Publication List

TB-LAMP

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Human
Diagnostics Worldwide

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Application in remote settings

A cost–benefit algorithm for rapid diagnosis of tuberculosis and rifampicin resistance detection during mass screening campaigns

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– BMC Infectious Diseases (2022) 22:219 –

Abstract

Background

Active tuberculosis (TB) case finding is important as it helps detect pulmonary TB cases missed by the other active screening methods. It requires periodic mass screening in risk population groups such as prisoners and refugees. Unfortunately, in these risk population groups periodic mass screening can be challenging due to lengthy turnaround time (TAT), cost and implementation constraints. The aim of this study was to evaluate a diagnostic algorithm that can reduce the TAT and cost for TB and Rifampicin resistance (RR) detection. The algorithm involves testing with TB-LAMP followed by Xpert MTB/RIF for positive TB-LAMP cases to diagnose TB during mass campaigns in prisons and refugee camps.

Methods

The National Tuberculosis Control Program (NTCP) organized routine TB mass-screening campaigns in 34 prisons and 3 villages with refugees camps in Cameroon in 2019. TB LAMP was used for initial TB diagnosis and all TB-LAMP positive cases tested with the Xpert MTB/RIF assay to determine RR. TAT and cost benefits analysis of the combined use of TB-LAMP and Xpert MTB/RIF assays was determined and compared to the Xpert MTB/RIF assay when used only.

Results

A total of 4075 sputum samples were collected from TB presumptive, 3672 cases in 34 prisons and 403 samples in 3 villages. Of the 4,075 samples screened with TB-LAMP, 135 were TB positive (3.31%) and run on the Xpert MTB/RIF. Of the 135 positives cases, Xpert MTB/RIF revealed 3 were RR (2.22%). The use of TB-LAMP followed by testing with Xpert MTB/RIF for TB and RR detection reduced the TAT by 73.23% in prisons and 74.92% in villages. In addition to a reduced TAT, the two molecular tests used in synergy is cost benefit from year 2 onwards.

Conclusions

This study demonstrates the advantages of a diagnostic algorithm based on an initial testing with TBLAMP followed by testing with Xpert MTB/RIF for TB diagnosis. This approach improved early and rapid TB detection with an added advantage of providing RR status. The proposed algorithm is effective and less costly from the second year of implementation and should be used by TB control programs.

Tuberculosis-loop-mediated isothermal amplification implementation in Cameroon: Challenges, lessons learned and recommendations.

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– African Journal of Laboratory Medicine | Vol 11, No 1 | a1792 | –

Abstract

Background

Until 2016, microscopy was the main tool for the early detection of pulmonary tuberculosis in Cameroon, especially in remote settings. Due to the poor sensitivity of microscopy, there was a need to implement a molecular assay in order to improve tuberculosis case detection.

Intervention

In 2017, tuberculosis loop-mediated isothermal amplification (TB-LAMP), a molecular rapid diagnostic test recommended by the World Health Organization, was implemented in Cameroon as a replacement test of microscopy for initial diagnosis of pulmonary tuberculosis and also as a follow-on test to microscopy for smear-negative sputum specimens. A roll out plan for TB-LAMP implementation in Cameroon had been developed from January 2017 to April 2017, followed by initial implementation at four sites in May 2017. Additional sites were added progressively.

Lessons Learnt

The use of TB-LAMP as a follow-on test to microscopy for smear-negative sputum specimens helped in the detection of tuberculosis in 14.77% of those who were sputum-smear negative in 2019. Tuberculosis-loop-mediated isothermal amplification usage as an initial test, followed by testing with Xpert MTB/RIF for rapid tuberculosis and rifampicin resistance detection during tuberculosis mass screening campaigns, reduced the turn-around time by 73.23% as compared to when the Gene Xpert instrument was used alone.

Recommendations

The implementation and scaling up of TB-LAMP in Cameroon contributed to increase access to tuberculosis molecular diagnosis in remote settings and as such improved tuberculosis case notification. However, to better enhance this notification and optimise the use of a TB-LAMP instrument, a suitable sample transport system is recommended.

Laboratory diagnosis of tuberculous meningitis in human immunodeficiency virus–seropositive patients: Correlation with the uniform case definition

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– S Afr J Infect Dis. 2020;35(1), a135 –

Abstract

Background

Laboratory confirmation of the diagnosis of tuberculous meningitis (TBM) has always been problematic. Using the uniform case definition suggested by Marais et al., we determined the sensitivity of a variety of laboratory tests.

Methods

Human immunodeficiency virus (HIV)–seropositive patients suspected of having subacute meningitis were included in the study. Using the uniform case definition, patients were divided into possible and probable cases of TBM. The following specific tests were done on the cerebrospinal fluid (CSF): layered Ziehl–Neelsen (ZN) staining, CSF culture and a panel of nucleic acid amplification tests (NAAT) consisting of the GenoType MTBDRplus assay, Cepheid Xpert MTB/RIF, the MTB Q-PCR Alert (Q-PCR) and the loop-mediated isothermal amplification (LAMP) assay. The sensitivity of each test was compared to the case definition and to each other.

Results

A total of 68 patients were evaluated. Using the uniform case definition only, without any of the specific laboratory tests, there were 15 probable cases (scores > 12) and 53 possible cases (scores 6–11) of TBM. When the uniform case definition was tested against any laboratory test, 12 of the 15 (80%) probable cases and 26 of the 53 (49.1%) possible cases had laboratory confirmation. When each test was compared to any other test, the sensitivities for the Xpert MTB/RIF, GenoType MTBDRplus, CSF culture, Q-PCR, LAMP and ZN layering were 63.2 (46.0–78.2), 76.3 (59.8–88.6), 65.7 (47.8–80.9), 81.1 (64.8–92.0), 70.3 (53.0–84.1) and 55.6 (38.1–72.1), respectively.

Conclusions

In this study, the GenoType MTBDRplus and the Q-PCR tests performed better than the Xpert MTB/RIF. Because the Xpert MTB/RIF is not good enough to 'rule out' TBM, a negative result should be followed up by another NAAT, such as the GenoType MTBDRplus or Q-PCR. The LAMP assay may be considered as the first test in resource-poor settings. At the time of the study, we did not have access to the Xpert MTB/RIF Ultra, which has now been recommended by the World Health Organization as the test of first choice. However, even this test has a similar limitation as the Xpert MTB/RIF, with two recent studies showing variable results.

Loop mediated isothermal amplification for the rapid diagnosis of pulmonary tuberculosis

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– *J. Evolution Med. Dent. Sci. 2019;8(29):2338-2341*–

Abstract

Background

Control of tuberculosis is often challenged by diagnostic methods which are time consuming, often less sensitive, expensive and inaccessible to most patients especially in the developing countries. The characteristics of loop-mediated isothermal amplification (LAMP) method make it a promising platform for the molecular detection of tuberculosis in developing countries. We wanted to evaluate the loop mediated isothermal amplification method for the rapid diagnosis of pulmonary tuberculosis (PTB) in low resource settings.

Methods

We conducted an observational study in the Microbiology department for a period of eighteen months on sputum samples collected from suspected cases of pulmonary tuberculosis which satisfied the inclusion as well as exclusion criteria. All these samples after processing were subjected to smear microscopy by acid fast staining, culture on Lowenstein-Jensen (LJ) medium and LAMP assay and results were compared to derive sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).

Results

A total of 110 samples were included in the study. Using culture as the reference standard, we found that the sensitivity and specificity for TB-LAMP assay were 98.3% and 98.03% respectively and PPV and NPV were 98.3% and 98.03% respectively. The AFB staining had a sensitivity of 91.5% and specificity of 98%.

Conclusions

Hence LAMP method is a reliable test for the diagnosis of tuberculosis which can be suited to resource limited settings. The method has very good positive and negative predictive value for pulmonary samples. It is a rapid technique when compared to conventional culture and simple and less expensive than other molecular based methods. Therefore, it can be applied as a point of care testing (POCT) method in resource limited settings.

Performance and impact of GeneXpert MTB/RIF® and Loopamp MTBC Detection Kit® assays on tuberculosis case detection in Madagascar

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– BMC Infectious Diseases (2019) 19:542–

Abstract

Background

Tuberculosis rapid molecular assays, including GeneXpert MTB/RIF® and Loopamp MTBC Detection Kit®, are highly sensitive and specific. Such performance does not automatically translate in improved disease control and highly depends on their use, local epidemiology and the diagnostic algorithms they're implemented within. We evaluate the performance of both assays and assess their impact on additional cases notification when implemented within WHO recommended tuberculosis diagnostic algorithms in Madagascar.

Methods

Five hundred forty eight presumptive pulmonary tuberculosis patients were prospectively recruited between November 2013 and December 2014 in Antananarivo, Madagascar, a high TB incidence sub-Saharan African urban setting. Both molecular assays were evaluated as first line or add-on testing following negative smear microscopy. Based on locally defined assay performance characteristics we measure the impact of both assays and WHO-recommended diagnostic algorithms on additional tuberculosis case notifications.

Results

High sensitivity and specificity was confirmed for both GeneXpert MTB/RIF® (86.6% (95% CI 81.1–90.7%) and 97.4% (95% CI 94.9–98.8%)) and Loopamp MTBC Detection Kit® (84.6% (95% CI 78.9–89.0%) and 98.4% (95% CI96.2–99.4%)). Implementation of GeneXpert MTB/RIF® and Loopamp MTBC Detection Kit® increased tuberculosis diagnostic algorithms sensitivity from 73.6% (95% CI 67.1–79.3%) up to 88.1% (95% CI 82.8–91.9%). This increase was highest when molecular assays were used as add-on testing following negative smear microscopy. As add-on testing, GeneXpert MTB/RIF® and Loopamp MTBC Detection Kit® respectively improved case detection by 23.8 and 21.2% ($p < 0.05$).

Conclusion

Including GeneXpert MTB/RIF® or Loopamp MTBC Detection Kit® molecular assays for TB detection on sputum samples from presumptive TB cases can significantly increase case notification in TB diagnostic centers. The TB case detection rate is further increased when those tests are use as second-line follow-on testing following negative smear microscopy results. A country wide scale-up and digital integration of molecular-based TB diagnosis assays shows promises for TB control in Madagascar.

Diagnostic accuracy of loop-mediated isothermal amplification assay for extra-pulmonary tuberculosis in Indian population

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– Journal of Microbiological Methods 158 (2019) 59–65–

Abstract

Background

Confirmatory diagnosis of extra-pulmonary tuberculosis remains a true challenge owing to difficulty in procuring appropriate specimen, inefficient laboratory methods and paucibacillary nature of infection. These obstructions become all the very difficult in pediatric EPTB cases, due to non-specific clinical signs and symptoms, low sensitivity of smear microscopy and culture, lack of awareness among clinicians, etc.

Aim of the study

The present study aimed to evaluate the diagnostic accuracy of rapid and cost-effective loopmediated isothermal amplification (LAMP) assay for EPTB diagnosis in children.

Methods

A total of 154 cases were analyzed by EPTB-site smear microscopy, culture, PCRs for IS6110, MPB64 & Pab genes, nested PCR and LAMP assay. Single-gene PCRs were performed by custom-synthesized primers. Nested PCR was performed using the 3B BIOTUB Kit and the LAMP assay was done using the Nu-LAMP TB kit.

Results

We observed that the molecular tests displayed 4-fold higher positivity rate (minimum 46%) in comparison to the microbiological tests (maximum 11.03%). In contrast to the composite reference standard, LAMP assay was found to be 79.6% sensitive and 78% specific for EPTB diagnosis in childhood cases.

Conclusions

Our results indicate that LAMP assay is a promising technique for efficient diagnosis of EPTB in children belonging to resource-limited regions.

Detecting Mycobacterium tuberculosis using the loop-mediated isothermal amplification test in South Africa

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– INT J TUBERC LUNG DIS 21(10):1154–1160–

Abstract

Setting

In South Africa, KwaZulu-Natal is the epicentre of the human immunodeficiency virus (HIV) epidemic, where approximately 70% of people with tuberculosis (TB) are co-infected with HIV. Undiagnosed TB contributes to high mortality in HIV-infected patients. Delays in diagnosing TB and treatment initiation result in prolonged transmission and increased infectiousness.

Objective

To evaluate the Loopamp™ MTBC Detection kit (TB-LAMP; based on the loop-mediated isothermal amplification assay), smear microscopy and Xpert test with the gold standard of mycobacterial culture.

Methods

Sputum samples were collected from 705 patients with symptoms of pulmonary TB attending a primary health care clinic.

