CBNAAT: Comparision of Diagnositc Yield in Sputum and Bal Fluid

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Abstract
Aims and Objectives: *To compare the diagnostic yield of CBNAAT method for BAL fluid and sputum for detection of mycobacterium to diagnose pulmonary tuberculosis.*
Material and Methods: *129 sputum and BAL specimens from 129 patients were studied which included 65 specimens from sputum culture positive TB patients and 64 specimens from sputum culture negative patients. Patients with Sputum culture negative for MTB were considered as control.*
Observation: *It was observed that out of 65 culture positive cases of pulmonary tuberculosis, 43 were sputum CBNAAT (+)ve and 54 were CBNAAT (+)ve in BAL. Sensitivity and specificity of CBNAAT for sputum was 66.15% and 100% respectively. Sensitivity and specificity of CBNAAT for BAL was 83.07% and 100% respectively.*
Conclusion: *our study suggests that BAL-CBNAAT shows additional advantage of confirmatory diagnosis of the disease even if sputum CBNAAT is negative.*

Introduction

Tuberculosis is caused by bacteria (mycobacterium tuberculosis) that most often affects lungs[1]. Tuberculosis occurs in every part of the world. Tuberculosis is one of the top ten causes of death worldwide. In 2017, 10 million people fell ill with TB, and 1.6 million died from the disease (including 0.3 million among people with HIV). With the pandemic of AIDS and emergence of drug resistant strains of mycobacterium tuberculosis, pulmonary tuberculosis has now become a major health problem to the world community[2].

TB spreads from person to person through air. When person with pulmonary TB, coughs, sneeze or spits they propel the bacteria and inhalation of these bacteria can cause TB infection[1].

Early and rapid diagnosis and treatment of the case is the most important step in reducing the TB incidence[3].

Global incidence is falling at about 2% per year. This needs to accelerate to a 4-5% annual decline to reach the 2020 milestones of the End TB strategy[4].

Lab diagnosis of TB is based on traditional method of smear microscopy by Ziel-neelsen staining and on sputum culture of Mycobacterium Tuberculosis. Sputum microscopy is rapid and inexpensive but bacterial concentration required is 10,000 Acid Fast Bacillii per ml or greater. It also lacks specificity and cannot distinguish various strains of mycobacterium. Culture of Mycobacterium tuberculosis is more sensitive and 10-100 viable bacilli are required but it takes long period to produce results.

The detection of Mycobacterium Tuberculosis by Cartridge Based Nucleic Acid Amplification Test (CBNAAT) has been found to be useful in diagnosis of pulmonary tuberculosis.

The CBNAAT is one of these newer methods that simultaneously identifies Mycobacterium tuberculosis and detects rifampicin resistance [5].

In our study we have compared the yield of CBNAAT method for BAL fluid and sputum for detection of mycobacterium to diagnose tuberculosis.

Material and Method

This was a hospital based comparative study, conducted in TB and chest Department of SN Medical College Agra

We have investigated presumptive pulmonary TB cases. Detailed clinical history was taken and chest x-ray & sputum smear microscopy after ZN staining was done.

All cases were sent to Intermediate reference laboratory National JALMA Institute for Leprosy and Other Mycobacterial Diseases for sputum culture for MTB. 129 sputum and BAL specimens from 129 patients were studied which included 65 specimens from sputum culture positive TB patients and 64 specimens from sputum culture negative patients. Patients with Sputum culture negative for MTB were considered as control.

Sputum samples were collected according to RNTCP guidelines and samples sent to Intermediate reference laboratory, State Tuberculosis Training & Demonstration Centre Agra for CBNAAT.

Bronchoalveolar lavage was taken in our bronchoscopy suit in the department of Respiratory Medicine, SN Medical College, Agra. BAL fluid sent to Intermediate reference laboratory State Tuberculosis Training & Demonstration Centre Agra for CBNAAT.

