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AN EVALUATION OF DIAGNOSTIC IMPORTANCE OF FIBREOPTIC BRONCHOSCOPY AND INDUCED SPUTUM IN THE DIAGNOSIS OF SPUTUM SMEAR-NEGATIVE PULMONARY TUBERCULOSIS

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ABSTRACT

Introduction: Induced sputum is less invasive and economical procedure than bronchoscopy. A single induced sputum sample and bronchoscopy are very useful for diagnosing of **Sputum smear-negative pulmonary tuberculosis (SSN-PTB)**. Our aim is to find out which procedure is better in diagnosis of sputum negative pulmonary tuberculosis.

Methods: It is a cross-sectional prospective study in which consecutive patient were selected with possibly active pulmonary tuberculosis, the diagnostic give way three induced sputum tests were weighed against with bronchoscopy. Patients whichever produced no sputum otherwise (acid fast) smear negative sputum. Bronchoscopy was only carried out if at least two induced sputum samples were smear negative.

Results: Of 147 patients who completed all tests, 51 (34 %) had smear negative and culture positive specimens, 26 (51%) on bronchoscopy and 49 (96%) on induced sputum ($p<0.005$). Two patients were culture positive on bronchoscopy alone compared with 25 patients on induced sputum alone; 24 were culture positive on both tests.

Conclusions: Induced sputum test is better than bronchoscopy in diagnosis of sputum negative TB patients. Three induced sputum tests without bronchoscopy should carry out in patients examined for possibly active or inactive tuberculosis who produce no sputum or have smear negative sputum. Nosocomial tuberculosis may be a risk factor for Induced sputum testing so it is recommended it should be performed in respiratory isolation conditions

Keywords: Sputum smear-negative pulmonary tuberculosis (SSN-PTB), Induced sputum, bronchoscopy

INTRODUCTION

Tuberculosis (TB), a significant preventable and treatable cause of death, is a foremost health problem globally. According to the recent estimates, there were 8.8 million new TB cases in 2005, 7.4 million of them in Asia and sub-Saharan Africa; 1.6 million people died of TB, including 1,95,000 patients co-infected with the human immunodeficiency virus (HIV).[1, 2] Detection of active pulmonary tuberculosis (PTB) disease is an important element of TB control as early treatment turn into these patients noninfectious and break up the chain of transmission of TB. According the programme conditions, Revised National Tuberculosis Control Programme (RNTCP) of Government of India, [3] the diagnosis of PTB is rely on sputum smear examination. Sputum microscopy is a highly specific test, an inexpensive, appropriate technology for periphery also and is an essential part of the

directly observed treatment, short-course (DOTS) strategy of the WHO.

On the other hand, in patients with a compatible clinical symptoms, sputum smears do not shows acid-fast bacilli (AFB) in all patients, 'smear negative - culture positive' state has been found in 22% to 61% of the cases.[4, 5] Mycobacterial cultures take at least six to eight weeks time for confirming the diagnosis and in so doing an important time is vanished or patient may receive empirical treatment. The clinicians still face Sputum smear-negative pulmonary tuberculosis **(SSN-PTB)** as a common problem in children who are unable to make a sufficient sample of sputum and patients with immunosuppressed states like AIDS patients, commonly have SSN-PTB. Delayed diagnosis may be an important cause of excess mortality in people living with HIV who have smear-negative pulmonary and extra pulmonary tuberculosis.

Bronchoscopy is commonly used for investigating patients with SSN-PTB. Still, there is a wide range in the diagnostic tests are available yield from bronchoscopy in suspected TB,[6,7] and bronchoscopy is expensive, needs experts to perform and some time inconvenient to patients. A cheaper non-invasive test which may adopt by RNTCP could be performed at peripheral centers and means of providing the same information as bronchoscopy would be beneficial.

Induced sputum testing has previously been reported to be a useful test in the diagnosis of subjects with SSN-PTB .[8] Mc Williams et al[9]compared the induced sputum test and bronchoscopy in the diagnosis of TB, and reported that the diagnostic value of induced sputum test was more than bronchoscopy. We have compared the results of three induced sputum tests with bronchoscopy washings in 200 patients with possibly active pulmonary tuberculosis.

METHODS

The present study, approved by the institutional ethics committee, was conducted in tertiary level hospital over a period from November 2010 to November 2011.

