in the USA.[3] Recent UK experience with the Determine® (Abbott Diagnostics, IL, USA), a visually read, qualitative immunochromatographic test for the detection of antibodies to HIV-1 and 2, suggests that the American experience can be replicated in a UK setting.[4] This method, using a finger prick whole blood sample, has shown almost 100% sensitivity and specificity, similar to several third-generation enzyme immunoassay (EIA) tests.[5]

Oral fluid sampling may confer added benefits to users over finger prick blood testing as it may be perceived as less invasive and is less painful. OraQuick® ADVANCE Rapid HIV-1/2 Test (OraQuick – OraSure Technologies Inc, Bethlehem, PA, USA) is Food and Drug Administration (FDA) approved and has been marketed in the USA for some years. It achieved 99.1% sensitivity and 99.6% specificity in a large Centers for Disease Control and Prevention (CDC) study.[5] In a recent field evaluation in India, it achieved 100% sensitivity and specificity.[6]

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OraQuick has only recently been Conformitée Européene (CE) marked and licensed for use in the UK. There are no published reports of its performance in a UK setting. The aim of this study was to evaluate the sensitivity, specificity and predictive values of OraQuick when used in four genitourinary (GU) medicine clinics in three East London National Health Service (NHS) trusts and compare the results with the standard laboratory based HIV antibody test.

METHODS

Patients attending the study clinics requesting an HIV test who were identified as having an increased risk for HIV infection were invited to take part in the study and written consent was obtained (Table 1). Patients were excluded if they were under 16 years old, highly anxious about HIV testing or were unable or unwilling to consent to an HIV test. Those who consented to take part in the study had an OraQuick oral fluid rapid test performed in parallel with their serum HIV test. They were also asked to complete an anonymous feedback questionnaire. Each participant's age, ethnicity, HIV risk and concurrent and previous sexually transmitted infections were also recorded. All participants underwent pre-test counselling and blood was taken for HIV-1/2 antibody EIA using ADVIA Centaur a third-generation immunoassay system (Siemens

Table 1 **Study inclusion criteria**

MSM
Patients from sub-Saharan Africa
Patients from other endemic areas where the HIV prevalence is >1%

MSM = Men who have sex with men

Healthcare Diagnostics, Tarrytown, NY, USA) as per routine practice. Oral fluid was collected by the participant, according to pack instructions, under direct staff supervision. The rapid tests were processed and read by clinic staff (nurses, doctors or health advisers) who had attended training from OraSure Technologies, the makers of OraQuick, prior to the beginning of the study. All rapid test results were verified by another trained member of clinical staff. All reactive specimens, on either OraQuick or EIA, were confirmed by Vidas immunoassay (BioMerieux, Mercy l'Etoile, France) and Biospot Immunocomb 1 and 2 Test (Orgenics, Yavne, Israel) which are the confirmatory tests used routinely in these testing sites.

HIV results were communicated either in person or by telephone or text, one to two weeks later in accordance with routine practice; results from OraQuick were not given to the patients during this study as the test was as yet unlicensed in the UK.

The staff involved in the study completed a feedback questionnaire to assess the feasibility and acceptability of this type of test.

Data were entered on to an excel database and sensitivity, specificity, positive predictive value and negative predictive value were calculated. The 95% confidence intervals (CI) were calculated in Excel as described by Gardner and Altman.[7]

Ethical approval for the study was granted by the East London and The City Research Ethics Committee.

RESULTS

A total of 820 oral fluid samples were tested. Demographic data were available from 812 participants (8 sets of missing data). Of those participants for whom data were available, 685 (84%) were men and 119 (15%) women, (the remainder not stated); 74% were men who have sex with men (MSM). The median age was 31 years. Of all the participants, 58% were Caucasian, 20% Black African and 19% of other ethnicities.

Forty-seven participants had a positive serum EIA test, which gave an HIV prevalence of 5.73%.

The sensitivity of OraQuick was 93.64% (95% CI 82.46–98.66%) and specificity 99.87% (99.28–100%). The positive predictive value was 97.78% (88.2–99.94%) and the negative predictive value 99.61% (98.87–99.92%). There were one false-positive and three false-negative results (Table 2). One test was rapid test, negative with initial equivocal serology; repeat serology on this patient confirmed a negative result.

Questionnaire data will be reported elsewhere.

Table 2 **Comparison of HIV status by OraQuick with those confirmed on serology**

	HIV positive	HIV negative
OraQuick® positive	44	1
OraQuick® negative	3	772

DISCUSSION

This is the first study to present data using the OraQuick in the UK. We included only high-risk patients in this study as this reflects the planned use of HIV rapid tests in our service.

