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Clinical evaluation of a hepatitis C antibody rapid immunoassay on self-collected oral fluid specimens☆

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ABSTRACT

We evaluated the performance of the OraQuick® HCV Rapid Antibody Test (Orasure Technologies, Inc., Bethlehem, PA) on oral fluid specimens when used by patients for self-testing. Participants used a set of instructions, self-collected their specimens, and interpreted their result. A researcher interpreted the test simultaneously and independently. Participants' true antibody status was determined by reviewing medical records or by a venipuncture blood sample. Sensitivity, specificity, and κ statistic were calculated. The sample included 95 participants (48 male and 47 female). Sensitivity and specificity on self-collected oral fluid samples were 88.4%% (95% CI, 74.9–96.1) and 100% (95% CI, 93–100), respectively, when patients interpreted the test results. Sensitivity and specificity were 97.7% (95% CI, 88–99.9) and 98% (95% CI, 89.6–100), respectively, when trained staff interpreted the result. κ statistic was 0.89 (95% CI 0.80–0.98). The rapid HCV test kit showed good performance when used for self-testing of oral fluid specimens.

1. Background

It is estimated that 3.5 million people in the United States are infected with the hepatitis C virus (Edlin et al., 2015) (HCV). HCV infection is a significant cause of cirrhosis, hepatocellular cancer, and mortality (El-Kamary et al., 2011). The CDC recommend screening for HCV infection among adults born 1945 through 1965 and high-risk groups such as injection drug users, persons with HIV infection, and hemodialysis patients (https://www.cdc.gov/hepatitis/hcv/guidelinesc.htm, n.d.). Current screening is conducted with either a rapid or a laboratory-based antibody test in a blood sample for detection of HCV antibodies. If the initial test is positive, an additional nucleic acid amplification test for HCV RNA follows to discern between active and prior infection (CDC, 2013).

The only FDA-approved rapid test in the United States is the OraQuick ® HCV Rapid Antibody Test (Orasure Technologies, Inc., Bethlehem, PA) that detects antibodies to HCV on serum and whole blood. The test has a Clinical Laboratory Improvements Amendments waiver, and it can be used in clinical and community settings, such as physician offices and community testing organizations.

The test kit may also detect HCV antibodies in oral fluid, and it is approved for use with oral fluid outside the United States. The manufacturer-reported sensitivity on oral fluid samples is 98.1% (96.6–99%) and the specificity is 99.6% (99.2–99.9%) (http://orc.orasure.com/default.aspx?pageid=1475, n.d.). Collecting oral fluid is a simple, non-invasive procedure that can be performed without special equipment even at home. Using oral fluid could simplify screening and help increase testing especially among high-risk and hard-to-reach populations. The goal of this study was to evaluate the performance of the OraQuick ® HCV Rapid Antibody Test in oral fluid when used by patients for self-testing.

2. Methods

2.1. Study subjects

Subjects were recruited from the Hepatology outpatient clinic of the UCLA Pfleger Liver Institute between February 2018 and August 2018. All subjects eligible for the study were adults who spoke and understood English. A trained researcher screened, consented, and recruited patients during clinic appointment.

2.2. Oral fluid sample collection

The oral fluid sample was self-collected by the patient using the non-invasive OraQuick® Rapid Antibody test kit (Orasure Technologies, Inc.,

Abbreviations: HCV, hepatitis C virus; UCLA, University of California, Los Angeles.

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Bethlehem, PA). Patients who used dentures were instructed to remove them prior to sample collection. Patients who consumed food or beverage or used oral care products were tested after 30 min following exposure in order to ensure accuracy for each test. Patients were given a visual guide with instructions on how to collect and test the oral fluid sample. The instruction sheet was based on manufacturer's instructions (http://orc.orasure.com/default.aspx?pageid=1484, n.d.). Patients would open the package and set up the test solution vial; then they would use the test device to collect the sample by swabbing once around the lower and upper outer gums. Once the patients completed the sample collection, they placed the collection device in the solution vial. Participants interpreted their result after 20 min. Patients were also given a visual guide to assist them in result interpretation as "Positive," "Negative," or "Invalid." Patients sealed their evaluation sheet in an envelope. Simultaneously, a trained researcher interpreted the rapid test and recorded the result separately.