Inclusion criteria comprised: Clinically suspected cases of pulmonary tuberculosis, aged 16-75 years, with three sputum smears negative for AFB and a chest radiograph suggestive of pulmonary tuberculosis was included in the study after obtaining an informed consent. **Exclusion criteria** were severe asthma or severe chronic obstructive pulmonary disease (COPD) (forced expiratory volume in 1 second (FEV1) <65% predicted), oral steroid treatment for either of these conditions in the previous month. Patients with bleeding diathesis, history of myocardial infarction or arrhythmia, extra-pulmonary tuberculosis, history of anti-tubercular treatment (ATT) for more than one month, and those with severe dyspnoea were excluded from the study. HIV-positive and non- cooperative patients were also excluded.

A detailed history, clinical examination, and routine investigations were carried out on suspected cases of tuberculosis. Three sputum samples (spot, morning and spot) were tested for presence of AFB in the smear. In patients with suspected smear negative pulmonary tuberculosis, a sputum sample was sent for sputum culture (BACTEC) and the patients were taken up for Induced sputum and bronchoscopy. Prior to the procedure an informed written consent was obtained from the patient. Each subject had been explained in detail about procedure, benefits of procedure and risk factor of it in lay local language and Prior to the procedure an informed written consent was obtained from the patient.

Induced sputum tests procedures

Patients were nebulized with 3% hypertonic saline solution delivered by an ultrasonic nebulizer. The inhalation continued until production of a sufficient sample of sputum or 20 minutes. The procedures were usually performed on three consecutive days. Patients with mild/moderate asthma or COPD received 2.5 mg salbutamol via a standard nebulizer before each induced sputum test. All subjects were supervised by an experienced nursing staff.

Bronchoscopy procedure: It was an elective procedure with the patient nil orally for 4-6 hours. Patients were pre-medicated with 0.6 mg atropine 30-45 minutes prior to bronchoscopy and mobilization was done with two per cent xylocaine via ultrasonic nebulizer. Fibreoptic bronchoscopy was performed by a respiratory physician. Olympus BF type E2 bronchoscope was used. Bronchial segments which were thought from the chest radiograph to be the site of active or inactive TB were washed with 40 ml normal saline. Usually 15-30 ml of fluid was instilled with each washing and about one- fourth to half of this volume was retrieved in the suction trap. Up to one-fourth of the instilled amount retrieved was considered successful. The bronchial washings were sent for AFB staining, AFB culture by BACTEC, and for cytology and cell count.

After the procedure, the patient was observed for development of pneumothorax, hemorrhage, infection and cardiac arrhythmias for 24-48 hours. The first sputum sample after bronchoscopy (post-bronchoscopic sputum) was collected and sent for analysis along with bronchial washings.

Specimens were processed using standard methodology13. Positive smears were confirmed by Ziehl-Neelsen staining. Specimens were cultured using Bactec 12B and Lowenstein-Jensen media.

Table 1. Tuberculosis diagnosis with Induced sputum and Bronchoscopy

	n	
(A) Excluded Patients		**%**
Active Tuberculosis	**27**	
Smear positive on induced sputum	*22*	*81.48*
Smear negative, culture positive subjects	*5*	*18.5*
No evidence of Tuberculosis	**26**	
Subtotal (A)	**53**	
(B) Subjects who completed study tests		
Active Tuberculosis	**51**	
Induced sputum only	*25*	*49.01*
Bronchoscopy only	*2*	*3.92*
Induced sputum and bronchoscopy	*24*	*47.05*
Active Non-tuberculosis mycobacteria	**2**	
Non-tuberculous mycobacteria (probable contaminant)	**5**	
No mycobacterial disease	**89**	
Subtotal (B)	**147**	
Total subjects (A+B)	**200**	

RESULTS

Subjects

Two hundred and sixty subjects were enrolled. Fifty three (26.5%) did not complete three induced sputum tests and/or bronchoscopy. So 147 (81 men and 66 women) took part in the study. Their median age was 38 years (range 15–85.One hundred and forty five of the 147 (96%) participants tolerated the induced sputum test without difficulty. Twenty five of 147 cannot tolerate Bronchoscopy procedure.

Diagnosis of pulmonary tuberculosis

Seventy eight cases of TB were diagnosed from 200 subjects (table 1). Among the 27 excluded subjects, 22 had smear positive induced sputum and did not proceed to bronchoscopy. Five of the remaining 20 subjects were diagnosed with TB and were excluded from the statistical comparison of induced sputum with bronchoscopy because of failure to complete all tests. All four were smear negative and culture positive on induced sputum, and two were culture positive on bronchial washings.

Fifty one of 147 subjects who completed all tests were diagnosed with smear negative, culture positive pulmonary TB. Forty nine of the 51 (96.7%) were identified by induced sputum testing and 26 (51%) by bronchoscopy. Two cases were diagnosed only by bronchoscopy, whereas induced sputum testing alone diagnosed 25. Twenty four were culture positive by both tests. Induced sputum was more sensitive than bronchoscopy ($p<0.005$, McNemar $\chi 2$test) in diagnosing active TB in this subject group.