Results

The TB-LAMP assay had significantly higher sensitivity than smear microscopy (72.6% vs. 45.4%, P, 0.001), whereas specificity was slightly lower (99% vs. 96.8%, P¼0.05), but significantly higher than Xpert (92.9%, P¼0.004). There was no significant difference in sensitivity of smear-positive, culture-positive and smear-negative, culture-positive sputum samples using TB-LAMP vs. Xpert (respectively 95.9%/55.9% vs. 97.6%/66.1%; P ¼0.65, P ¼ 0.27). The positive predictive value of TB-LAMP was significantly higher than that of Xpert (87.5% vs. 77.0%; P ¼ 0.02), but similar to that of smear microscopy (94.2%; P ¼ 0.18). The negative predictive value was respectively 91.9%, 92.5% (P ¼ 0.73) and 83.1% (P ¼ 0.0001).

Conclusion

Given its ease of operability, the TB-LAMP assay could be implemented as a point-of-care test in primary health care settings, and contribute to reducing treatment waiting times and TB prevalence.

Comparative Evaluation of the Loop-Mediated Isothermal Amplification Assay for Detecting Pulmonary Tuberculosis

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– Ann Lab Med 2018;38:119-124–

Abstract

Background

Early detection of tuberculosis (TB) is challenging in resource-poor settings because of limited accessibility to molecular diagnostics. The aim of this study was to evaluate the performance of the loop-mediated isothermal amplification kit (TB-LAMP) for TB diagnosis compared with conventional and molecular tests.

Methods

A total of 290 consecutive sputum samples were collected from May till September, 2015. All samples were processed using the N-Acetyl-L-cysteine (NALC) NaOH method and tested by smear microscopy, solid and liquid culture, real-time PCR, and TB-LAMP.

Results

The sensitivity of TB-LAMP for smear-positive and smear-negative samples with culture positivity was 92.0% and 58.8%, respectively. TB-LAMP was positive in 14.9% of TB culture-negative samples; however, all those samples were also positive by real-time PCR. In addition, none of the samples positive for nontuberculous mycobacteria by culture were positive by TB-LAMP. The overall agreement between TB-LAMP and real-time PCR was good; however, the concordance rate was significantly lower for real-time PCR positive samples with Ct values of 30–35.

Conclusions

TB-LAMP could replace smear microscopy and increase TB diagnostic capacity when Xpert MTB/RIF is not feasible because of poor infrastructure.

Performance of loop-mediated isothermal amplification assay in the diagnosis of pulmonary tuberculosis in a high prevalence TB/HIV rural setting in Uganda

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– BMC Infectious Diseases (2018) 18:87–

Abstract

Background

The Smear microscopy lacks sensitivity especially in HIV co-infection, resulting in undiagnosed tuberculosis (TB) and high mortality. The loop-mediated isothermal amplification (TB-LAMP) assay can be staged with minimal infrastructure, is rapid, low cost and detection can be with the naked eye. We assessed feasibility and performance of Eiken TB-LAMP test at point-of-need in TB diagnosis in a high prevalence TB/HIV rural setting in Uganda.

Methods

From October 2013-February 2014, TB-LAMP testing was performed on sputum specimens from outpatient presumptive TB adults at a district hospital and two low-level health centers in Kiboga District where smear microscopy is the available routine diagnostic option. TB-LAMP was performed by a technician after a week of training in the district hospital. The technician had no prior experience in the technology. Samples from the low-level health centers were transported to the district hospital for TB-LAMP.

Results

Of the 233 presumptive TB (126 at hospital); 113 (48.5%) were HIV-infected; 129 (55%) male; median age 40 (IQR 30-53). Compared to MTB culture, overall sensitivity and specificity of TB-LAMP were 55.4% (95 CI 44.1-66.3) and 98.0% (95 CI 94.3-99.6) respectively. Among HIV-infected participants, TB-LAMP sensitivity and specificity were 52.3% (95 CI 36.7-67.5%) and 97.1% (95 CI 89.9-99.6) respectively; and 24.4% (95% CI 12.9-39.5) and 98.6% (95% CI 95.1-99.8) respectively among smear-negatives. TB-LAMP sensitivity and specificity were 62.2% (95% CI 44.8-77.5) and 97.8% (95% CI 92.1-99.7) in the hospital setting where central testing occurred compared to 50.0% (95% CI 34.9-65.1) and 98.4% (95% CI 91.2-100) respectively in low-level health centers where specimens were transported centrally.

Conclusions

In this high prevalence TB/HIV rural setting, TB-LAMP performs better than conventional smear microscopy in diagnosis of MTB among presumptive TB patients although the sensitivity is lower than that reported by the World Health Organization. TB-LAMP can easily be performed following a short training period and in absence of sophisticated infrastructure and expertise.

Comparative study of Loopamp™ *Mycobacterium tuberculosis* Complex Kit for Rapid Detection of *Mycobacterium tuberculosis* Complex in Cameroon

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– Biomed Biotechnol Res J 2018;2:46-52–

Abstract

Background

The most practical test for identifying tuberculosis (TB) in developing countries remains smear microscopy. However, due to its low sensitivity, a new point-of-care diagnostic method has been developed. The purpose of this study was to assess the performance of TB-Loop-mediated isothermal amplification (TB-LAMP) test on sputum samples of suspected TB cases.

Methods

Suspected pulmonary TB patients (527) from Jamot Hospital and without any history of anti-TB treatment were consecutively included in the study. Smear microscopy, TB-LAMP, GeneXpert® MTB/RIF, and liquid culture using BACTEC 960 Mycobacteria Growth Indicator Tube (MGIT) were performed on sputum samples collected from these patients. The sensitivity and specificity of TB-LAMP were compared with smear microscopy and GeneXpert® MTB/RIF. MGIT culture was the gold standard.

Results

TB-LAMP and smear microscopy showed sensitivities of 82.6% (95% confidence interval [CI], 76.9–87.2) and 53.6% (95% CI, 46.8–60.3), respectively, and specificities of 96.0% (95% CI, 93.2–97.7) and 99.0% (95% CI, 97.1–99.7), respectively. The sensitivity and specificity of TB-LAMP were similar to GeneXpert®, (89.9%; 95% CI, 85.0–93.3 and 97.0%; 95% CI, 94.4–98.4).

Conclusions

TB-LAMP is more sensitive than currently used microscopy. It presents a favorable diagnostic tool for TB in peripheral laboratories with limited equipment, such as those in developing countries.

Comparison of TB-LAMP, GeneXpert MTB/RIF and culture for diagnosis of pulmonary tuberculosis in The Gambia

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– J Infect; 72(3): 332-337–

Abstract

Background

Diagnosis of tuberculosis (TB) remains difficult, particularly in resource-limited settings. The development of nucleic acid-based tests for detection of *Mycobacterium tuberculosis* complex (MTBC) has significantly increased sensitivity compared to conventional smear microscopy and provides results within a matter of hours compared to weeks for the current gold-standard, liquid culture.

Methods

In this study we performed side-by-side comparison of mycobacterial detection assays on sputum samples from 285 subjects presenting with symptoms suggestive of TB in The Gambia and a cross-sectional cohort of 156 confirmed TB patients with a median of 2 months of treatment. A novel assay, Loop-Mediated Amplification test for TB (TB-LAMP), was compared to smear microscopy, MGIT culture and GeneXpert MTB/RIF for all samples.

Results

When culture was used as the reference standard, we found an overall sensitivity for TB-LAMP of 99% (95% CI: 94.5-99.8) and specificity of 94% (95% CI: 89.3-96.7). When latent class analysis was performed, TB-LAMP had 98.6% (95% CI: 95.9-100) sensitivity and 99% (95% CI: 98.2-100) specificity compared to 91.1% (95% CI: 86.1-96) sensitivity and 100% (95% CI: 98.2-100) specificity for MGIT culture. GeneXpert had the highest sensitivity 99.1% (95% CI: 97.1-100) but the lowest specificity 96% (95% CI: 92.6-98.3). Both TB-LAMP and GeneXpert showed high sensitivity and specificity regardless of age or strain of infection.

Conclusions

Our findings show the diagnostic utility of both GeneXpert and TB-LAMP in The Gambia. Whilst TB-LAMP requires less infrastructure, it is unable to detect drug-resistant patterns and therefore would be most suitable as a screening test for new TB cases in peripheral health clinics.

Rapid Laboratory Diagnosis of Pulmonary Tuberculosis

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– Int J Mycobacteriol 2017;6:296-301–

Abstract

Background

Tuberculosis (TB) ranks as the second leading cause of death from an infectious disease worldwide. Early diagnosis of Mycobacterium tuberculosis in clinical samples becomes important in the control of TB both for the treatment of patients and for curbing of disease transmission to the others in the community. The study objective was to perform Ziehl-Neelsen (ZN) staining, fluorochrome staining, line probe assay (LPA), and loop-mediated isothermal amplification (LAMP) assay for rapid detection of pulmonary TB (PTB) and to compare the results of LPA and LAMP in terms of sensitivity, specificity, and turnaround time.

Methods

A total of 891 sputum samples from clinically diagnosed/suspected cases of TB were subjected to ZN and fluorochrome staining. Smear positive samples were subjected to LPA, and smear negative were cultured on Lowenstein-Jensen media. A total of 177 samples were subjected to liquid culture and LAMP. Conventional culture was considered as "gold standard" for calculation of parameters.

Results

Light-emitting diode fluorescence microscopy had the same sensitivity as ZN with similar high specificity. LPA was performed on 548 sputum samples which includes 520 smear positive and 28 smear negative culture positive samples and multidrug-resistant TB was detected in 32.64%. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of TB-LAMP on direct sputum samples was found to be 98.96%, 95%, 96%, and 98.70%, respectively, when compared with ZN smear microscopy. By considering culture as "gold standard," LAMP showed a sensitivity, specificity, PPV, and NPV of 98.94%, 96.34%, 96.90%, and 98.75%, respectively. The sensitivity and PPV of TB-LAMP were 98.97% and 96%, respectively, when compared with LPA.

Conclusions

A successful rapid laboratory diagnosis of PTB is possible when one combines the available methodology of microscopy, culture as well as molecular techniques. The LAMP assay was found to be simple, self-contained, and efficacious for early diagnosis of suspected cases of PTB with advantages of having a high throughput, no requirements of sophisticated equipment, and complex biosafety facilities.

Comparison of loop-mediated isothermal amplification assay and smear microscopy with culture for the diagnostic accuracy of tuberculosis

Baye Gelaw, Yitayal Shiferaw, Marta Alemayehu and Abate Assefa Bashaw

– BMC Infect Dis. 2017; 17: 79–

Abstract

Background

Tuberculosis (TB) caused by *Mycobacterium tuberculosis* is one of the leading causes of death from infectious diseases worldwide. Sputum smear microscopy remains the most widely available pulmonary TB diagnostic tool particularly in resource limited settings. A highly sensitive diagnostic with minimal infrastructure, cost and training is required. Hence, we assessed the diagnostic performance of Loop-mediated isothermal amplification (LAMP) assay in detecting *M.tuberculosis* infection in sputum sample compared to LED fluorescent smear microscopy and culture.

Method

A cross-sectional study was conducted at the University of Gondar Hospital from June 01, 2015 to August 30, 2015. Pulmonary TB diagnosis using sputum LED fluorescence smear microscopy, TB-LAMP assay and culture were done. A descriptive analysis was used to determine demographic characteristics of the study participants. Analysis of sensitivity and specificity for smear microscopy and TB-LAMP compared with culture as a reference test was performed. Cohen's kappa was calculated as a measure of agreement between the tests.

Results

A total of 78 pulmonary presumptive TB patients sputum sample were analyzed. The overall sensitivity and specificity of LAMP were 75 and 98%, respectively. Among smear negative sputum samples, 33.3% sensitivity and 100% specificity of LAMP were observed. Smear microscopy showed 78.6% sensitivity and 98% specificity. LAMP and smear in series had sensitivity of 67.8% and specificity of 100%. LAMP and smear in parallel had sensitivity of 85.7% and specificity of 96%. The agreement between LAMP and fluorescent smear microscopy tests was very good ($\kappa = 0.83$, *P*-value ≤0.0001).

Conclusions

TB-LAMP showed similar specificity but a slightly lower sensitivity with LED fluorescence microscopy. The specificity of LAMP and smear microscopy in series was high. The sensitivity of LAMP was insufficient for smear negative sputum samples.

