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Role of Bronchoscopy in Diagnosing Sputum Negative Pulmonary Tuberculosis: A Retrospective Study

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Abstract
Objective: *To evaluate the significance of bronchoscopy in detecting additional cases of pulmonary tuberculosis which are not detected by AFB smear microscopy or by GeneXpert of sputum sample.*
Method: *With the Pulmonary Department of tertiary healthcare centre, we retrospectively reviewed records of 127 patients from April 2019 to December 2019 who underwent three diagnostic tests for pulmonary tuberculosis- AFB smear microscopy, GeneXpert of sputum and GeneXpert of bronchoalveolar lavage (BAL) sample obtained by bronchoscopy. The results of the BAL sample were compared with the other two to check if it detected more cases of tuberculosis.*
Result: *The result of GeneXpert of BAL sample obtained after bronchoscopy showed a concordance of 82.68% with the result of AFB sputum smear and a concordance of 81.10% with the result of GeneXpert of sputum. It detected an additional 17.32% of pulmonary tuberculosis cases.*
Conclusion: *Incorporating bronchoscopy in diagnosing pulmonary tuberculosis led to a detection of an additional 17.32% of cases.*
Keywords: *bronchoscopy, bronchoalveolar lavage, pulmonary tuberculosis.*

Introduction

Tuberculosis remains a major cause of ill health and is one of the top 10 causes of death worldwide in spite of availability of targeted drugs. Currently, the world and many high TB burden countries including India are not on track to reach the 2020 milestones of the End TB Strategy. The burden of drug-resistant TB is of major interest and concern at global, regional and country levels. In 2018, there were approximately half a million (range, 417 000–556 000) new cases of rifampicin-resistant TB (of which 78% had multidrug-resistant TB). The three countries with the largest share of the global burden were India (27%), China (14%) and the Russian Federation (9%)[1].

Prompt and accurate diagnosis followed by provision of appropriate treatment in line with international standards prevents deaths and limits ill health among people who develop tuberculosis. It also prevents further transmission of infection to others.

There are numerous tests available for the diagnosis of tuberculosis. The acid-fast bacillus (AFB) smear is still employed for diagnosing active pulmonary tuberculosis despite being invented decades ago. However, AFB smear microscopy is known to have

a low sensitivity and, because it cannot distinguish between *Mycobacterium tuberculosis* and nontuberculous mycobacteria, low specificity[2,3]. Culture although gold standard, takes longer time for positivity. Whereas, Nucleic acid amplification techniques such as GeneXpert, due to its rapidity help in early diagnosis and management of tuberculosis. In addition, they can detect a resistance to rifampicin[2].

World Health Organization recommends bacteriological confirmation of pulmonary tuberculosis (PTB) by the detection of acid-fast bacilli (AFB) in respiratory specimens. However about 40-60% of patients with PTB suspected clinically or radiologically may fail to produce sputum, or when it is available, AFB may be negative on repeated smear examination. These sputum smear negative patients and those who fail to produce any sputum can be diagnosed by flexible fibre optic bronchoscopy.[4]

In India, a sputum AFB smear microscopy and GeneXpert of sputum sample are done initially to diagnose pulmonary TB. Bronchoscopy and bronchoalveolar lavage (BAL) is usually performed when there is suspicion of sputum smear negative TB, failure to expectorate sputum of adequate quality and quantity and suspicion of false negative. GeneXpert of the BAL sample is done for an accurate diagnosis since it is a faster and more sensitive method in detecting tuberculosis compared to AFB smear microscopy.

There are older studies available which investigate the importance of BAL sample obtained by bronchoscopy.[4,5] In these studies, the BAL samples are subjected to AFB smear. Since GeneXpert is a more sensitive method of diagnosing TB, the BAL samples in this study were subjected to GeneXpert instead to get a more accurate picture.

Methodology

The retrospective study was conducted a tertiary healthcare centre in Navi Mumbai in the state of Maharashtra. The study comprises of 127 patient's records. Every suspected case of pulmonary tuberculosis who had undergone all three- AFB sputum smear microscopy, GeneXpert of sputum and GeneXpert of BAL sample were included in the study. Cases which had record of extra-pulmonary instead of pulmonary samples of all three tests were excluded.