2.3. Under evaluation test device

The OraQuick HCV rapid test (Orasure Technologies, Inc., Bethlehem, PA) is a lateral flow device that detects antibodies to HCV (http://orc.orasure.com/default.aspx?pageid=1484, n.d.). It is FDA-approved for use on serum and whole blood samples but not for use on oral fluid specimens. Antigen from the core, NS3, and NS4 regions of HCV genome is immobilized on a single test in a nitrocellulose strip contained with the device. Reactive results present as 2 reddish-purple lines on the test strip at the test zone, while nonreactive results present as 1 line.

2.4. Reference standard comparison

The HCV antibody status of participants was determined by reviewing their medical record or laboratory testing. Participants were considered positive for antibodies if they had a positive HCV antibody test in the past 6 months or if they tested positive for antibodies on the laboratory test ordered at the same day the oral fluid sample was collected. The venipuncture blood sample was collected and tested for HCV antibodies using the ADVIA Centaur® HCV Assay (Siemens, Pleasanton, CA).

2.5. Statistical analysis

Sensitivity and specificity were calculated along with their respective 95% exact confidence interval (95% CI). The medical record test result or the ADVIA test result was considered the true antibody status of the participants. Cohen's κ statistic was used to assess the degree of interrater agreement between patient and trained personnel result interpretation. Data analysis was performed using the IBM ® SPSS ® Statistics version 24.

2.6. Human subjects

The UCLA Institutional Review Board reviewed and approved the study with IRB #17-001268.

3. Results

3.1. Study population

From February 2018 to August 2018, we enrolled 101 participants. Eventually, 95 out of 101 participants were included in the data analysis. Six out of 101 participants were excluded due to missing laboratory test results. Table 1 shows the detailed demographic characteristics of the sample. Half of the participants were male, and the majority of the study population was white (54%) and Hispanic/Latino (26%).

Table 1
Participant demographics, UCLA Hepatology clinic, 2018.

Demographics (n = 95)		
Sex	*N*	%
Female	47	49.5%
Male	48	50.5%
Age in years		
Mean (SD)	57.6 (13.9)	
Range	20–86	
Race/ethnicity		
White	51	53.7%
Black	5	5.3%
Latino	26	27.4%
Asian	5	5.3%
Unknown/other	8	8.4%

3.2. Sensitivity and specificity

Of the 95 subjects, 44 were classified as HCV antibody positive (46.3%) (7 were tested the same day they were enrolled, and 37 had tested in the past 6 months before enrollment). The sensitivity and specificity of the under-evaluation test using self-collected oral fluid specimens were 88.4% (95% CI, 74.9–96.1) and 100% (95% CI, 93–100), respectively, when patients interpreted the test results, whereas the clinical sensitivity and specificity were 97.7% (95% CI, 88.0–99.9) and 98% (95% CI, 89.6–100), respectively, when the test was interpreted by trained personnel (Table 2). The difference in the observed sensitivity and specificity test result reading (patient versus staff) was not statistically significant ($\chi^2 = 2.68$, $P = 0.10$ and $\chi^2 = 0.01$, $P = 0.92$). The κ coefficient was 0.89 (95% CI 0.80–0.98), indicating very good agreement between patient and trained personnel's result interpretation (Table 3). Five participants that were classified as "HCV antibody positive" interpreted their result as "Negative," while staff interpreted their result as "Positive." In 1 case, a participant interpreted their result as "Invalid," while the trained researcher interpreted as "Positive."