Clinical Performances of Pure TB-Lamp Kit for *M. tuberculosis* Complex Detection in Sputum Samples

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– J of Tuberculosis Research, 2016, 5, 129-138–

Abstract

Tuberculosis represents a main concern for public health worldwide. In poor countries, the most prevalent method for bacteriological confirmation remains Smear Sputum Microscopy (SSM). This study objective was to assess clinical performances of Loop Mediated Isothermal Amplification for TB detection (Lamp-TB). Sputum of patients presenting symptoms consistent with tuberculosis were collected according to the National Tuberculosis Control Programme guidelines in Centre Antituberculeux de Yopougon. SSM after Ziehl-Neelsen staining and TB-Lamp were blindly performed with spot sputum specimen. Samples, transported at Institut Pasteur de Cote d'Ivoire were decontaminated according to N-acetyl-L-cystein (NALC) method. In Mycobacteria Growth Indicator Tube (MGIT), 500 μl of pellet were inoculated and incubated in MGIT 960 instrument. MPT64 antigen was detected on positive culture. Of 500 patients enrolled, 469 were included. Clinical isolates of M. tuberculosis Complex were detected for 157 (33.5%). Comparatively to culture, Sensitivity and Specificity of SSM were 86% (95% Confidence interval (CI): 81% - 91%) 96% (95%IC: 94% - 98%) respectively. TB-Lamp Sensitivity was 92% (95%CI: 88% - 96%), and Specificity 94% (95%CI: 91% - 97%). Positive Predictive Value of SSM and TB-Lamp was 91.8% and 88.8% respectively. Negative Predictive Value of TB-Lamp assay was 95.7% whereas this of SSM was 93.3%. Positive Likelihood Ratio was 15.3 for TB-Lamp and 21.5 for SSM 21.5 whereas negative Likelihood of TB-Lamp was lower than SSM. Active tuberculosis was detected in162/469 (34.5%) with TB-Lamp and 147 (31.3%) with SSM. TB-Lamp assay performances estimated from sputum samples may improve detection of active TB cases in routine.

Feasibility and Operational Performance of Tuberculosis Detection by Loop-Mediated Isothermal Amplification Platform in Decentralized Settings: Results from a Multicenter Study

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– J Clin Microbiol. 2016 Aug;54(8):1984-91–

Abstract

Currently available nucleic acid amplification platforms for tuberculosis (TB) detection are not designed to be simple or inexpensive enough to implement in decentralized settings in countries with a high burden of disease. The loop-mediated isothermal amplification platform (LAMP) may change this. We conducted a study in adults with symptoms suggestive of TB in India, Uganda, and Peru to establish the feasibility of using TB-LAMP (Eiken Chemical Co.) in microscopy laboratories compared with using smear microscopy against a reference standard of solid and liquid cultures. Operational characteristics were evaluated as well. A total of 1,777 participants met the eligibility criteria and were included for analysis. Overall, TB-LAMP sensitivities among culture-positive samples were 97.2% (243/250; 95% confidence interval [CI], 94.3% to 98.2%) and 62.0% (88/142; 95% CI, 53.5% to 70.0%) for smear-positive and smear-negative TB, respectively, but varied widely by country and operator. Specificities ranged from 94.5% (446/472; 95% CI, 92.0% to 96.4%) to 98.0% (350/357; 95% CI, 96.0% to 99.2%) by country. A root cause analysis identified high temperatures, high humidity, and/or low reaction volumes as possible causes for false-positive results, as they may result in nonspecific amplification. The study was repeated in India with training focused on vulnerable steps and an updated protocol; 580 participants were included for analysis. Specificity in the repeat trial was 96.6% (515/533; 95% CI, 94.7% to 97.9%). To achieve acceptable performance of LAMP at the microscopy center level, significant training and infrastructure requirements are necessary.

Accuracy of LAMP-TB Method for Diagnosing Tuberculosis in Haiti

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– Jap J Infect Dis; 69(6): 488-492–

Abstract

The procedure of ultra-rapid extraction (PURE) and loop-mediated isothermal amplification for tuberculosis (LAMP-TB) is a simple and rapid manual tuberculosis diagnostic with medium-throughput capability. Because of its simplicity, this method could be useful in resource-limited conditions such as microscopy centers in developing countries. This study was conducted to evaluate the clinical performance of this method in a point-of-care setting. The performance was compared to that of smear microscopy and liquid culture in a hospital laboratory in Haiti, which is considered a representative facility for the implementation of this method. The sensitivity, based on culture-positivity, was 86% (95% confidence interval: 81.3-90.3%) and that based on the smear-negative and culture-positive results was 51% (38.7-63.5%). The specificity based on sample negativity for both smear and culture was 98.4% (96.8-99.2). These results are nearly equivalent to those of a clinical study performed in Japan and are comparable with those of other nucleic acid amplification methods. Thus, approximately 18% more tuberculosis patients could be identified by adding the LAMP-TB method to routine smear microscopy in field settings in Haiti. In addition, it is suggested that local technicians could perform LAMP-TB after only short-term training.

Diagnostic Accuracy of the PURE-LAMP Test for Pulmonary Tuberculosis at the County-Level Laboratory in China

Xichao Ou, Qiang Li, Hui Xia, Yu Pang, Shengfen Wang, Bing Zhao, Yuanyuan Song, Yang Zhou, Yang Zheng, Zhijian Zhang, Zhiying Zhang, Junchen Li, Haiyan Dong, Jack Zhang, Kai Man Kam, Junying Chi, Shitong Huan, Daniel P. Chin, Yanlin Zhao

– PLoS One; 9(5): e94544–

Abstract

Background

Early and effective detection of *Mycobacterium tuberculosis* (MTB), particularly in smear-negative tuberculosis (TB), is a priority for global TB control. Loop-mediated isothermal amplification with a procedure for ultra rapid DNA extraction (PURE-LAMP) can detect TB in sputum samples rapidly and with high sensitivity and specificity. However, the PURE-LAMP test has not been effectively evaluated, especially in resource-limited laboratories. In this study, we evaluated the performance of the PURE-LAMP test for TB detection in TB suspects from two county-level TB dispensaries in China.

Methods

From April 2011 to February 2012, patients with suspected TB were continuously enrolled from two county-level TB laboratories in China. Three sputum samples (spot, night, and morning sputum) were collected from each recruited patient. Detection of MTB by PURE-LAMP was compared to a reference standard L-J culture. The results showed that the sensitivity of the PURE-LAMP test based on spot sputum for MTB detection was 70.67%, while the sensitivity of the PURE-LAMP test based on spot sputum for MTB detection in smear positive and culture positive patients and smear negative and culture positive patients was 92.12% and 53.81%, respectively. The specificity of PURE-LAMP based on spot sputum for MTB detection was 98.32%. The sensitivity and specificity of the PURE-LAMP test based on three sputa combination for MTB detection was 88.80% and 96.86%, respectively. The results also showed that the PURE-LAMP test had a significantly lower contamination rate than did solid culture.

Conclusions

The study suggested that, in peripheral-level TB laboratories in China, the PURE-LAMP test showed high sensitivity and specificity for TB detection in TB suspects, making it a more effective, rapid, and safe method worthy of broader use in the future.

Application in Reference Centers

Performance of the TB-LAMP diagnostic assay in reference laboratories: Results from a multicentre study

Thu Hang Pham, Jonathan Peter, Fernanda C.Q. Mello, Tommy Parraga, Nguyen Thi Ngoc Lan, Pamela Nabeta, Eloise Valli, Tatiana Caceres, Keertan Dheda, Susan E. Dorman, Doris Hillemann, Christen M. Gray, Mark D. Perkins
– International Journal of Infectious Diseases 68 (2018) 44–49–

Abstract

Objective

Loop To evaluate the diagnostic performance of TB-LAMP, a manual molecular tuberculosis (TB) detection method, and provide comparison to the Xpert MTB/RIF assay.

Methods

In a large multicentre study, two sputum samples were collected from participants with TB symptoms in reference laboratories in Peru, South Africa, Brazil, and Vietnam. Each sample was tested with TB-LAMP. The reference standard consisted of four direct smears, four cultures, and clinical and radiological findings. Individuals negative on conventional tests were followed up after 8 weeks. The Xpert MTB/RIF assay was performed on fresh or frozen samples as a molecular test comparison.

Results

In A total of 1036 adults with suspected TB were enrolled. Among 375 culture-confirmed TB cases with 750 sputum samples, TB-LAMP detected 75.6% (95% confidence interval (CI) 71.8–79.4%), including 97.9% (95% CI 96.4–99.4%) of smear-positive TB samples and 46.6% (95% CI 40.6–52.7%) of smear-negative TB samples. Specificity in 477 culture-negative participants not treated for TB (954 sputum samples) was 98.7% (95% CI 97.9–99.6%). TB-LAMP test results were indeterminate in 0.3% of cases.

Conclusions

Both TB-LAMP detects nearly all smear-positive and half of smear-negative TB cases and has a high specificity when performed in reference laboratories. Performance was similar to the Xpert MTB/RIF assay.

Cost-Utility Analysis of Molecular Testing for Tuberculosis Diagnosis in Suspected Pulmonary Tuberculosis in Thailand

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Clinico Economics and Outcomes Research 2022:14

Abstract

Purpose

Given the lack of economic evaluation study of molecular testing in Thailand, this study aimed to evaluate the cost-utility of molecular testing algorithms including Xpert MTB/RIF and the loop-mediated isothermal amplification (TB-LAMP) in the general population suspected of having pulmonary TB based on a societal perspective.

Methods

hybrid decision tree Markov model using a 1-month cycle length was used to evaluate costs and outcomes of five TB diagnostic algorithms: 1) sputum smear microscopy (SSM) with culture and drug susceptibility testing (DST), 2) Xpert MTB/RIF addon,3) Xpert MTB/RIF initial, 4) TB-LAMP add-on, and 5) TB-LAMP initial during a lifetime period. All costs were calculated in 2021 Baht, and results were presented as an incremental cost-effectiveness ratio (ICER) for molecular testing compared with SSM with culture. One-way sensitivity and probability analyses were used to evaluate uncertainty input parameters.

Results

TB-LAMP was less expensive overall (6565 Baht) than Xpert MTB/RIF (7010 Baht) and SSM with culture (6845 Baht). Molecular testing was projected to improve quality adjusted life year (QALY) by 0.53 to 0.94 years. In comparison to SSM with culture and DST, providing an initial TB-LAMP test was the most preferred choice. Xpert MTB/RIF Initial had the lowest ICER (197 Baht per QALY gained), followed by TB-LAMP Add-on (993 Baht per QALY gained) and Xpert MTB/RIF Add-on (3940 Baht perQALY gained). One-way sensitivity analysis uncovered that sensitivity of TB-LAMP was greater than that of other parameters.

Conclusions

Providing molecular testing including Xpert MTB/RIF and TB-LAMP as either initial or add-on test for TB diagnosis was more cost-effective than SSM with culture and DST in the general population with suspected pulmonary TB in Thailand. Our study could provide useful evidence to policymakers advocating for inclusion of molecular testing in the universal health coverage benefit package in Thailand.

Comparison to Smear Microscopy

Evaluation of Loopamp Assay for the Diagnosis of Pulmonary Tuberculosis in Cambodia

Sokleaph Cheng, Sok Heng Pheng, Seiha Heng, Guy B. Marks, Anne-Laure Bañuls, Tan Eang Mao, Alexandra Kerléguer

– Hindawi. BioMed Research International. Volume 2020, Article ID 6828043 –

Abstract

The Loopamp™ MTBC kit (TB-LAMP) is recommended by WHO for Mycobacterium tuberculosis complex detection in lowincome countries with a still low drug-resistant tuberculosis (TB) rate. This study is aimed at testing its feasibility in Cambodia on sputa collected from presumptive tuberculosis patients. 499 samples were tested at a smear microscopy center and 200 at a central-level mycobacteriology laboratory. Using mycobacterial cultures as reference, TB-LAMP results were compared with those of LED fluorescent microscopy (LED-FM) and Xpert® MTB/RIF. At the microscopy center, TB-LAMP sensitivity was higher than that of LED-FM (81.5% [95% CI, 74.5-87.6] versus 69.4% [95% CI, 62.2-76.6]), but lower than that of the Xpert assay (95.5% [95% CI 92.3-98.8]). At the central-level laboratory, TB-LAMP sensitivity (92.8% [95% CI, 87.6-97.9]) was comparable to that of Xpert (90.7% [95% CI, 85.0-96.5]) using stored sample. No significant difference in terms of specificity between TB-LAMP and Xpert assays was observed in both study sites. In conclusion, our data demonstrate that TB-LAMP could be implemented at microscopy centers in Cambodia to detect TB patients. In addition, TB-LAMP can be a better choice to replace smear microscopy for rapid TB diagnosis of new presumptive TB patients, in settings with relative low prevalence of drug-resistant TB and difficulties to implement Xpert assay.

Loop mediated isothermal amplification for the rapid diagnosis of pulmonary tuberculosis

Ganga Raju Krishna, Chithra Valsan, Sathiavathy K. A.

– *J. Evolution Med. Dent. Sci. 2019;8(29):2338-2341*–

Abstract

Background

Control of tuberculosis is often challenged by diagnostic methods which are time consuming, often less sensitive, expensive and inaccessible to most patients especially in the developing countries. The characteristics of loop-mediated isothermal amplification (LAMP) method make it a promising platform for the molecular detection of tuberculosis in developing countries. We wanted to evaluate the loop mediated isothermal amplification method for the rapid diagnosis of pulmonary tuberculosis (PTB) in low resource settings.