Any new HIV rapid test should have performance comparable with tests already in routine use. For the purposes of this study, we determined a performance meeting or approaching that of both the ADVIA Centaur (our current test) and Determine® (the most commonly used rapid test in the UK) to be acceptable. Current EIA screening in our service achieves 99.86% specificity and 100% sensitivity.[8] In this study, the sensitivity of OraQuick was lower (93.64%) but the specificity was comparable (99.87%) with this.

The reduced sensitivity in our study was due to the occurrence of three misinterpreted tests, which we have included as false-negative results. Excluding these data from analysis increases the sensitivity of OraQuick to 100% (95% CI 91.96–100%) and the negative predictive value to 100% (95% CI 99.52–100%). All three rapid tests were read by study staff towards the beginning of the study and interpreted as negative but on investigation, we believe that a faint positive line was present on all three. Advice was sought from both Bio-Stat Limited and OraSure Technologies Inc. A re-training session using a low titre panel ensured that staff understood that a faint line can be extremely faint and no further tests were misread as negative beyond this point in the study; however, this demonstrated the importance of regular staff training and quality control procedures when rapid tests are used.

The three cases were investigated in detail and this will be reported elsewhere. In at least one of the three cases, an extended window period leading to delayed conversion to antibody positivity may have been a factor in the negative rapid test result; indeed this patient was strongly rapid test positive on repeat testing three months later. It has been noted that conversion to antibody positivity in oral fluid samples may take longer than with whole blood or serum, adding about two weeks to the window period.[4,9] However, the exact period does depend on which serum and oral fluid tests are being compared.[10]

Rapid testing has the potential to increase uptake of HIV testing. In the United States, rapid tests have already led to an increase in HIV testing. One large study reported a 36% increase in testing with a consequent increase in the detection of previously undiagnosed HIV-infected individuals.[3] In the UK, The Health Protection Agency estimates 73,000 adults in the UK are living with HIV of whom 29% (21,600) are currently unaware of their infection.[11] The high proportion (a quarter of HIV-infected heterosexual men and women and almost half of men who have sex with men) of people leaving GU medicine clinics who are unaware of their HIV infection is of particular concern. The proportion of people remaining undiagnosed is even higher among those with an acute STI (40% and 59%, respectively). In addition, the UK is the only country in western or central Europe to show a rise in HIV infections.[12] This has been recognized by The Department of Health and the reduction of undiagnosed HIV infection has been one of their main strategies to reduce rates of HIV transmission.[13]

HIV rapid tests can be based on either oral fluid or whole blood from a finger prick. To be suitable for screening in a sexual health or outreach setting, rapid tests should be highly (>99%) sensitive and specific.[2] A large study evaluating the Determine® (finger prick) HIV rapid test in 1623 patients in

London achieved a sensitivity of 100% and specificity of 99.9%, a positive predictive value of 97.5% and a negative predictive value of 100%.[2] Furthermore, it scored full marks when assessed on technical aspects and a review of independent evaluations reported a sensitivity of 100%, and specificity of 99.4%.[14,15]

Disadvantages of Determine® include the multistep procedure, the need for capillary tubes, chase buffer solution, lancets, safety goggles, sharps bins, means of safe disposal of samples (resulting in both inconvenience and additional costs) and the fact that once taken, the sample must be processed immediately. One of the advantages of OraQuick is that samples can be tested up to 10 minutes after collection – an advantage in some clinical settings. Other advantages are its simplicity: the procedure is so simple that the sample can be self taken and that, having a single use vial containing a premeasured amount of a buffered developer solution, it needs no special equipment. Given that oral fluid may not be considered potentially infectious unless it contains blood, the disposal of samples is also much easier.

An independent review of rapid tests found OraQuick to be simple to perform and it was the preferred oral fluid test.[16,17] Like Determine®, it achieved maximum marks in a World Health Organization technical assessment, and was shown to be highly sensitive and specific (98.1 and 100%, respectively).[18] Our data support these observations: overall, results were easy to interpret, regardless of whether they were positive or negative and staff found the procedure easy to learn and to perform. In our study, patients responded positively to the availability of a non-invasive test.

The main disadvantage of OraQuick is that at 20 minutes, it takes slightly longer than other rapid tests, including Determine®, to provide results for oral fluid samples.

Current UK guidelines[10,19] recommend that, in general, oral fluid testing should be avoided. However, at the time these guidelines were developed, there were no oral fluid rapid screening tests available in the UK and the level of evidence for this recommendation was acknowledged to be low (IVc). The position has now changed with the CE marking and marketing of OraQuick.

