Clinical Performance of the FilmArray™ BioThreat-E test for diagnosing Ebola Virus Disease in “alternate” specimen types: urine and saliva


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BACKGROUND

The current Ebola outbreak has highlighted the need for efficient diagnostic tools. Diagnosis of Ebola Virus Disease (EVD) has relied on RT-PCR techniques on blood specimens. Non-invasive diagnosis would make the management of patients easier, faster, and safer for healthcare workers. The FilmArray (FA) system (BioFire Diagnostics, a bioMérieux company) is an automated and qualitative in vitro diagnostic platform that combines nucleic acid purification and nested multiplex RT-PCR. BioFire Defense has developed a commercially available FA test (BioThreat-E) designed to detect Ebola virus, Zaire strain from whole blood and urine. The system is a highly accurate, fast, and easy-to-use PCR molecular diagnostic instrument which delivers test results in approximately one hour using a closed, sample-to-answer system. Based on in vitro technical performance obtained on spiked-whole blood and urine specimens, an Emergency Use Authorization was obtained from the FDA on August 10, 2015 (1). In the meantime, published data have demonstrated that the FilmArray panels are effective tests for evaluating patients with EVD (3-4) and a clinical field trial was conducted in Guinea to assess the clinical performance(10,7),(986,987)

DESIGN OF THE STUDY

The study was conducted between March 7, 2015 and July 24, 2015 at the “Laboratoire des Fèvers Hémorragiques Viraîles” in Donka National Hospital (Conakry, Guinée), which is the Reference Laboratory for Hemorrhagic Fevers in Guinée. The study did not involve with patient management according to routine practice in Conakry and Coyer Treatment Center. No specific invasive intervention was required for this research protocol. One additional EDTA tube was drawn from a single patient during the sampling for the evaluation of the BioThreat-E test on blood. Two additional non-invasive samples were taken whenever possible: one urine sample, and one saliva sample using a swab and a transport medium (UTM viral transport Media,Copan) availability of both depending on the condition of the patient and the management constraints in the context of the Ebola clinic. The protocol was approved by the Guinean Ethical Committee.

RESULTS

From March 7 to July 24, 156 EVD-suspected patients were enrolled; 55 were declared positive according to the previous criteria and 37 were able to provide saliva and/or urine samples: 35 positive patients conducted a saliva sample and 3 positive patients provided a urine sample:

• 34 out of the 35 saliva samples were positive with the BioThreat-E test
• 3 out of the 3 urine samples were positive with the BioThreat-E test

Only one saliva sample was negative. The Ct value of the corresponding blood sample with the Altona technique was 23.49, and the duration of the disease declared by this patient at admission was 14 days. For the 32 patients who gave a saliva sample and for whom we could obtain this data, the mean duration of the disease was 5.06 days, ranging from 2 to 14 days, with 28 patients between 2 and 8 days, 3 patients between 10 and 12 days, and one patient only at 14 days.

One explanation for the single negative saliva sample in a positive patient could be a faster clearance of the virus in saliva than in blood, as previously described (6). However, taking into account the facts that the discordant saliva sample could be retested by the BioThreat-E assay the following day and gave a positive result and the analysis of the melting curve data for the first BioThreat-E test, it is highly unlikely that a low concentration of Ebola Zaire nucleic acid was present in the sample and “missed” on the first run. These data suggest that a user error during the first test was most likely the cause of these discrepant results on a single saliva specimen.

This field study showed that the BioFire FA BioThreat-E assay can be used on saliva and on urine specimens in EVD suspected cases. Of the 38 samples included in this study, we obtained an almost perfect concordance (97.37 %) between blood and the non-invasive saliva and urine samples. Healthcare staff found that urine was more difficult to obtain for practical reasons. Saliva, collected by a swab and then placed into transport medium, is much easier to collect and preferred by the workers. More data need to be collected for a better knowledge of the viral kinetics in different body fluids but we believe that using a very sensitive molecular technique like the FilmArray BioThreat-E assay on non-invasive specimens, especially saliva, could be very useful for the rapid diagnosis of EVD, easy and ongoing surveillance of this infection, and management of suspected cases, even outside of well equipped and specialized settings.

References

3) Lakht A.A. et al. Use of FilmArray™ system for detection of Zaire ebolavirus in a small Hospital, Aba, Sierra Leone. J Clin Microbiol. 2015 Jul;53(7):2066-74
4) Southern T.B. et al. Comparison of FilmArray and quantitative Real-Time Reverse Transcription PCR for detection of Zaire ebolavirus from clinical and chestral specimens. J Clin Microbiol. 2015 Sep;53(9):6956-60

The status for EVD was defined for each patient based on the result of routine testing on serum using the following techniques: 1) Quantitect® Probe RT-PCR (Qiagen) and 2) RealStar® Filovirus Type RT-PCR Kit 1.0 (Altona). Positive patients: patients enrolled in the study showing positive results with the two routine PCR tests performed in the lab, Negative patients: patients enrolled in the study showing negative results with the two routine PCR tests performed in the lab, Equivocal patients: all other results showing a discrepancy between the two routine tests.

BioThreat-E test was performed on all the available stored saliva and urine samples, for positive patients only.

• This test has not been FDA cleared or approved;
• This test has been authorized only for an Emergency Use Authorization for use by CLIA Moderate and High Complexity Laboratories;
• This test has been authorized only for the detection of Ebola Zaire virus (detected in the West African outbreak in 2014) and not for any other viruses or pathogens;
• This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of in vitro diagnostics for detection of Ebola Zaire virus under section 564(b)(1) of the Act, 22 U.S.C § 3606b-3(b)(1), unless the authorization is terminated or revoked sooner.

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