Methods

We conducted an observational study in the Microbiology department for a period of eighteen months on sputum samples collected from suspected cases of pulmonary tuberculosis which satisfied the inclusion as well as exclusion criteria. All these samples after processing were subjected to smear microscopy by acid fast staining, culture on Lowenstein-Jensen (LJ) medium and LAMP assay and results were compared to derive sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).

Results

A total of 110 samples were included in the study. Using culture as the reference standard, we found that the sensitivity and specificity for TB-LAMP assay were 98.3% and 98.03% respectively and PPV and NPV were 98.3% and 98.03% respectively. The AFB staining had a sensitivity of 91.5% and specificity of 98%.

Conclusions

Hence LAMP method is a reliable test for the diagnosis of tuberculosis which can be suited to resource limited settings. The method has very good positive and negative predictive value for pulmonary samples. It is a rapid technique when compared to conventional culture and simple and less expensive than other molecular based methods. Therefore, it can be applied as a point of care testing (POCT) method in resource limited settings.

Feasibility and Performance of Loop-Mediated Isothermal Amplification Assay in the Diagnosis of Pulmonary Tuberculosis in Decentralized Settings in Eastern China

Zhongdong Wang, Haiyan Sun, Zhisheng Ren, Bai Xue,Jie Lu, Huaqiang Zhang

– BioMed Research International (2019) 19 –

Abstract

Early diagnosis is essential for the control and prevention of tuberculosis (TB). The objective of this study was to investigate the feasibility and performance of loop-mediated isothermal amplification (LAMP) in the diagnosis of pulmonary TB in county-level microscopy centers in Qingdao, Eastern China. A total of 523 presumptive TB patients were consecutively recruited between July 2017 and April 2018, and 22 patients were excluded from the analysis. Of 102 culture-positive cases, TB-LAMP identified 91 cases, demonstrating a sensitivity of 89.2%. In comparison, the sensitivity of routine smear microscopy was 69.6% (71/102), which was significantly lower than that of TB-LAMP (P=0.001). In addition, TB-LAMP sensitivities in smear-positive and smear-negative samples were 98.6% and 67.7%, respectively. In conclusion, our data demonstrate that TB-LAMP outperforms conventional smear microscopy in TB diagnosis, which could be used as an alternative method for smear microscopy in resource-limited settings in China.

Performance and impact of GeneXpert MTB/RIF® and Loopamp MTBC Detection Kit® assays on tuberculosis case detection in Madagascar

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– BMC Infectious Diseases (2019) 19:542–

Abstract

Background

Tuberculosis rapid molecular assays, including GeneXpert MTB/RIF® and Loopamp MTBC Detection Kit®, are highly sensitive and specific. Such performance does not automatically translate in improved disease control and highly depends on their use, local epidemiology and the diagnostic algorithms they're implemented within. We evaluate the performance of both assays and assess their impact on additional cases notification when implemented within WHO recommended tuberculosis diagnostic algorithms in Madagascar.

Methods

Five hundred forty eight presumptive pulmonary tuberculosis patients were prospectively recruited between November 2013 and December 2014 in Antananarivo, Madagascar, a high TB incidence sub-Saharan African urban setting. Both molecular assays were evaluated as first line or add-on testing following negative smear microscopy. Based on locally defined assay performance characteristics we measure the impact of both assays and WHO-recommended diagnostic algorithms on additional tuberculosis case notifications.

Results

High sensitivity and specificity was confirmed for both GeneXpert MTB/RIF® (86.6% (95% CI 81.1–90.7%) and 97.4% (95% CI 94.9–98.8%)) and Loopamp MTBC Detection Kit® (84.6% (95% CI 78.9–89.0%) and 98.4% (95% CI96.2–99.4%)). Implementation of GeneXpert MTB/RIF® and Loopamp MTBC Detection Kit® increased tuberculosis diagnostic algorithms sensitivity from 73.6% (95% CI 67.1–79.3%) up to 88.1% (95% CI 82.8–91.9%). This increase was highest when molecular assays were used as add-on testing following negative smear microscopy. As add-on testing, GeneXpert MTB/RIF® and Loopamp MTBC Detection Kit® respectively improved case detection by 23.8 and 21.2% ($p < 0.05$).

Conclusion

Including GeneXpert MTB/RIF® or Loopamp MTBC Detection Kit® molecular assays for TB detection on sputum samples from presumptive TB cases can significantly increase case notification in TB diagnostic centers. The TB case detection rate is further increased when those tests are use as second-line follow-on testing following negative smear microscopy results. A country wide scale-up and digital integration of molecular-based TB diagnosis assays shows promises for TB control in Madagascar.

Detecting *Mycobacterium tuberculosis* using the loop-mediated isothermal amplification test in South Africa

S. Reddy, S. Ntoyanto, Y. Sakadavan, T. Reddy, S. Mahomed, M. Dlamini, B. Spooner, G. Ramjee, A. Coutsoudis, N. Ngomane, K. Naidoo, K. Mlisana, P. Kiepiela

– INT J TUBERC LUNG DIS 21(10):1154–1160

Abstract

Setting

In South Africa, KwaZulu-Natal is the epicentre of the human immunodeficiency virus (HIV) epidemic, where approximately 70% of people with tuberculosis (TB) are co-infected with HIV. Undiagnosed TB contributes to high mortality in HIV-infected patients. Delays in diagnosing TB and treatment initiation result in prolonged transmission and increased infectiousness.

Objective

To evaluate the Loopamp™ MTBC Detection kit (TB-LAMP; based on the loop-mediated isothermal amplification assay), smear microscopy and Xpert test with the gold standard of mycobacterial culture.

Methods

Sputum samples were collected from 705 patients with symptoms of pulmonary TB attending a primary health care clinic.

Results

The TB-LAMP assay had significantly higher sensitivity than smear microscopy (72.6% vs. 45.4%, P, 0.001), whereas specificity was slightly lower (99% vs. 96.8%, P¼0.05), but significantly higher than Xpert (92.9%, P¼0.004). There was no significant difference in sensitivity of smear-positive, culture-positive and smear-negative, culture-positive sputum samples using TB-LAMP vs. Xpert (respectively 95.9%/55.9% vs. 97.6%/66.1%; P ¼0.65, P ¼ 0.27). The positive predictive value of TB-LAMP was significantly higher than that of Xpert (87.5% vs. 77.0%; P ¼ 0.02), but similar to that of smear microscopy (94.2%; P ¼ 0.18). The negative predictive value was respectively 91.9%, 92.5% (P ¼ 0.73) and 83.1% (P ¼ 0.0001).

Conclusion

Given its ease of operability, the TB-LAMP assay could be implemented as a point-of-care test in primary health care settings, and contribute to reducing treatment waiting times and TB prevalence.

Comparative Evaluation of the Loop-Mediated Isothermal Amplification Assay for Detecting Pulmonary Tuberculosis

Chang-Ki Kim, Eun A Cho, Dong Mi Shin, Sung Won Choi and So Youn Shin

– Ann Lab Med 2018;38:119-124–

Abstract

Background

Early detection of tuberculosis (TB) is challenging in resource-poor settings because of limited accessibility to molecular diagnostics. The aim of this study was to evaluate the performance of the loop-mediated isothermal amplification kit (TB-LAMP) for TB diagnosis compared with conventional and molecular tests.

Methods

A total of 290 consecutive sputum samples were collected from May till September, 2015. All samples were processed using the N-Acetyl-L-cysteine (NALC) NaOH method and tested by smear microscopy, solid and liquid culture, real-time PCR, and TB-LAMP.

Results

The sensitivity of TB-LAMP for smear-positive and smear-negative samples with culture positivity was 92.0% and 58.8%, respectively. TB-LAMP was positive in 14.9% of TB culture-negative samples; however, all those samples were also positive by real-time PCR. In addition, none of the samples positive for nontuberculous mycobacteria by culture were positive by TB-LAMP. The overall agreement between TB-LAMP and real-time PCR was good; however, the concordance rate was significantly lower for real-time PCR positive samples with Ct values of 30–35.

Conclusion

In TB-LAMP could replace smear microscopy and increase TB diagnostic capacity when Xpert MTB/RIF is not feasible because of poor infrastructure.

Performance of loop-mediated isothermal amplification assay in the diagnosis of pulmonary tuberculosis in a high prevalence TB/HIV rural setting in Uganda

Lydia Nakiyingi, Prossy Nakanwagi, Jessica Briggs, Tifu Agaba, Frank Mubiru, Mark Mugenyi, Willy Ssengooba, Moses L. Joloba and Yukari C. Manabe

– BMC Infectious Diseases (2018) 18:87–

Abstract

Background

The Smear microscopy lacks sensitivity especially in HIV co-infection, resulting in undiagnosed tuberculosis (TB) and high mortality. The loop-mediated isothermal amplification (TB-LAMP) assay can be staged with minimal infrastructure, is rapid, low cost and detection can be with the naked eye. We assessed feasibility and performance of Eiken TB-LAMP test at point-of-need in TB diagnosis in a high prevalence TB/HIV rural setting in Uganda.

Methods

From October 2013-February 2014, TB-LAMP testing was performed on sputum specimens from outpatient presumptive TB adults at a district hospital and two low-level health centers in Kiboga District where smear microscopy is the available routine diagnostic option. TB-LAMP was performed by a technician after a week of training in the district hospital. The technician had no prior experience in the technology. Samples from the low-level health centers were transported to the district hospital for TB-LAMP.

Results

Of the 233 presumptive TB (126 at hospital); 113 (48.5%) were HIV-infected; 129 (55%) male; median age 40 (IQR 30-53). Compared to MTB culture, overall sensitivity and specificity of TB-LAMP were 55.4% (95 CI 44.1-66.3) and 98.0% (95 CI 94.3-99.6) respectively. Among HIV-infected participants, TB-LAMP sensitivity and specificity were 52.3% (95 CI 36.7-67.5%) and 97.1% (95 CI 89.9-99.6) respectively; and 24.4% (95% CI 12.9-39.5) and 98.6% (95% CI 95.1-99.8) respectively among smear-negatives. TB-LAMP sensitivity and specificity were 62.2% (95% CI 44.8-77.5) and 97.8% (95% CI 92.1-99.7) in the hospital setting where central testing occurred compared to 50.0% (95% CI 34.9-65.1) and 98.4% (95% CI 91.2-100) respectively in low-level health centers where specimens were transported centrally.

Conclusions

In this high prevalence TB/HIV rural setting, TB-LAMP performs better than conventional smear microscopy in diagnosis of MTB among presumptive TB patients although the sensitivity is lower than that reported by the World Health Organization. TB-LAMP can easily be performed following a short training period and in absence of sophisticated infrastructure and expertise.

Comparative study of Loopamp™ *Mycobacterium tuberculosis* Complex Kit for Rapid Detection of *Mycobacterium tuberculosis* Complex in Cameroon

Valerie Flore Donkeng Donfack, Laure Ngando, Eric Walter Yone Pefura, Dieudonné Shubesi Che, Ghislaine Ateba, Jean Joel Rim Bigna, Jean Louis Abena Foe, Christopher Kuaban, Sara Eyangoh

– Biomed Biotechnol Res J 2018;2:46-52–

Abstract

Background

The most practical test for identifying tuberculosis (TB) in developing countries remains smear microscopy. However, due to its low sensitivity, a new point-of-care diagnostic method has been developed. The purpose of this study was to assess the performance of TB-Loop-mediated isothermal amplification (TB-LAMP) test on sputum samples of suspected TB cases.

Methods

Suspected pulmonary TB patients (527) from Jamot Hospital and without any history of anti-TB treatment were consecutively included in the study. Smear microscopy, TB-LAMP, GeneXpert® MTB/RIF, and liquid culture using BACTEC 960 Mycobacteria Growth Indicator Tube (MGIT) were performed on sputum samples collected from these patients. The sensitivity and specificity of TB-LAMP were compared with smear microscopy and GeneXpert® MTB/RIF. MGIT culture was the gold standard.

Results

TB-LAMP and smear microscopy showed sensitivities of 82.6% (95% confidence interval [CI], 76.9–87.2) and 53.6% (95% CI, 46.8–60.3), respectively, and specificities of 96.0% (95% CI, 93.2–97.7) and 99.0% (95% CI, 97.1–99.7), respectively. The sensitivity and specificity of TB-LAMP were similar to GeneXpert®, (89.9%; 95% CI, 85.0–93.3 and 97.0%; 95% CI, 94.4–98.4).

Conclusions

TB-LAMP is more sensitive than currently used microscopy. It presents a favorable diagnostic tool for TB in peripheral laboratories with limited equipment, such as those in developing countries.