Our data suggest that OraQuick offers a real alternative to the currently used HIV point of care tests, with a performance that is equivalent to that of both Determine® and conventional EIA tests. We believe that OraQuick has the potential to increase HIV testing and diagnosis in the culturally diverse population of East London and elsewhere in the UK.

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REFERENCES

1 Winter AJ, Sulaiman Z, Hawkins D. BASHH Clinical Governance Committee Guidance on the appropriate use of HIV point of care tests. *Int J STD AIDS* 2006;**17**:802–5
2 Dewsnap CH, McOwan A. A review of HIV point-of-care-tests. *Int J STD AIDS* 2006;**17**:357–9
3 San Antonio-Gaddy M, Richardson-Moore A, Burstein GR, *et al.* Rapid HIV antibody testing in the New York State anonymous HIV counseling and testing program: experience from the field. *J Acquir Immune Defic Syndr* 2006;**43**:446–50
4 Giles RE, Crocker S, Perry KR, Parry JV, Mortimer PP. *Abbott Determine HIV-1/2 Simple/Rapid Test Device. Medical Devices Agency Evaluation Report*, 1998. See [http://www.hpa-midas.org.uk/reports/reports_hiv.asp] (last checked 25 January 2008)
5 Delaney KP, Branson BM, Uniyal A, *et al.* Performance of an oral fluid rapid HIV-1/2 test: experience from four CDC studies. *AIDS* 2006;**20**:1655–60
6 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* 2007;**2**:e367
7 Gardner MJ, Altman DG. Calculating confidence intervals for proportions and their differences. In: Gardner MJ, Altman DG, eds. *Statistics with Confidence*. London: BMJ Publishing Group, 1989:28–33
8 HIV 1/0/2 Enhanced 03162506 Rev A, 2005–2012. *ADVIA Centaur Assay Manual*. Tarrytown, NY: Bayer HealthCare LLC, 2005
9 Gallo D, George JR, Fitchen JH, *et al.* Evaluation of a system using oral mucosal transudate for HIV-1 antibody screening and confirmatory testing. Orasure Clinical Trials Group. *JAMA* 1997;**277**:254–8
10 Rogstad KE, Palfreeman A, Rooney G, *et al. United Kingdom National Guidelines on HIV Testing 2006, Clinical Effectiveness Group British Association of Sexual Health and HIV*. See [http://www.bashh.org/guidelines/2006/hiv_testing_june06.pdf] (last checked November 2007)
11 The UK Collaborative Group for HIV and STI Surveillance. *Testing Times. HIV and Other Sexually Transmitted Infections in the United Kingdom*. London: Health Protection Agency, Centre for Infections, 2007. See [http://www.hpa.org.uk/infections/topics_az/hiv_and_sti/Default.htm] (last checked January 2008)
12 Joint United Nations Programme on HIV/AIDS (UNAIDS) and World Health Organization (WHO). *AIDS Epidemic Update, December 2007*. See [http://www.unaids.org/en/KnowledgeCentre/HIVData/EpiUpdate/EpiUpdArchive/2007/default.asp] (last checked January 2008)
13 The National Strategy for Sexual Health and HIV, Department of Health, 21 July 2001. See [http://www.dh.gov.uk/dr_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_4058945.pdf] (last checked January 2008)
14 World Health Organization. *HIV Assays: Operational Characteristics (Phase I) Report 12*. See [http://www.who.int/diagnostics_laboratory/publications] (last checked November 2007)
15 Branson BM. Point-of-care rapid tests for HIV antibodies. *J Lab Med* 2003;**27**:288–95
16 ECRI Institute. Rapid HIV test kits (evaluation). Health Devices 2006 May;35(5):157–77. See [http://www.ecri.org] (last checked March 2008)
17 Rapid HIV testing: 2005 update (slide presentation online). See [www.cdc.gov/hiv/rapid_testing] (last checked March 2008)
18 World Health Organization. *HIV Assays: Operational Characteristics (Phase I) Report 14*. See [http://www.who.int/diagnostics_laboratory/publications] (last checked March 2008)
19 Smit EJ. Screening guidelines for sexually transmitted Infections: human immunodeficiency virus (HIV). In: *Screening Guideline Steering Group Sexually Transmitted Infections: UK National Screening and Testing Guidelines*. See [http://www.bashh.org/guidelines/2006/sti_screening_guidelines_ v14_0806.pdf] (last checked February 2008)

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