CBNAAT: Cartridge-based nucleic acid amplification test (CBNAAT) is a recently introduced polymerase chain reaction (PCR) based method for detection of Tuberculosis.It also detects rifampicin resistance as it targets the rpoB gene of mycobacteria. CBNAAT is a Mycobacterium tuberculosis-specific automated, cartridgebased nucleic acid amplification assay, having fully integrated and automated amplification and detection using real-time PCR, providing results within 100 minutes. It is a highly specific test as it uses 3 specific primers and 5 unique molecular probes to target the rpoB gene of M. tuberculosis, which is the critical gene associated with rifampicin resistance[6].

Observation

The present study was conducted on 129 patients of presumptive tuberculosis, out of which 65 patients Sputum Culture positive cases and 64 patients were Sputum Culture Negative cases, attended department of TB and chest diseases, SN Medical College, Agra.

Group	Total	Sputum for CBNAAT		BAL for CBNAAT	
		(+)ve	(-)ve	(+)ve	(-)ve
Pul. TB	65	43	22	54	11
Sputum Culture Negative cases	64	0	64	0	64

It was observed that out of out of 65 culture positive cases of pulmonary tuberculosis, 43 were sputum CBNAAT (+)ve and 54 were CBNAAT (+)ve in BAL.

Sputum for CBNAAT	No. of cases	Control	Total
Positive	43 (True positive)	0 (False positive)	43
Negative	22 (False negative)	64 (True negative)	86
Total	65	64	129

Sensitivity   = 43/65 = 66.15%   (+)vePredictive Value   = 43/43 =98.4%
Specificity   = 65/65 =100.0%   (-)ve predictive Value   = 64/86 = 75.44%

BAL for CBNAAT	No. of cases	Control	Total
Positive	54 (True positive)	0 (False positive)	54
Negative	11 (False negative)	64 (True negative)	75
Total	65	64	129

Sensitivity   = 54/65 = 83.07%   (+)vePredictive Value   = 54/54 =100.0%
Specificity   = 64/64 =100.0%   (-)ve predictive Value   = 64/75 = 85.33%

Discussion

CBNAAT should not be thought as a substitute for culture and SM. However, it can act as an adjuvant of traditional tests and clinical data for confirming TB. It cannot be used for monitoring the therapeutic response as it can produce false-positive results in presence of non-viable TB bacteria; though identification of M. tuberculosis out of Non-Tubercular Mycobacterium (NTM) is possible by it[7]. Thus, CBNAAT is helpful diagnostic test towards AFB smear-positive patients for rapidly detection of pulmonary TB and getting it differentiated from NTM[8].

A study conducted by Avashia S et al., reported 47.2% gain in respect of sputum positivity among smear negative TB cases[9]. The results of the present study have concurrence with this where 66.15% yield for sputum CBNAAT and for BAL-CBNAAT it was 83.07%. This 16.92 % increase in the yield arising out of BAL-CBNAAT over and above the yield of sputum CBNAAT was also revealed to be statistically significant. Here, the yield of 16.92% sputum positive patients would be taken as a major gain from the epidemiological point of view so far as the transmission of TB concerns.

A Cochrane systematic review done in 2013 showed high accuracy of CBNAAT compared to culture. It showed about 88% sensitivity and 98% specificity for pulmonary TB in adults. Among smear-negative TB patients, Xpert had a sensitivity of 67%[10]. Ioannidis P et al., reported that GeneXpert MTB/RIF assay has positive predictive values for pulmonary and extra-pulmonary samples 93.5% and 50%, whereas negative predictive values for those are 91.7% and 100%, respectively. In case of microscopically negative specimens, the figures are 79% and 95.6%[11]. In our study sensitivity and specificity of sputum for CBNAAT to detect AFB in smear negative cases is 66.15% and 100.0%.

Conclusion

Our study reaffirmed the usefulness of the CBNAAT over and above the traditional smear microscopy for a significantly higher yield. It leads to early detection and treatment of TB for stopping the transmission of the disease in the community. BAL-CBNAAT shows additional advantage of confirmatory diagnosis of the disease even if sputum CBNAAT is negative. Simplicity, sensitivity, speed and automation of CBNAAT makes this technique a very attractive tool for diagnosis of Mycobacterium tuberculosis from smear negative cases of TB suspects. With the added advantage of detection of multi-drug resistant cases, it seems to be another mile stone in 'End TB' strategy.

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