Comparison of loop-mediated isothermal amplification assay and smear microscopy with culture for the diagnostic accuracy of tuberculosis

Baye Gelaw, Yitayal Shiferaw, Marta Alemayehu and Abate Assefa Bashaw

– BMC Infect Dis. 2017; 17: 79–

Abstract

Background

Tuberculosis (TB) caused by *Mycobacterium tuberculosis* is one of the leading causes of death from infectious diseases worldwide. Sputum smear microscopy remains the most widely available pulmonary TB diagnostic tool particularly in resource limited settings. A highly sensitive diagnostic with minimal infrastructure, cost and training is required. Hence, we assessed the diagnostic performance of Loop-mediated isothermal amplification (LAMP) assay in detecting *M.tuberculosis* infection in sputum sample compared to LED fluorescent smear microscopy and culture.

Method

A cross-sectional study was conducted at the University of Gondar Hospital from June 01, 2015 to August 30, 2015. Pulmonary TB diagnosis using sputum LED fluorescence smear microscopy, TB-LAMP assay and culture were done. A descriptive analysis was used to determine demographic characteristics of the study participants. Analysis of sensitivity and specificity for smear microscopy and TB-LAMP compared with culture as a reference test was performed. Cohen's kappa was calculated as a measure of agreement between the tests.

Results

A total of 78 pulmonary presumptive TB patients sputum sample were analyzed. The overall sensitivity and specificity of LAMP were 75 and 98%, respectively. Among smear negative sputum samples, 33.3% sensitivity and 100% specificity of LAMP were observed. Smear microscopy showed 78.6% sensitivity and 98% specificity. LAMP and smear in series had sensitivity of 67.8% and specificity of 100%. LAMP and smear in parallel had sensitivity of 85.7% and specificity of 96%. The agreement between LAMP and fluorescent smear microscopy tests was very good ($\kappa = 0.83$, *P*-value ≤0.0001).

Conclusions

TB-LAMP showed similar specificity but a slightly lower sensitivity with LED fluorescence microscopy. The specificity of LAMP and smear microscopy in series was high. The sensitivity of LAMP was insufficient for smear negative sputum samples.

Comparison to Gene Xpert/RIF

Evaluation of TB-LAMP assay for detection of *Mycobacterium tuberculosis* in children

Rakesh Yadav, Priya Daroch, Parakriti Gupta, Pankaj Vaidya, Meenu Singh, Joseph L. Mathew, Sunil Sethi
– J Infect Dis. 2021;53(12), 942-946 –

Abstract

Background

Paediatric tuberculosis remains a major public health problem in developing countries. The diagnosis of tuberculosis in children is challenging because of the paucibacillary nature of the disease, due to which more sensitive nucleic acid amplification tests are needed. In this study, we determined the accuracy of WHO endorsed TB-LAMP assay for detection of *Mycobacterium tuberculosis* in children.

Methods

This was a prospective study conducted between March to July, 2018. A total of 177 samples from consecutive suspected TB children were received for microbiological diagnosis of TB. All tests for *Mycobacterium tuberculosis* detection were performed in parallel (smear microscopy, mycobacterial culture, Xpert MTB/RIF and TB-LAMP). The diagnostic accuracy of index test i.e. TB LAMP were determined using mycobacterial culture as a reference standard.

Results

Of the 177 samples, 2 (1.1%) were excluded from the study. Among 175 samples, TB-LAMP and Xpert MTB/RIF were positive in 27 (15.4%) and 25 (14.3%) samples, respectively. The sensitivity of both Xpert MTB/RIF and TB-LAMP was same, i.e. 84% (95%CI: 63.9–95.5%), when culture was considered as the reference standard. The specificity, positive predictive value and negative predictive value of TB-LAMP assay was 96% (95%CI: 91.5–98.5%), 77.8% (95%CI: 61.1–88.6%) and 97.3% (95%CI: 93.6–98.9%), respectively.

Conclusions

For the detection of *M. tuberculosis* in paediatric samples, TB-LAMP showed a sensitivity and specificity comparable to Xpert MTB/RIF.

Laboratory diagnosis of tuberculous meningitis in human immunodeficiency virus–seropositive patients: Correlation with the uniform case definition

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– S Afr J Infect Dis. 2020;35(1), a135 –

Abstract

Background

Laboratory confirmation of the diagnosis of tuberculous meningitis (TBM) has always been problematic. Using the uniform case definition suggested by Marais et al., we determined the sensitivity of a variety of laboratory tests.

Methods

Human immunodeficiency virus (HIV)–seropositive patients suspected of having subacute meningitis were included in the study. Using the uniform case definition, patients were divided into possible and probable cases of TBM. The following specific tests were done on the cerebrospinal fluid (CSF): layered Ziehl–Neelsen (ZN) staining, CSF culture and a panel of nucleic acid amplification tests (NAAT) consisting of the GenoType MTBDRplus assay, Cepheid Xpert MTB/RIF, the MTB Q-PCR Alert (Q-PCR) and the loop-mediated isothermal amplification (LAMP) assay. The sensitivity of each test was compared to the case definition and to each other.

Results

A total of 68 patients were evaluated. Using the uniform case definition only, without any of the specific laboratory tests, there were 15 probable cases (scores > 12) and 53 possible cases (scores 6–11) of TBM. When the uniform case definition was tested against any laboratory test, 12 of the 15 (80%) probable cases and 26 of the 53 (49.1%) possible cases had laboratory confirmation. When each test was compared to any other test, the sensitivities for the Xpert MTB/RIF, GenoType MTBDRplus, CSF culture, Q-PCR, LAMP and ZN layering were 63.2 (46.0–78.2), 76.3 (59.8–88.6), 65.7 (47.8–80.9), 81.1 (64.8–92.0), 70.3 (53.0–84.1) and 55.6 (38.1–72.1), respectively.

Conclusions

In this study, the GenoType MTBDRplus and the Q-PCR tests performed better than the Xpert MTB/RIF. Because the Xpert MTB/RIF is not good enough to 'rule out' TBM, a negative result should be followed up by another NAAT, such as the GenoType MTBDRplus or Q-PCR. The LAMP assay may be considered as the first test in resource-poor settings. At the time of the study, we did not have access to the Xpert MTB/RIF Ultra, which has now been recommended by the World Health Organization as the test of first choice. However, even this test has a similar limitation as the Xpert MTB/RIF, with two recent studies showing variable results.

Evaluation of Loopamp Assay for the Diagnosis of Pulmonary Tuberculosis in Cambodia

Sokleaph Cheng, Sok Heng Pheng, Seiha Heng, Guy B. Marks, Anne-Laure Bañuls, Tan Eang Mao, Alexandra Kerléguer

– Hindawi. BioMed Research International. Volume 2020, Article ID 6828043 –

Abstract

The Loopamp™ MTBC kit (TB-LAMP) is recommended by WHO for Mycobacterium tuberculosis complex detection in lowincome countries with a still low drug-resistant tuberculosis (TB) rate. This study is aimed at testing its feasibility in Cambodia on sputa collected from presumptive tuberculosis patients. 499 samples were tested at a smear microscopy center and 200 at a central-level mycobacteriology laboratory. Using mycobacterial cultures as reference, TB-LAMP results were compared with those of LED fluorescent microscopy (LED-FM) and Xpert® MTB/RIF. At the microscopy center, TB-LAMP sensitivity was higher than that of LED-FM (81.5% [95% CI, 74.5-87.6] versus 69.4% [95% CI, 62.2-76.6]), but lower than that of the Xpert assay (95.5% [95% CI 92.3-98.8]). At the central-level laboratory, TB-LAMP sensitivity (92.8% [95% CI, 87.6-97.9]) was comparable to that of Xpert (90.7% [95% CI, 85.0-96.5]) using stored sample. No significant difference in terms of specificity between TB-LAMP and Xpert assays was observed in both study sites. In conclusion, our data demonstrate that TB-LAMP could be implemented at microscopy centers in Cambodia to detect TB patients. In addition, TB-LAMP can be a better choice to replace smear microscopy for rapid TB diagnosis of new presumptive TB patients, in settings with relative low prevalence of drug-resistant TB and difficulties to implement Xpert assay.

Performance and impact of GeneXpert MTB/RIF® and Loopamp MTBC Detection Kit® assays on tuberculosis case detection in Madagascar

Niaina Rakotosamimanana, Simon Grandjean Lapierre, Vaomalala Raharimanga, Mamy Serge Raherison, Astrid M. Knoblauch, Antso Hasina Raherinandrasana, Andrianantenaina Rakotoson, Julio Rakotonirina, Voahangy Rasolofo

– BMC Infectious Diseases (2019) 19:542–

Abstract

Background

Tuberculosis rapid molecular assays, including GeneXpert MTB/RIF® and Loopamp MTBC Detection Kit®, are highly sensitive and specific. Such performance does not automatically translate in improved disease control and highly depends on their use, local epidemiology and the diagnostic algorithms they're implemented within. We evaluate the performance of both assays and assess their impact on additional cases notification when implemented within WHO recommended tuberculosis diagnostic algorithms in Madagascar.

Methods

Five hundred forty eight presumptive pulmonary tuberculosis patients were prospectively recruited between November 2013 and December 2014 in Antananarivo, Madagascar, a high TB incidence sub-Saharan African urban setting. Both molecular assays were evaluated as first line or add-on testing following negative smear microscopy. Based on locally defined assay performance characteristics we measure the impact of both assays and WHO-recommended diagnostic algorithms on additional tuberculosis case notifications.

Results

High sensitivity and specificity was confirmed for both GeneXpert MTB/RIF® (86.6% (95% CI 81.1–90.7%) and 97.4% (95% CI 94.9–98.8%)) and Loopamp MTBC Detection Kit® (84.6% (95% CI 78.9–89.0%) and 98.4% (95% CI96.2–99.4%)). Implementation of GeneXpert MTB/RIF® and Loopamp MTBC Detection Kit® increased tuberculosis diagnostic algorithms sensitivity from 73.6% (95% CI 67.1–79.3%) up to 88.1% (95% CI 82.8–91.9%). This increase was highest when molecular assays were used as add-on testing following negative smear microscopy. As add-on testing, GeneXpert MTB/RIF® and Loopamp MTBC Detection Kit® respectively improved case detection by 23.8 and 21.2% ($p < 0.05$).

Conclusion

Including GeneXpert MTB/RIF® or Loopamp MTBC Detection Kit® molecular assays for TB detection on sputum samples from presumptive TB cases can significantly increase case notification in TB diagnostic centers. The TB case detection rate is further increased when those tests are use as second-line follow-on testing following negative smear microscopy results. A country wide scale-up and digital integration of molecular-based TB diagnosis assays shows promises for TB control in Madagascar.

Cost and affordability analysis of TB-LAMP and Xpert MTB/RIF assays as routine diagnostic tests in peripheral laboratories in Malawi and Vietnam

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– J Glob Health Sci. 2019 Jun;1(1):e22

Abstract

Background

While the incidence of tuberculosis (TB) is declining globally, the rate of decline is far too slow to meet the 2035 end TB targets. Use of rapid molecular diagnostics that can be deployed in peripheral settings has the potential to address gaps in TB care cascade, improve case detection, and ultimately limit the on-going transmission of the disease.

Methods

We assessed the costs and affordability of 2 commercial nucleic acid amplification test (NAAT)—loop-mediated isothermal amplification assay for TB (TB-LAMP) and Xpert MTB/RIF (Xpert)—used at the peripheral laboratories in Malawi and Vietnam. Costs were assessed from the health service provider perspective using bottom-up method. Categorized documentation of resources uses for each diagnostic test was done using a standardized time-and-motion form directly observing each laboratory procedure. Affordability was assessed as a proportion of total first-year implementation and operational costs of respective diagnostics against the national TB program budget for 2014.

Results

Unit costs of TB-LAMP and Xpert varied depending on the daily test volumes and the test kit costs were the primary cost driver. Unused equipment capacity costs were also an important cost driver at low testing volumes and was more significant for Xpert. Weighted average per-test cost of nationwide implementation of respective diagnostics was between $14.37–$15.85 for TB-LAMP and $20.06–$26.86 for Xpert for Vietnam and Malawi. Both NAATs would account for a significant portion of or exceeded the national TB program budget if complete nationwide roll-out to peripheral laboratory were considered.

Conclusion

While TB-LAMP is a lower cost alternative to Xpert as an upfront NAAT for TB in peripheral settings, cost-utility against Xpert and other alternatives and optimized implementation strategies must be carefully evaluated through additional model-based studies to better inform policy and program decisions to expand the coverage of rapid diagnostics for TB.