Of 49 subjects who were culture positive on sputum testing, twelve were positive on one test, thirteen were positive on two tests, and 24 were positive on all three samples. Non-tuberculous mycobacteria were cultured from induced sputum in seven subjects. Single cultures of Mycobacterium gordonae (n=2) and M triviale (n=1) were assumed to be contaminants. In one subject M avium intracellulare complex was cultured from all three induced sputum samples, but bronchial washings were culture negative.

DISCUSSION

This study has shown that induced sputum testing is a safe, effective means of obtaining specimen for AFB and culture in suspected **pulmonary tuberculosis** cases. It is also more sensitive than bronchoscopy for detecting active pulmonary TB in **Sputum smear-negative pulmonary tuberculosis (SSN-PTB)**. These results differ from those of Anderson[10] which suggest that a single induced sputum test and bronchoscopy have similar diagnostic ability. In the study by Anderson [10] there were 101 subjects, of whom 20/26 (77%) were culture positive on sputum testing and 19/20 (95%) had culture positive bronchial washings[10] .The observations of McWilliams et al [9] were also showing a relationship with our study. McWilliams et al found induced sputum gave a diagnosis of TB in smear negative patients about 96.07%.[9] In the present study, induced sputum made available a diagnosis of smear negative, culture positive TB in 49/51 subjects (96.07%). This result was significantly better than bronchoscopy, which gave the diagnosis in only 25/51 cases (51%).

The discrepancy between the results of the present study and those of Anderson may comprise several reasons. Lignocaine can inhibit the growth of M tuberculosis in vitro.[11] If more lignocaine was used in the present study in some TB cases, this might reveal the apparent false negative rate of bronchoscopy.

The volume of bronchial lavage fluid may be a reason. About 40 ml was lavaged per segment and usually 15-30 ml of fluid was instilled with each washing in our study

compared with 50–60 ml by Anderson et al. The same type of ultrasonic nebulizer and the same tonicity of saline were used in all three studies.[9, 10]

Different patient populations, dissimilar procedural techniques, and different levels of laboratory specialization may also responsible enrolment of sputum smear negative PTB patients. These differences may be related to, different For example, in our study, most of the patients were referred from outpatient clinics (primary health care units) whose laboratories are not specialized in the diagnosis of TB, and some of the results for these patients may therefore have been falsely negative.

On the other hand, to a certain extent bronchoscopy under diagnosing TB in our study but we consider that the induced sputum procedure gave an undervalue of TB in other studies. With three induced sputum procedures the diagnosis was made in 25 patients (49.01%) with all three induced sputum specimens, in fourteen (27%) with two specimens, and in ten (19%) with only one specimen. Obviously, only single induced sputum may have the potential for false negative results. The present study confirms the results of McWilliams et al [9]Al-Zahrani et al[12]who showed that increasing number of tests may pick up the diagnostic yield of induced sputum testing.

Induced sputum testing has some disadvantages also. The staff who supervise the tests have the risk of transmission of TB.[13] The risk of transmission may be less with induced sputum if proper safety measures are applied [14] bronchoscopy procedure requires a doctor and an assistant are to be in attendance throughout while sputum induction involves only one staff member who does not need to be present during each test. Bronchoscopy was evaded in 22 subjects who had smear positive induced sputum in the present study. A key protection measure with sputum testing is that it should only be performed in a separate room that has a proper ventilation requirement for TB isolation.

In our study one induced sputum test performed each day for 3 days. Whether improved convenience and reduced indirect costs could be achieved by performing the three tests over 1–2 days, without reducing the diagnostic yield, remains untested. Positive induced sputum cultures for non-tuberculous mycobacterium in seven of 200 subjects (3.5%) shows that, like bronchoscopy, [15–19] induced sputum carry a low risk of false positive mycobacterial cultures. However, bronchoscopy is a costly test,[9,20] is an invasive procedure, and is not widely available in the developing countries and resource poor settings. Therefore, depending on the circumstances in which the patient is being evaluated, bronchoscopy should be used with care. In resource poor settings, where transmission of TB is high, sputum induction with hypertonic saline can be useful in adding to the diagnostic yield.

If the patient suspected to have SSNPTB still remains induced sputum smear-negative, despite these potential problems, we believe the advantages of induced sputum outweigh the disadvantages. Bronchoscopy is a semi-invasive procedure. Replacing it with induced sputum testing removes the need for sedation and the risk from bronchoscopy, albeit low, of nosocomial infection.