4. Discussion

In this study, we evaluated the performance of the OraQuick ® HCV Rapid Antibody test when used by patients for self-testing of self-collected oral fluid specimens. To our knowledge, this is the first study in which participants collected and interpreted their test results using the OraQuick test (Ibrahim et al., 2015; Lee et al., 2010; Smith et al., 2011). The test kit showed very good performance when used by patients, but there was a small not statistically significant difference in the clinical performance of the test when interpreted by the patients compared to trained staff.

In this study, the test kit's sensitivity was lower compared to the one reported by the manufacturer (http://orc.orasure.com/default.aspx?pageid=1484, n.d.) but similar to other clinical evaluation studies. Indeed, Ibrahim et al. (2015) reported sensitivity of 88.3% and specificity of 100% on a sample of patients of an infectious diseases clinic. Similarly, Pallarés et al. (2018) reported sensitivity of 89.9% and specificity 100% on oral fluid. It should be noted that, in both studies, trained staff collected, tested the sample on site, and interpreted the result. Consequently, use by untrained users may not significantly affect the performance of the test.

Sample collection, as well as errors, due to subjective reading and interpretation of results could have an impact on the sensitivity of the test. The test kit is designed to be used by trained personnel. Certification and training can be acquired online on the manufacturer's website and include a brief online provider-oriented training session. In our study, participants were provided printed graphical instructions on test kit use and an adequate amount of time to review and understand the instructions. Our team developed this tool based on the manufacturer's

Table 2
Performance of the OraQuick® HCV Rapid Antibody Test in self-collected oral fluid specimens, UCLA Hepatology clinic, 2018.

	HCV Ab+	Sensitivity (95% CI)	HCV Ab−	Specificity (95% CI)
Patient interpretation	38/43	88.4% (74.9–96.1)	51/51	100% (93–100)
Personnel interpretation	43/44	97.7% (88–99.9)	50/51	98% (89.6–100)

Table 3
Cohen's κ of the OraQuick® HCV Rapid Antibody Test in self-collected oral fluid specimen, UCLA Hepatology clinic, 2018.

		Staff		Total	Cohen's κ (95% CI)
		Positive	Negative		
Patient	Positive	38	0	38	0.89 (0.80–0.98)
	Negative	5	51	56	
Total		43	51		

instructions (http://orc.orasure.com/default.aspx?pageid=1484, n.d.). Participants found using the kit easy, but they reported difficulty reading the result lines. Perhaps, minor modifications on the test kit could facilitate result interpretation.

There were a few limitations in our study. Firstly, the small sample size affects the accuracy of our estimates on the performance. Secondly, the convenience sample of patients we used may be susceptible to interpretation bias, as patients who have been tested and/or treated for HCV infection in the past knew their HCV antibody status.

Our results show that the Oraquick HCV test kit could be potentially used for self-testing of self-collected oral fluid specimens by untrained users. Increasing the availability of an HCV self-test kit could be part of expanded screening approaches and could prove helpful in reaching marginalized populations or underserved communities. Future studies should examine the performance of the test kit for self-testing in different high-risk populations in nonclinical settings, as well as evaluate the impact of self-testing on the efforts of elimination of hepatitis C infection among these populations.

5. Conclusion

The rapid HCV test kit showed good performance when used for self-testing of oral fluid specimens. There was high agreement between patients and trained personnel on the interpretation of rapid HCV test kit results.

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Ethics approval and consent to participate

The UCLA Institutional Review Board reviewed and approved the study with IRB #17-001268.

Consent for publication

All authors read and approved the final manuscript.

Availability of data and material

All data generated or analyzed during this study are available from the principal investigator on reasonable request.

Competing interest

All authors do not have a commercial or other association that might pose a conflict of interest.

Authors' contributions

1. MK: data acquisition, drafting, results interpretation, data/statistical analysis, writing manuscript, and critically thinking about manuscript content.
2. CS: provided valuable insights for revising the manuscript and result interpretation.
3. PT: provided valuable insights for revising manuscript.
4. SS: co-principal investigator and provided valuable insights for revising manuscript.
5. JDK: principal investigator and provided valuable insights in study design, analysis, and manuscript preparation.

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