Detecting *Mycobacterium tuberculosis* using the loop-mediated isothermal amplification test in South Africa

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– INT J TUBERC LUNG DIS 21(10):1154–1160

Abstract

Setting

In South Africa, KwaZulu-Natal is the epicentre of the human immunodeficiency virus (HIV) epidemic, where approximately 70% of people with tuberculosis (TB) are co-infected with HIV. Undiagnosed TB contributes to high mortality in HIV-infected patients. Delays in diagnosing TB and treatment initiation result in prolonged transmission and increased infectiousness.

Objective

To evaluate the Loopamp™ MTBC Detection kit (TB-LAMP; based on the loop-mediated isothermal amplification assay), smear microscopy and Xpert test with the gold standard of mycobacterial culture.

Methods

Sputum samples were collected from 705 patients with symptoms of pulmonary TB attending a primary health care clinic.

Results

The TB-LAMP assay had significantly higher sensitivity than smear microscopy (72.6% vs. 45.4%, P, 0.001), whereas specificity was slightly lower (99% vs. 96.8%, P¼0.05), but significantly higher than Xpert (92.9%, P¼0.004). There was no significant difference in sensitivity of smear-positive, culture-positive and smear-negative, culture-positive sputum samples using TB-LAMP vs. Xpert (respectively 95.9%/55.9% vs. 97.6%/66.1%; P ¼0.65, P ¼ 0.27). The positive predictive value of TB-LAMP was significantly higher than that of Xpert (87.5% vs. 77.0%; P ¼ 0.02), but similar to that of smear microscopy (94.2%; P ¼ 0.18). The negative predictive value was respectively 91.9%, 92.5% (P ¼ 0.73) and 83.1% (P ¼ 0.0001).

Conclusion

Given its ease of operability, the TB-LAMP assay could be implemented as a point-of-care test in primary health care settings, and contribute to reducing treatment waiting times and TB prevalence.

Performance of the TB-LAMP diagnostic assay in reference laboratories: Results from a multicentre study

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– International Journal of Infectious Diseases 68 (2018) 44–49–

Abstract

Objective

Loop To evaluate the diagnostic performance of TB-LAMP, a manual molecular tuberculosis (TB) detection method, and provide comparison to the Xpert MTB/RIF assay.

Methods

In a large multicentre study, two sputum samples were collected from participants with TB symptoms in reference laboratories in Peru, South Africa, Brazil, and Vietnam. Each sample was tested with TB-LAMP. The reference standard consisted of four direct smears, four cultures, and clinical and radiological findings. Individuals negative on conventional tests were followed up after 8 weeks. The Xpert MTB/RIF assay was performed on fresh or frozen samples as a molecular test comparison.

Results

In A total of 1036 adults with suspected TB were enrolled. Among 375 culture-confirmed TB cases with 750 sputum samples, TB-LAMP detected 75.6% (95% confidence interval (CI) 71.8–79.4%), including 97.9% (95% CI 96.4–99.4%) of smear-positive TB samples and 46.6% (95% CI 40.6–52.7%) of smear-negative TB samples. Specificity in 477 culture-negative participants not treated for TB (954 sputum samples) was 98.7% (95% CI 97.9–99.6%). TB-LAMP test results were indeterminate in 0.3% of cases.

Conclusions

Both TB-LAMP detects nearly all smear-positive and half of smear-negative TB cases and has a high specificity when performed in reference laboratories. Performance was similar to the Xpert MTB/RIF assay.

Comparative study of Loopamp™ *Mycobacterium tuberculosis* Complex Kit for Rapid Detection of *Mycobacterium tuberculosis* Complex in Cameroon

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– Biomed Biotechnol Res J 2018;2:46-52–

Abstract

Background

The most practical test for identifying tuberculosis (TB) in developing countries remains smear microscopy. However, due to its low sensitivity, a new point-of-care diagnostic method has been developed. The purpose of this study was to assess the performance of TB-Loop-mediated isothermal amplification (TB-LAMP) test on sputum samples of suspected TB cases.

Methods

Suspected pulmonary TB patients (527) from Jamot Hospital and without any history of anti-TB treatment were consecutively included in the study. Smear microscopy, TB-LAMP, GeneXpert® MTB/RIF, and liquid culture using BACTEC 960 Mycobacteria Growth Indicator Tube (MGIT) were performed on sputum samples collected from these patients. The sensitivity and specificity of TB-LAMP were compared with smear microscopy and GeneXpert® MTB/RIF. MGIT culture was the gold standard.

Results

TB-LAMP and smear microscopy showed sensitivities of 82.6% (95% confidence interval [CI], 76.9–87.2) and 53.6% (95% CI, 46.8–60.3), respectively, and specificities of 96.0% (95% CI, 93.2–97.7) and 99.0% (95% CI, 97.1–99.7), respectively. The sensitivity and specificity of TB-LAMP were similar to GeneXpert®, (89.9%; 95% CI, 85.0–93.3 and 97.0%; 95% CI, 94.4–98.4).

Conclusions

TB-LAMP is more sensitive than currently used microscopy. It presents a favorable diagnostic tool for TB in peripheral laboratories with limited equipment, such as those in developing countries.

Comparison of TB-LAMP, GeneXpert MTB/RIF and culture for diagnosis of pulmonary tuberculosis in The Gambia

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– J Infect; 72(3): 332-337–

Abstract

Background

Diagnosis of tuberculosis (TB) remains difficult, particularly in resource-limited settings. The development of nucleic acid-based tests for detection of *Mycobacterium tuberculosis* complex (MTBC) has significantly increased sensitivity compared to conventional smear microscopy and provides results within a matter of hours compared to weeks for the current gold-standard, liquid culture.

Methods

In this study we performed side-by-side comparison of mycobacterial detection assays on sputum samples from 285 subjects presenting with symptoms suggestive of TB in The Gambia and a cross-sectional cohort of 156 confirmed TB patients with a median of 2 months of treatment. A novel assay, Loop-Mediated Amplification test for TB (TB-LAMP), was compared to smear microscopy, MGIT culture and GeneXpert MTB/RIF for all samples.

Results

When culture was used as the reference standard, we found an overall sensitivity for TB-LAMP of 99% (95% CI: 94.5-99.8) and specificity of 94% (95% CI: 89.3-96.7). When latent class analysis was performed, TB-LAMP had 98.6% (95% CI: 95.9-100) sensitivity and 99% (95% CI: 98.2-100) specificity compared to 91.1% (95% CI: 86.1-96) sensitivity and 100% (95% CI: 98.2-100) specificity for MGIT culture. GeneXpert had the highest sensitivity 99.1% (95% CI: 97.1-100) but the lowest specificity 96% (95% CI: 92.6-98.3). Both TB-LAMP and GeneXpert showed high sensitivity and specificity regardless of age or strain of infection.

Conclusions

Our findings show the diagnostic utility of both GeneXpert and TB-LAMP in The Gambia. Whilst TB-LAMP requires less infrastructure, it is unable to detect drug-resistant patterns and therefore would be most suitable as a screening test for new TB cases in peripheral health clinics.

General

A cost–benefit algorithm for rapid diagnosis of tuberculosis and rifampicin resistance detection during mass screening campaigns

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– BMC Infectious Diseases (2022) 22:219 –

Abstract

Background

Active tuberculosis (TB) case finding is important as it helps detect pulmonary TB cases missed by the other active screening methods. It requires periodic mass screening in risk population groups such as prisoners and refugees. Unfortunately, in these risk population groups periodic mass screening can be challenging due to lengthy turnaround time (TAT), cost and implementation constraints. The aim of this study was to evaluate a diagnostic algorithm that can reduce the TAT and cost for TB and Rifampicin resistance (RR) detection. The algorithm involves testing with TB-LAMP followed by Xpert MTB/RIF for positive TB-LAMP cases to diagnose TB during mass campaigns in prisons and refugee camps.

Methods

The National Tuberculosis Control Program (NTCP) organized routine TB mass-screening campaigns in 34 prisons and 3 villages with refugees camps in Cameroon in 2019. TB LAMP was used for initial TB diagnosis and all TB-LAMP positive cases tested with the Xpert MTB/RIF assay to determine RR. TAT and cost benefits analysis of the combined use of TB-LAMP and Xpert MTB/RIF assays was determined and compared to the Xpert MTB/RIF assay when used only.

Results

A total of 4075 sputum samples were collected from TB presumptive, 3672 cases in 34 prisons and 403 samples in 3 villages. Of the 4,075 samples screened with TB-LAMP, 135 were TB positive (3.31%) and run on the Xpert MTB/RIF. Of the 135 positives cases, Xpert MTB/RIF revealed 3 were RR (2.22%). The use of TB-LAMP followed by testing with Xpert MTB/RIF for TB and RR detection reduced the TAT by 73.23% in prisons and 74.92% in villages. In addition to a reduced TAT, the two molecular tests used in synergy is cost benefit from year 2 onwards.

Conclusions

This study demonstrates the advantages of a diagnostic algorithm based on an initial testing with TBLAMP followed by testing with Xpert MTB/RIF for TB diagnosis. This approach improved early and rapid TB detection with an added advantage of providing RR status. The proposed algorithm is effective and less costly from the second year of implementation and should be used by TB control programs.

Evaluation of TB-LAMP assay for detection of *Mycobacterium tuberculosis* in children

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–INFECTIOUS DISEASES (2021); VOL. 0; 1-5–

Abstract

Background

Paediatric tuberculosis remains a major public health problem in developing countries. The diagnosis of tuberculosis in children is challenging because of the paucibacillary nature of the disease, due to which more sensitive nucleic acid amplification tests are needed. In this study, we determined the accuracy of WHO endorsed TB-LAMP assay for detection of *Mycobacterium tuberculosis* in children.

Methods

This was a prospective study conducted between March to July, 2018. A total of 177 samples from consecutive suspected TB children were received for microbiological diagnosis of TB. All tests for *Mycobacterium tuberculosis* detection were performed in parallel (smear microscopy, mycobacterial culture, Xpert MTB/RIF and TB-LAMP). The diagnostic accuracy of index test i.e. TB LAMP were determined using mycobacterial culture as a reference standard.

Results

Of the 177 samples, 2 (1.1%) were excluded from the study. Among 175 samples, TB-LAMP and Xpert MTB/RIF were positive in 27 (15.4%) and 25 (14.3%) samples, respectively. The sensitivity of both Xpert MTB/RIF and TB-LAMP was same, i.e. 84% (95%CI: 63.9–95.5%), when culture was considered as the reference standard. The specificity, positive predictive value and negative predictive value of TB-LAMP assay was 96% (95%CI: 91.5–98.5%), 77.8% (95%CI: 61.1–88.6%) and 97.3% (95%CI: 93.6–98.9%), respectively.

Conclusions

For the detection of M. tuberculosis in paediatric samples, TB-LAMP showed a sensitivity and specificity comparable to Xpert MTB/RIF.

Diagnostic accuracy of TB-LAMP for pulmonary tuberculosis: a systematic review and meta-analysis

Priya B. Shete, Katherine Farr, Luke Strnad, Christen M. Gray, Adithya Cattamanchi

– BMC Infectious Diseases (2019) 19:268–

Abstract

Background

The need for a rapid, molecular test to diagnose tuberculosis (TB) has prompted exploration of TB-LAMP (Eiken; Tokyo, Japan) for use in resource-limited settings. We conducted a systematic review to assess the accuracy of TB-LAMP as a diagnostic test for pulmonary TB.

Methods

We analyzed individual-level data for eligible patients from all studies of TB-LAMP conducted between Jan 2012 and October 2015 to compare the diagnostic accuracy of TB-LAMP with that of smear microscopy and Xpert MTB/RIF® using 3 reference standards of varying stringency. Pooled sensitivity and specificity and pooled differences in sensitivity and specificity were estimated using random effects meta-analysis. Study quality was evaluated using QUADAS-2.

Results

Four thousand seven hundred sixty individuals across 13 studies met eligibility criteria. Methodological quality was judged to be low for all studies. TB-LAMP had higher sensitivity than sputum smear microscopy (pooled sensitivity difference + 13·2, 95% CI 4·5–21·9%) and similar sensitivity to Xpert MTB/RIF (pooled sensitivity difference − 2·5, 95% CI -8·0 to + 2·9) using the most stringent reference standard available. Specificity of TB-LAMP was similar to that of sputum smear microscopy (pooled specificity difference − 1·8, 95% CI -3·8 to + 0·2) and Xpert MTB/RIF (pooled specificity difference 0·5, 95% CI -0·9 to + 1·8).

Conclusions

From the perspective of diagnostic accuracy, TB-LAMP may be considered as an alternative test for sputum smear microscopy. Additional factors such as cost, feasibility, and acceptability in settings that continue to rely on sputum smear microscopy should be considered when deciding to adopt this technology. Xpert MTB/RIF should continue to be preferred in settings where resource and infrastructure requirements are adequate and where HIV co-infection or drug-resistance is of concern.

