Original Article

Comparison of Induced Sputum and Bronchoalveolar Lavage Fluid Examination in the Diagnosis of Sputum Negative Pulmonary Tuberculosis

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Abstract

Background. Tuberculosis (TB) is one of the common infections in the world, especially in developing countries like India. Therefore, early diagnosis is important. This study was undertaken to compare the yield of sputum induction with bronchoalveolar lavage (BAL) in smear-negative suspected pulmonary TB patients in a tertiary care hospital in Agra.

Methods. Fifty patients were included in the study. In all patients, induced sputum, fibreoptic bronchoscopy and BAL fluid were subjected to diagnostic testing.

Results. On acid-fast smear examination, induced sputum and BAL fluid tested positive in 27/50 and 25/50 patients, respectively with a sensitivity of 83.3% and 90% respectively ($p<0.0001$). On comparing sputum induction *versus* BAL on culture, 30 patients were positive by sputum induction and 27 patients were positive on BAL fluid, with the sensitivity of 85.7% and 77.1%, respectively. The results showed that the sputum induction showed a significantly higher yield than that of BAL fluid ($p=0.0013$).

Conclusion. Sputum induction offers an alternative approach in the diagnosis of smear-negative suspected pulmonary TB patients and would enhance sensitivity for the diagnosis of TB. **[Indian J Chest Dis Allied Sci 2016;58:173-175]**

Key words: Sputum negative pulmonary TB, BAL, Induced sputum.

Introduction

Tuberculosis (TB) is one of the most common infections in the world, especially in developing countries. India has more new TB cases annually than any other country.[1] The World Health Organization (WHO) recommends the detection of acid-fast bacilli (AFB) in respiratory specimens as the initial approach to the diagnosis of pulmonary TB (PTB).[2] However, this method has a low sensitivity and has little value in patients who cannot produce sputum spontaneously.[3,4] Early diagnosis to reduce the period of infectivity is considered to be one of the most effective TB control strategies. However, the isolation of *Mycobacterium tuberculosis* is difficult in children, human immunodeficiency virus (HIV) co-infected people, and others with paucibacillary disease. It follows that strategies to improve the bacteriologic confirmation of PTB by the optimisation of sputum collection are of great importance for the control of the epidemic.[5]

Mycobacterial culture being gold standard and a fundamental tool for the diagnosis of PTB has got its limitation of low sensitivity. Gastric lavage and fiberoptic bronchoscopy (FOB) have been regarded as the useful diagnostic procedures in persons with paucibacillary TB. However, these methods are relatively invasive and not always accessible in TB-endemic settings.[5] Sputum induction is a safe procedure with a high diagnostic yield and a high agreement with results of FOB for the diagnosis of PTB. In areas where FOB is not readily available, sputum induction offers an alternative or additional approach to the diagnosis of sputum smear-negative PTB (SSNPTB).[6]

In resource-limited countries where FOB in every case of SSNPTB is not feasible, sputum induction for diagnostic testing offers an alternative approach for diagnosing such cases. With this aim, the present study was undertaken on 50 patients to compare efficacy of sputum induction *versus* bronchoalveolar lavage (BAL) in the diagnosis of SSNPTB.

Material and Methods

This study was conducted between August 2009 and July 2012 in the Postgraduate Departments of Medicine and Pathology, S.N. Medical College and Hospital, Agra. Sixty patients were admitted with clinical and radiological evidence of PTB but were sputum smear-negative on both occasions (morning and spot). The patients presented with a wide variety of symptoms including cough, expectoration, fever with evening rise of temperature, haemoptysis, dyspnoea and chest pain. Radiologically, patients were categorised into those with cavitatory or non-

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cavitatory lesions. Of these, 10 patients were excluded as four patients did not give consent and six patients had some contraindications (3 were severely hypoxic, 2 had ischaemic heart disease and 1 had deranged coagulation profile). Fifty patients were included in the study. The enrolled patients were subjected to a protocol, which include detailed history regarding modes of onset, duration of illness, history of drug intake and radiological evidence of PTB.

One hour before bronchoscopy, all individuals inhaled 5mL of 3% hypertonic saline solution by nebuliser and then were asked to cough. Specimens achieved by this method (induced-sputum) were collected.

All patients were fasting for at least four hours prior to bronchoscopy and pre-medicated 30 to 45 minutes before the procedure with intra-muscular injection of atropine 0.6mg and 10mg of diazepam administered orally. Local anaesthesia to upper respiratory tract was administered using 4% xylocaine through a nebuliser, just before the procedure. Thorough examination of the bronchial tree was carried out. The bronchoscope was then wedged into the segmental and sub-segmental bronchi and BAL was taken from the involved area. For BAL fluid, sterilised buffered normal saline at body temperature was used; 20mL of this was instilled through the bronchoscope and promptly aspirated using low pressure suction. Total of 8-10 aliquotes (150-200 mL) were instilled. Lavage fluid was collected into a non-siliconised sterilised container. All samples of induced sputum by 3% hypertonic saline and BAL fluid was examined for AFB by Ziehl-Neelsen (Z-N) staining and was cultured for *Mycobacterium tuberculosis* on Lowenstein-Jensen (L-J) medium in our hospital.