AFB Smear Microscopy was prepared in D Y Patil Hospital's highly accredited EQA laboratory. The samples were all of sputum, collected in a sterile container. The smears were examined under oil immersion lens after being subjected to Z-N staining. GeneXpert tests were conducted in the D Y Patil Hospital laboratory and included samples of sputum as well as BAL. Bronchoscopy and BAL was performed according to the joint guidelines of Indian Chest Society, National College of Chest Physicians and Indian Association of Bronchoscopy in D Y Patil Hospital, Nerul.

After the data had been collected of these cases, they were computerised on a Microsoft Excel sheet. The results of the tests were entered in addition to basic patient information such as name, age, sex, address and date of test. The data was then analysed and tabulated and the results were given in percentage.

Result

A total of 127 patient records were collected for this study. These records provide information about the results of three diagnostic tests- AFB pre bronchoscopy sputum smear, GeneXpert of pre bronchoscopy sputum and GeneXpert of bronchoalveolar lavage (BAL) sample obtained after bronchoscopy. The findings of the results are summarized in Table 1.

Table 1

AFB sputum smear microscopy	GeneXpert of sputum sample	GeneXpert of BAL sample	Total cases
Negative	Negative	MTB Not Detected	103
Negative	Negative	MTB Detected	24
Positive	Negative	MTB Not Detected	0
Positive	Negative	MTB Detected	0

In 103 cases, all three methods concord their results and do not detect the presence of tuberculosis in the patient. 24 out of the total 127 cases detect tuberculosis after bronchoscopy was introduced when the other two methods were unable to do so. Hence, the GeneXpert of the BAL sample obtained after bronchoscopy is able to detect an additional 17.32% cases of tuberculosis. There are no cases in the study in which a detection of tuberculosis by either AFB smear microscopy or GeneXpert of sputum was contradicted by the result of GeneXpert of BAL after bronchoscopy.

Out of the total 24 MTB detected cases from the GeneXpert of BAL sample, 4 showed resistance to the first line anti-TB drug rifampicin and the other 20 were sensitive to it. Hence, 16.67% of the MTB detected cases showed a high possibility of multi-drug resistant TB. The detection of these MDR cases would have been missed if bronchoscopy was not incorporated. This would add to the global threat of rising prevalence of MDR-TB.

The result of GeneXpert of BAL sample obtained after bronchoscopy shows a total concordance of 82.68% with the result of AFB sputum smear and a total concordance of 81.10% with the result of GeneXpert of sputum.

Discussion

In the study there are 22 cases i.e. 17.32% where tuberculosis is detected by GeneXpert of BAL sample and not detected by the other two methods. The lack of detection by AFB smear can be due to technical errors of preparing and staining smear in microscopy or because the patient did not excrete Mycobacterium tuberculosis in sputum at the time of collection of the sample. Inability to secrete the bacteria in sputum during sample collection could be the reason for a false negative by the GeneXpert of sputum method. These obstacles are overcome by performing bronchoscopy and using a BAL sample. By employing bronchoscopy, a targeted extraction of BAL sample based on chest radiography is possible. As a result, the BAL sample shows lower chances of inadequate quality and quantity as compared to sputum sample. Bronchoscopy is essential in suspected patients who are unable to expectorate sputum and sputum induction has also failed. This makes bronchoscopy a necessary tool in eliminating tuberculosis since the WHO Expert Committee on Tuberculosis recommends that patients of pulmonary tuberculosis in whom the disease has not been confirmed bacteriologically should not be started on anti-tubercular treatment until the diagnosis can be confirmed bacteriologically. Additionally, immunosuppressed patients like the ones suffering from HIV are more likely to be sputum smear negative. Hence, the use of bronchoscopy becomes very important in these susceptible patients.

From this study we can conclude that incorporating bronchoscopy in diagnosing tuberculosis led to a detection of an additional 17.32% of cases. These cases would have otherwise been undiagnosed and possibly later present as multi-drug resistant tuberculosis and with a higher bacillary load.

Limitation

It should be noted that since GeneXpert uses DNA amplification technique to detect the presence of Mycobacterium tuberculosis, small traces of bacteria can also be detected. It also picks up dead bacilli seen in patients with a past history of pulmonary tuberculosis and can give a false positive.

Conclusion

The introduction of bronchoscopy detected an additional 17.32% cases of pulmonary TB. These cases would have otherwise been undiagnosed and added to the national and global tuberculosis burden.

Declaration of Conflict of Interest: There is no conflict of interest

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