Diagnostic Performance of Loop-mediated Isothermal Amplification test for TB

DIAGNOSTIC PERFORMANCE OF LOOP-MEDIATED ISOTHERMAL AMPLIFICATION TEST FOR TB

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BACKGROUND

Direct sputum smear microscopy (DSSM) is currently being used as the primary test for diagnosing tuberculosis (TB) in the country despite its reported poor sensitivity. This can lead to false negative cases that remain undetected and untreated, contributing to continued TB transmission. The Procedure for Ultra-Rapid DNA Extraction with Loop-mediated Isothermal AMPlification for TB (PURE-TB-LAMP) assay is a viable alternative to DSSM, having received recommendation from the World Health Organization in 2016 as a replacement test for DSSM and as a follow-on test for smear-negative patients. PURE-TB-LAMP is designed as a point-of-care test, with similar low biosafety requirements as microscopy. This study is part of a collaboration program between DOH and JICA aiming to evaluate the said test in local field conditions, starting with a phase I evaluation performed in a central laboratory setting.

PURE TB LAMP process overview. The conduct of the assay can be divided into three major parts, namely: 1) lysis by heat treatment; 2) DNA extraction by filtration through a special absorbent material (PURE); and, 3) amplification of DNA fragments specific to *Mycobacterium tuberculosis* under one temperature condition (LAMP). Results are visualized against the ultraviolet lamp unit of the PURE TB LAMP machine, with presence of TB bacilli indicated by fluorescence. The whole process takes about one hour, with a maximum of 14 samples per run in one machine.

SETTING

Recruitment of study participants was done at 28 health centers in the cities of Muntinlupa and Las Piñas. All laboratory processes were conducted at the National TB Reference Laboratory (NTRL) of the Research Institute for Tropical Medicine.

OBJECTIVES

1. Determine the diagnostic performance of PURE TB LAMP using liquid culture as reference standard
2. Compare diagnostic performance of PURE TB LAMP with LED fluorescent smear microscopy using liquid culture as reference standard
3. Compare diagnostic performance of PURE TB LAMP with Xpert® MTB/RIF using liquid culture as reference standard
4. Assess operational usability of PURE-TB-LAMP in terms of perceived ease of use, hands-on time, and acceptability as appraised by end-users

METHODOLOGY

The present study is a cross-sectional evaluation of PURE TB LAMP. Participants were prospectively enrolled from patients presenting with signs and symptoms of pulmonary TB and/or a chest X-ray indicative of the disease. Patients less than 18 years old and are undergoing TB treatment during recruitment (within at least 60 days) were excluded.

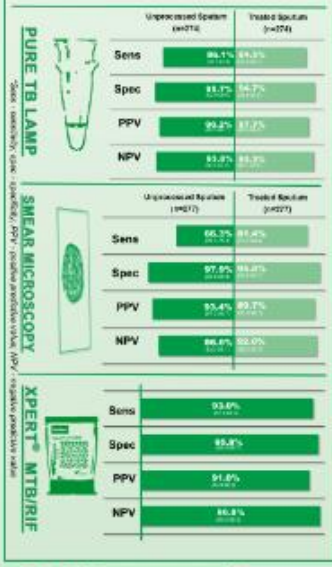
Enrolled participants were asked to submit the usual two samples for routine diagnosis. Samples were either collected on the spot ("spot" specimen) or the following morning. For the study procedures, one of the two samples submitted (at least 4mL) were transported to NTRL for laboratory processing, as detailed below:

All patient samples underwent six different TB diagnostic procedures. Sensitivity, specificity, and positive and negative predictive values for each test were computed using results from BACTEC MGIT automated liquid culture system as the reference standard. Values for the 95% confidence intervals of each measure were likewise computed. Statistical differences of specific parameters between each test was determined using McNemar test or exact McNemar test, as appropriate. P<0.05 was considered as significant.

Two laboratory staff who performed the PURE TB LAMP test were asked to evaluate the assay in terms of ease of use, hands-on time, and acceptability.

RESULTS

DIAGNOSTIC PERFORMANCE COMPARISON



A total of 279 sputum samples were collected from the study participants, 277 of which were included in the final analyses. Isolates with missing results for the particular test being evaluated were excluded in their respective analyses.

In raw, unprocessed samples, PURE TB LAMP sensitivity was found to be **better than smear microscopy (86.1% vs. 66.3%; p<0.001)** and **comparable to Xpert® MTB/RIF (93.0%; p=0.109)**. In NALC-NaOH-treated samples, smear microscopy and PURE TB LAMP **performed similarly (84.5% vs. 81.4%;p=0.617)**. The three tests also have comparable specificities for both unprocessed and NALC-NaOH-treated samples.

A further analysis of the diagnostic performance of PURE TB LAMP assay in smear-negative samples that tested positive in culture showed a sensitivity of **58.6% (95%CI, 40.7-76.6)** and **71.4% (95%CI, 54.7-88.2)** in unprocessed and treated samples respectively. Of the 213 samples that tested smear-negative, 21 samples were found PURE-TB-LAMP positive (and culture-positive), indicating that **10% of the samples initially identified as smear negative were in fact positive for TB bacilli and were correctly screened by PURE TB LAMP.**

Comparison of the diagnostic performance of PURE TB LAMP and Xpert® MTB/RIF in unprocessed samples showed **no significant difference (p = 0.109) and are thus comparable.**

The two end-users of the PURE TB LAMP generally gave **positive feedback** on the test, citing **ease of interpreting the results** and **shorter time needed to perform the test compared to microscopy**. However, a few issues and barriers to effective uptake of the test were noted, including **limited visibility in the pipetting tip** provided with the assay for sputum transfer, **perceived risk of cross contamination**, and **complexity of the steps of the assay.**

CONCLUSIONS AND RECOMMENDATIONS

The PURE TB LAMP assay has good diagnostic performance and has received positive feedback from its end-users. Values observed for its diagnostic performance were comparable, if not better, to those observed from studies conducted in other countries. Observed diagnostic performance is consistent with those in the WHO policy guidance. However, these may vary when the test is performed in its intended setting of use, as peripheral laboratories have very different conditions compared to a reference laboratory. Further study validating its diagnostic performance at the point-of-care setting and with a larger number of samples involved is recommended for a more precise and robust measure of how PURE TB LAMP will perform in local field conditions.

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Inclusion of TB diagnostics on the WHO Essential Diagnostics List

C. Gilpin, K. Weyer

– *INT J TUBERC LUNG DIS 22(8):827–828–*

As ON 16 MAY 2018, the World Health Organization (WHO) published its first Model List of Essential In Vitro Diagnostics (EDL), a catalogue of the tests needed to diagnose the most common medical conditions as well as selected global priority diseases, including tuberculosis (TB), the leading single infectiouscause of mortality worldwide. The EDL focuses on diagnostics that 'satisfy the priority health care needs of the population and which are selected with due regard to disease prevalence and public health relevance, evidence of efficacy and accuracy, and comparative cost-effectiveness, similar to the definition of an essential medicine.' It contains 113 products used in human specimens such as blood, urine and sputum: 58 tests are listed for detection and diagnosis of a wide range of common conditions, providing an essential package for screening and management of patients. The remaining 55 tests are designed for the detection, diagnosis and monitoring of selected priority diseases such as TB, the human immunodeficiency virus, malaria, hepatitis B and C, human papillomavirus and syphilis. The EDL was developed following extensive consultation within the WHO and externally. The draft list was then reviewed by the recently established WHO Strategic Advisory Group of Experts on In Vitro Diagnostics (SAGE-IVD). Specifically, the general laboratory diagnostics were compiled based on existing WHO guidelines and technical manuals and priority medical devices lists. The technologies specific to the diagnosis of TB are referred to in the EDL, with links to the respective guidelines. These commercial IVDs include molecular line probe assays (LPAs) for the detection of resistance to first- and second-line anti-tuberculosis medicines (Hain Lifesciences, Germany; Nipro Corporation, Japan), Xpert MTB/RIF and Xpert MTB/RIF Ultra for the detection of TB and rifampicin resistance (Cepheid, Sunnyvale, CA, USA), interferon- gamma release assays (IGRAs) (Qiagen, Valencia, CA, USA; Oxford Immunotec, Oxford, UK) and the tuberculin skin test (TST) for the diagnosis of latent tuberculous infection, the lateral flow lipoarabinomannin assay (LF-LAM) to assist in the diagnosis of TB in seriously ill human immunodeficiency virus positive individuals (Alere, Waltham, MA, USA), loop-mediated isothermal amplification (TB-LAMP) for the diagnosis of pulmonary TB (Eiken Chemical Co, Tokyo, Japan), the automated liquid culture and drug susceptibility testing MGIT system (BD, Franklin Lakes, CA, USA) and light emitting diode (LED) fluorescence microscopy.

For the development of guidelines on TB diagnostics, the WHO uses the international GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach to assess the quality of evidence and to develop and report recommendations. TB diagnostics currently recommended by the WHO comprise relatively unique and complex technologies, developed almost exclusively by singlesource manufacturers. These technologies are applicable to specific patient populations and require dedicated levels of laboratory infrastructure, biosafety and technical training. In vitro results should be used to guide appropriate treatment, especially for drugresistant TB. The latest WHO policies for TB diagnosis, treatment and care have therefore been consolidated into a concise compendium. The WHO End TB Strategy calls for universal access to testing and treatment for TB, including drug-resistant forms of the disease. The EDL serves as a guiding reference for countries to update or develop their own lists of essential diagnostics based on their local context and disease epidemiology. Ensuring that WHO-recommended TB diagnostics are included in national EDLs is an important first step on the path to reaching universal coverage. Moreover, ensuring that the required laboratory infrastructure, high-quality laboratory supplies and training of laboratory workers to accurately conduct TB testing are included in adequately budgeted plans for national laboratory services is imperative for scale-up and to truly benefit patients.

Rapid molecular assays for detection of tuberculosis

Rkia Eddabra and Hassan Ait Benhassou

– Pneumonia (2018) 10:4–

Abstract

Tuberculosis (TB) is an infectious disease that remains an important public health problem at the global level. It is one of the main causes of morbidity and mortality, due to the emergence of antibiotic resistant *Mycobacterium* strains and HIV co-infection. Over the past decade, important progress has been made for better control of the disease. While microscopy and culture continue to be indispensible for laboratory diagnosis of tuberculosis, the range of several molecular diagnostic tests, including the nucleic acid amplification test (NAAT) and whole-genome sequencing (WGS), have expanded tremendously. They are becoming more accessible not only for detection and identification of *Mycobacterium tuberculosis* complex in clinical specimens, but now extend to diagnosing multidrugresistant strains. Molecular diagnostic tests provide timely results useful for high-quality patient care, low contamination risk, and ease of performance and speed. This review focuses on the current diagnostic tests in use, including emerging technologies used for detection of tuberculosis in clinical specimens. The sensitivity and specificity of these tests have also been taken into consideration.

Commercial products to preserve specimens for tuberculosis diagnosis: a systematic review

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– INT J TUBERC LUNG DIS 22(7):741–753–

Abstract

Setting

Eliminating tuberculosis in high-burden settings requires improved diagnostic capacity. Important tests such as Xpert MTB/RIF and culture are often performed at centralised laboratories that are geographically distant from the point of specimen collection. Preserving specimen integrity during transportation, which could affect test performance, is challenging.

Objective

To conduct a systematic review of commercial products for specimen preservation for a World Health Organization technical consultation.

Design

Databases were searched up to January 2018. Methodological quality was assessed using Quality Assessment of Technical Studies, a new technical study quality-appraisal tool, and Quality Assessment of Diagnostic Accuracy Studies. Studies were analysed descriptively in terms of the different products, study designs and diagnostic strategies used.

Results

Four products were identified from 16 studies: PrimeStore-Molecular-Transport-Medium (PS-MTM), FTA card, GENO_CARD (all for nucleic acid amplification tests [NAATs]) and OMNIgene_SPUTUM (OMS; culture, NAATs). PS-MTM, but not FTA card or GENO_CARD, rendered *Mycobacterium tuberculosis* non-culturable. OMS reduced Löwenstein-Jensen but not MGIT™ 960™ contamination, led to delayed MGIT time-to-positivity, resulted in Xpert performance similar to cold chain-transported untreated specimens, and obviated the need for N-acetyl-L-cysteine-sodium hydroxide decontamination. Data from paucibacillary specimens were limited. Evidence that a cold chain improves culture was mixed and absent for Xpert. The effect of the product alone could be discerned in only four studies.

Conclusions

Limited evidence suggests that transport products result in test performance comparable to that seen in cold chain-transported specimens.