Statistical Analysis

Data were analysed using Statistical Package for Social Sciences (SPSS). For calculation of sensitivity and total number of positive cases (a+b) either by BAL or induced sputum or both was taken as gold standard.

Results

Of the 50 patients studied, 30 were males; their age ranged between 14-60 years. On AFB smear examination, induced sputum and BAL fluid tested positive in 27/50 and 25/50 patients, respectively. Among 25 BAL smear-positive cases, 22 were also positive by induced sputum examination and three were positive alone in BAL (Table 1). Among 27 induced sputum cases, five tested positive exclusively in induced sputum smear (Kappa=0.68) examination. Fisher's test demonstrated a significant relationship between these two methods (p<0.0001).

Table 1. Results of AFB microscopy by Z-N staining (n=50)

AFB	BAL	SI	BAL + SI
Positive	25	27	30
Negative	25	23	20

Definitions of abbreviations: AFB=Acid-fast bacilli; Z-N=Ziehl-Neelsen; BAL=bronchoalveolar lavage; SI=Sputum induction

Table 2. Results of mycobacterial culture on L-J medium (n=50)

Mycobacterial Culture on L-J Medium	BAL	SI	BAL + SI
Positive	27	30	35
Negative	23	20	15

Definitions of abbreviations: L-J=Lowenstein-Jensen; BAL=Bronchoalveolar lavage; SI=Sputum induction

Thirty patients were positive by induced sputum culture and 27 were positive by BAL culture. Among 27 BAL culture positive cases, 22 were also positive by induced sputum culture and five cases alone in BAL culture (Table 2). Among 30 induced sputum culture positive cases, 8 were alone positive in induced sputum culture (Kappa=0.47) examination. Fisher's test demonstrated a significant relationship between these two methods (p=0.0013).

Radiologically, 21 (42%) patients had cavitary lesions; 15/21 of these tested positive on mycobacterial culture. Twenty-nine (58%) had non-cavitatory lesions; 20/29 of these tested positive on mycobacterial culture. The sensitivity for diagnosis of TB in cavitatory lesions was 42.8% while in non-cavitatory lesions, it was 57.1% (Table 3).

Table 3. Diagnostic confirmation

Chest Radiograph Appearance	Positive by SI Culture Only	Positive by BAL Culture Only	Positive Both SI and BAL Mycobacterial	Total Cases Diagnosed	Sensitivity (%)
Cavitatory (n=21)	2	3	10	15	42.8
Non-cavitatory (n=29)	6	2	12	20	57.14

Definitions of abbreviations: SI=Sputum induction; BAL=Bronchoalveolar lavage

Discussion

In a study from Brazil,[6] the efficacy of induced sputum and FOB were studied in patients with HIV infection and negative sputum sample. The sensitivity of AFB smears of specimens obtained by inducted sputum and BAL fluid was found to be 34% and 38%, respectively. The authors concluded that induced-sputum is a safe and reliable diagnostic tool.[6] In New Zealand, Mc

Williams *et al*[7] compared induced-sputum and bronchoscopy sampling with radiologic findings and concluded that the induced-sputum sampling is positive with higher prevalence in patients with radiologic pattern of active TB, despite the fact that expense of induced-sputum is one-sixth of bronchoscopy.

Schoch and colleagues[8] demonstrated that clinical signs and radiologic findings are not sensitive enough for TB diagnosis. They also showed that bronchoscopy is more accurate than induced-sputum technique.[8]

In Canada, Al Zahrani and associates[9] found out that intermittent repeats of induced-sputum technique (up to three times) would increase its specificity from 64% to 97%. Repeating would also augment the culture sensitivity from 70% to 99%.[9] Parry and colleagues[10] proposed induced-sputum approach for patients who cannot produce sputum or have negative smear TB. Kartalogu *et al*[11] reported that though gastric lavage fluid is not a diagnostic method, mycobacterial culture of gastric lavage fluid is helpful.

In Bangladesh, Ganguly *et al*[12] evaluated the sensitivity of AFB-smears in samples from sputum induction and BAL as 74% and 58%, respectively in their study of 52 sputum smear-negative cases. In another study[13] the sensitivity of smear and culture of induced-sputum were reported to be 80% and 87%, respectively. Our study also showed similar results with sensitivity (on AFB smear examination) of sputum induction and BAL to be 90% and 83.3%, respectively. AFB culture also showed a sensitivity of 85.7% and 77.1% for sputum induction and BAL, respectively.

Conclusions

Sputum induction offers an alternative or additional approach to the diagnosis of smear-negative suspected pulmonary tuberculosis patients and would enhance sensitivity for the diagnosis of tuberculosis. We believe that sampling via induced-sputum method as a non-invasive approach is cheaper, with less side-effects, more comfortable and has less anxiety, and suited for resource-poor areas. It also has very less contraindications and lesser risk of nosocomial infection as compared to BAL. Nevertheless, repeated sampling would increase the diagnostic accuracy.

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