In summary, we have shown that sputum induced is a safe procedure with a high diagnostic yield and a high agreement with results of fiberoptic bronchoscopy for the diagnosis of SSN-PTB. In areas where fiberoptic bronchoscopy is not readily available, and as part of the workup of suspected TB prior to bronchoscopy, sputum induced test offers an alternative or additional approach to the diagnosis of sputum–smear-negative TB, and would enhance sensitivity for the diagnosis of TB

in resource-poor areas. These results guide us to recommend that three induced sputum tests (with proper safety measures) should be adopt at periphery primary health centers in the investigation of possibly active, sputum smear negative, pulmonary TB. Bronchoscopy will still be required if TB is excluded and tumour or other pathology is included in the differential diagnosis.

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REFERENCES

1. World Health Organization. Global tuberculosis control surveillance, planning, financing. WHO Report 2007.Geneva: World Health Organization; 2007. WHO/HTM/TB/2007.376
2. Dye C. Global epidemiology of tuberculosis. *Lancet* 2006;367: 938-40.
3. TB India 2007. *RNTCP Status Report.* New Delhi: Central TB Division, Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India; 2007.
4. Narain R, Subbarao MS, Chandrasekhar P, Pyarelal.Microscopy positive and microscopy negative cases of pulmonary tuberculosis. *Am Rev Respir Dis* 1971; 103: 761-3.
5. Kim TC, Blackman RS, Heatwole KM, Rochester DF. Acid fast bacilli in sputum smears of patients with pulmonary tuberculosis: prevalence and significance of negative smears pretreatment and positive smears post treatment. *Am Rev Respir Dis* 1984; 29: 264-8.
6. Arshad Altaf Bachh, Rahul Gupta, Inaamul Haq, Hanumant Ganapati Varudkar. Diagnosing sputum/smear-negative pulmonary tuberculosis: Does fibre-optic bronchoscopy play a significant role? Lung india,2010, 27 : 2, 58-62
7. Willcox PA, Benetar SR, Potgieter PD. Use of the flexible fibreoptic bronchoscope in diagnosis of sputum-negative pulmonary tuberculosis. Thorax1982;37:598–601.
8. Merrick ST, Sepkowitz KA, Walsh J, et al. Comparison of induced versus expectorated sputum for diagnosis of pulmonary tuberculosis by acid fast smear. Am J Infect Control1997;25:463–6.
9. T McWilliams, A U Wells, A C Harrison, S Lindstrom, R J Cameron, E Foskin Induced sputum and bronchoscopy in the diagnosis of pulmonary tuberculosis Thorax 2002;57:1010–1014
10. Anderson C, Inhaber N, Menzies D. Comparison of sputum induction with fiber-optic bronchoscopy in the diagnosis of tuberculosis. Am J Respir Crit Care Med1995;52:1570–4.
11. Schmidt RM, Rosenkranz HS. Anti microbial activity of local anaesthetics: lidocaine and procaine. J Infect Dis1970;121:597–607
12. Al Zahrani K, Al Jahdali H, René P, et al. Yield of smear, culture and amplification tests from repeated sputum induction for the diagnosis of pulmonary tuberculosis. Int J Tuberc Lung Dis2001;5:855–60.
13. Larson JL, Ridzon R, Hannan MH. Sputum induction versus fibreoptic bronchoscopy in the diagnsosis of tuberculosis. Am J Respir Crit Care Med2001;163:1279–80.

14. Centres for Disease Control. Guidelines for preventing the transmission of Mycobacterium tuberculosis in healthcare facilities, 1994. MMWR1994;43: RR-13
15. Leers W. Disinfecting endoscopes: how not to transmit Mycobacterium tuberculosis by bronchoscopy. Can Med Assoc J1980;123:275–83.
16. Nelson KE, Larson PA, Schraufnagel DE, et al. Transmission of tuberculosis by flexible fiberbronchoscopes. Am Rev Respir Dis1983;127:97–100.
17. Steere AC, Corrales J, and von Graevenitz A. A cluster of Mycobacterium gordonae isolates from bronchoscopy specimens. Am Rev Respir Dis1979;120:214–6.
18. Dawson DJ, Armstrong JG, and Blacklock ZM. Mycobacterial cross-contamination of bronchoscopy specimens. Am Rev Respir Dis1982;126:1095–7.
19. Pappas SA, Schaaff DM, DiCostanzo MB et al. Contamination of flexible fibreoptic bronchoscopes. Am Rev Respir Dis1983;127:391–2.
20. Lim TK, Cherian J, Poh KL, Leong TY. The rapid diagnosis of smear-negative pulmonary tuberculosis: a cost-effectiveness analysis. *Respirology* 2000; 5: 403-9.