Point of care diagnostics for tuberculosis

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– Pulmonol. 2018;24(2):73---85–

Abstract

The goals of the End TB strategy, which aims to achieve a 90% reduction in tuberculosis (TB) incidence and a 95% reduction in TB mortality by 2035, will not be achieved without new tools to fight TB. These include improved point of care (POC) diagnostic tests that are meant to be delivered at the most decentralised levels of care where the patients make the initial contact with the health system, as well as within the community. These tests should be able to be performed on an easily accessible sample and provide results in a timely manner, allowing a quick treatment turnaround time of a few minutes or hours (in a single clinical encounter), hence avoiding patient loss-to-follow-up. There have been exciting developments in recent years, including the WHO endorsement of Xpert MTB/RIF, Xpert MTB/RIF Ultra, loop-mediated isothermal amplification (TB-LAMP) and lateral flow lipoarabinomannan (LAM). However, these tests have limitations that must be overcome before they can be optimally applied at the POC. Furthermore, worrying short- to medium-term gaps exist in the POC diagnostic test development pipeline. Thus, not only is better implementation of existing tools and algorithms needed, but new research is required to develop new POC tests that allow the TB community to truly make an impact and find the ‘‘missed TB cases’’.

Evaluation of the Analytical Performance of the PURE-TB-LAMP Assay for Tuberculosis Detection

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– Medical Research Archives; Assay for tuberculosis detection; Volume 1; Issue 2–

Abstract

Given the prevalence and lethality of tuberculosis (TB) in developing countries, there is an ongoing need for rapid, simple, and low-cost detection method that nonetheless sensitive and highly specific. The present study evaluated the basic performance of a novel TB detection method combining procedure for ultra-rapid extraction (PURE) and loop-mediated isothermal amplification for TB (TB-LAMP). The PURE-TB-LAMP assay detected four *Mycobacterium tuberculosis* complexes and did not show any cross-reactivity with 18 species of non-TB mycobacteria (NTM) or with 10 species of other bacteria that cause respiratory tract infections such as Streptococcus pneumonia, underscoring its high specificity for TB detection. The analytical sensitivity of the assay was 100 CFU/ml for M. tuberculosis strain H37Rv cell and was unaffected by the presence of excess amounts of *M. avium* cells (a typical NTM species) or human genomic DNA. Moreover, when used with a range of artificial specimens prepared by spiking known amounts of cultured M. tuberculosis cells, the PURE method efficiently removed various inhibitory materials from a variety of samples such as sputum, urine, simulated gastric fluid, and whole blood, demonstrating the applicability of this assay to these samples. These results suggest that the PURE-TB-LAMP assay is a highly effective and accessible TB detection method that can be useful in resource-limited communities.

Loop-mediated isothermal amplification as alternative to PCR for the diagnosis of extra-pulmonary tuberculosis

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– J Clin Microbiol. 2016 Aug;54(8):1984-91–

Abstract

Background

The main challenge in combatting extra-pulmonary tuberculosis (EPTB) is the lack of a rapid, reliable and inexpensive diagnostic test for the detection of *Mycobacterium tuberculosis*.

Objective

To evaluate the diagnostic potential of an L-serine dehydratase gene (sdaA) loop-mediated isothermal amplification (LAMP) assay for the detection of M. tuberculosis in clinical specimens from presumptive EPTB patients.

Methods

An in-house sdaA LAMP assay was used to analyse clinical specimens (n = 315) for the diagnosis of EPTB compared with culture and the composite reference standard (CRS) comprising culture and polymerase chain reaction (PCR) using insertion sequence (IS) 6110 and mpb64 as target genes.

Results

The sdaA LAMP assay showed the highest sensitivity (93.3%) in comparison to culture; the sensitivity of IS6110 PCR, mpb64 and sdaA PCR assay was respectively 80%, 86.7% and 90%. In comparison to CRS, the LAMP assay had a sensitivity of 92.5% and a specificity of 99.2%, with a high positive (121.11) and a low negative likelihood ratio (0.08).

Conclusions

Due to its speed, simplicity, sensitivity and specificity, the sdaA LAMP assay is a potential diagnostic test for the diagnosis of EPTB, particularly in resource-limited settings.

Loop-mediated isothermal amplification of DNA

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– Nucleic Acids Res; 28(12): e63–

Abstract

We have developed a novel method, termed loop-mediated isothermal amplification (LAMP), that amplifies DNA with high specificity, efficiency and rapidity under isothermal conditions. This method employs a DNA polymerase and a set of four specially designed primers that recognize a total of six distinct sequences on the target DNA. An inner primer containing sequences of the sense and antisense strands of the target DNA initiates LAMP. The following strand displacement DNA synthesis primed by an outer primer releases a single-stranded DNA. This serves as template for DNA synthesis primed by the second inner and outer primers that hybridize to the other end of the target, which produces a stem-loop DNA structure. In subsequent LAMP cycling one inner primer hybridizes to the loop on the product and initiates displacement DNA synthesis, yielding the original stem-loop DNA and a new stem-loop DNA with a stem twice as long. The cycling reaction continues with accumulation of 10(9) copies of target in less than an hour. The final products are stem-loop DNAs with several inverted repeats of the target and cauliflower-like structures with multiple loops formed by annealing between alternately inverted repeats of the target in the same strand. Because LAMP recognizes the target by six distinct sequences initially and by four distinct sequences afterwards, it is expected to amplify the target sequence with high selectivity.

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Unitaid

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Parasite There are currently some products that have been marketed for several years with an intended use in peripheral settings. However, of these only one technology has been sufficiently evaluated in a variety of settings in order to now be approved by WHO, the Loopamp™ MTBC Detection kit from Eiken Chemical Corp. (Japan).6 Since 2012, this test has undergone 20 evaluation studies in 17 countries. This is the first NAAT product specifically designed for use in microscopy-level facilities to receive WHO endorsement, which had two conditional recommendations for the use of the assay instead of conventional SSM where patients present with symptoms of TB or as a follow-on test where follow-on testing of conventional SSM results is necessary.
The first version of the assay was released in 2011 by the company and has undergone some modifications since in terms of specimen and reaction volumes and the protocol used for the assay. The assay is well suited to resource-limited settings as the equipment is relatively simple and several user steps are added to reduce instrumentation complexity, including sample preparation and the interpretation of test results (Figure 17). The assays can be batched and up to 14 samples can be screened in a single run with control reactions. The assay uses 60 µL of raw sputum that is transferred to the sample preparation tube. MTB cells are inactivated and lysed via a combination exposure to highly alkaline conditions and temperature (90 °C) for 5 minutes. The sample preparation tube interlocks with a sample neutralization tube where the pH of the heated sample is neutralized. The final step is the addition of an applicator tube whereby ~30 µL of the liquid treated sputum contents can be expressed into a reaction tube. The assay reagents are stored as a glassified pellet inside each reaction tube lid. The DNA extracts are added to the tube strip, the caps are then closed and the tube strips inverted for 2 minutes to wet the reagents and then mixed to permit their introduction to the samples. The assay uses LAMP, an isothermal manual DNA amplification method that takes 40 minutes to perform at 67 °C in this assay. After incubation, the reactions are terminated by briefly heating at an elevated temperature. The results of each reaction are scored visually by the user via fluorescence, which is generated when DNA is amplified by the TB-LAMP reaction. The light source is supplied with the instrument and the user compares the green fluorescence of the positive control to each test. A negative control provides further user input to score any negative tests. The summary data from the 2016 WHO policy guidance document noted the pooled sensitivity of TB-LAMP was higher than for SSM, ranging from 77.7% to 80.3%. The pooled sensitivity for the TB-LAMP among SSM positive patients ranged from 95.2% to 96.6% across studies, depending on the reference standard used.6 The pooled specificity of the assays was also slightly variant depending on the reference methods used to qualify results with ranges from 97.7% to 98.1%. Eiken Chemical Corp. has partnered with HUMAN Diagnostics Worldwide (Germany) to globally distribute and market the assay and instrumentation necessary to perform the Loopamp™ MTBC Detection kit. Training requirements for LAMP is similar to the amount of training for smear microscopy.175 These products have been available since Q4 2016 and eligible countries and negotiated pricing can be accessed on the FIND website.20 The Loopamp™ Pure DNA Extraction kit costs €298.20 (90 extractions), the Loopamp™ MTB Detection Kit is €352.50 (2 x 48 reactions) and the instrument is €2450.00.

Analytical sensitivity and specificity of a loop-mediated isothermal amplification (LAMP) kit prototype for detection of *Trypanosoma cruzi* DNA in human blood samples

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Abstract

In This study aimed to assess analytical parameters of a prototype LAMP kit that was designed for detection of Trypanosoma cruzi DNA in human blood. The prototype is based on the amplification of the highly repetitive satellite sequence of T.cruzi in microtubes containing dried reagents on the inside of the caps. The reaction is carried out at 65°C during 40 minutes. Calcein allows direct detection of amplified products with the naked eye. Inclusivity and selectivity were tested in purified DNA from Trypanosoma cruzi stocks belonging to the six discrete typing units (DTUs), in DNA from other protozoan parasites and in human DNA. Analytical sensitivity was estimated in serial dilutions of DNA samples from Sylvio X10 (Tc I) and CL Brener (Tc VI) stocks, as well as from EDTA-treated or heparinized blood samples spiked with known amounts of cultured epimastigotes (CL Brener). LAMP sensitivity was compared after DNA extraction using commercial fiberglass columns or after "Boil & Spin" rapid preparation. Moreover, the same DNA and EDTA-blood spiked samples were subjected to standardized qPCR based on the satellite DNA sequence for comparative purposes. A panel of peripheral blood specimens belonging to Chagas disease patients, including acute, congenital, chronic and reactivated cases (N = 23), as well as seronegative controls (N = 10) were evaluated by LAMP in comparison to qPCR. LAMP was able to amplify DNAs from T. cruzi stocks representative of the six DTUs, whereas it did not amplify DNAs from Leishmania sp, T. brucei sp, T. rangeli KPN+ and KPN-, P. falciparum and non-infected human DNA. Analytical sensitivity was 1x10-2 fg/µL of both CL Brener and Sylvio X10 DNAs, whereas qPCR detected up to 1x 10-1 fg/µL of CL Brener DNA and 1 fg/µl of Sylvio X10 DNA. LAMP detected 1x10-2 parasite equivalents/mL in spiked EDTA blood and 1x10-1 par.eq/mL in spiked heparinized blood using fiberglass columns for DNA extraction, whereas qPCR detected 1x10-2 par.eq./mL in EDTA blood. Boil & Spin extraction allowed detection of 1x10-2 par.eq /mL in spiked EDTA blood and 1 par.eq/ml in heparinized blood. LAMP was able to detect T.cruzi infection in peripheral blood samples collected from well-characterised seropositive patients, including acute, congenital, chronic and reactivated Chagas disease. To our knowledge, this is the first report of a prototype LAMP kit with appropriate analytical sensitivity for diagnosis of Chagas disease patients, and potentially useful for monitoring treatment response.

Evaluation of a loop-mediated amplification test for rapid diagnosis of tuberculosis in Ghana

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Abstract

Background

The unavailability of cheap but rapid, highly sensitive and specific diagnostic tools for tuberculosis (TB) remains a major setback for the global efforts to end TB by the year 2035. Nucleic acid-based TB diagnostic assays remain the most recommended and the Gene Xpert MTB/RIF (Cepheid Sunnyvale, United States) is the most widely used which has an added advantage of detecting rifampicin resistance. However, the machinery requirement of the GeneXpert MTB/RIF makes it unsuitable for use in rural and resource-limited settings eventually challenging the global efforts to end TB by the year 2035. Loop-mediated amplification (LAMP) of DNA technology presents a cheap alternative for the precision diagnosis of TB.

Objective

In this study, we evaluated the specificity and sensitivity of the TB-LAMP assay kit manufactured by Human Diagnostics
Worldwide (Geneva, Switzerland) for the diagnosis of TB in Ghana.

Methods

We assessed the performance of the TB-LAMP assay against a panel of genotyped mycobacteria (including members of the Mycobacterium tuberculosis complex (MTBC) and a couple of nontuberculous mycobacteria) and sputum samples collected from presumptive TB patients using sputum culture as reference diagnostic assay

Results

The TB-LAMP assay was found to be very specific in detecting members of the MTBC as positive samples whereas the nontuberculous mycobacteria were all negative. Using sputum culture as a reference, the TB-LAMP assay was found to have 99.2% sensitivity, 97.2% specificity, 98.5% positive predictive value (PPV), 98.6% negative predictive value (NPV) and 98.5% accuracy for detection of MTBC among sputum samples collected from presumptive TB patients in Ghana. The TB-LAMP assay additionally showed 100% accuracy in detecting members of the MTBC among a panel of mycobacterium.

Conclusion

The TB-LAMP is highly sensitive and specific for the diagnosis of TB. It is thence recommended for use as a primary screening tool before referral for culture and sensitivity assays for better management of TB.

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