Use of flexible bronchoscopy for rapid diagnosis of suspected tubercular cases in rural India

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Abstract
Background: Reaching a correct diagnosis is a challenge for physicians treating any of the 30% to 50% of pulmonary tuberculosis patients who have negative sputum cultures or who present with no sputum. Flexible bronchoscopy acquires special importance for these cases for whom empirical anti-tuberculosis therapy is the only option left. In our study we aimed to assess the diagnostic yield of flexible bronchoscopy in patients, suspected to have tuberculosis, whose sputum smears were negative.

Methodology: In our hospital-based cross-sectional study, 42 patients were enrolled by consecutive sampling. Flexible bronchoscopy and selective bronchial washings were done in all patients.

Results: Bronchoscopy lavage smears were positive for M. tuberculosis in 10 (23.8%) patients. Fifteen (35.7%) patients had positive culture.

Conclusion: Flexible bronchoscopy has an important role in the diagnosis of patients suspected to have tuberculosis, whose sputum smears are negative or who can not produce sputum.

Key words: flexible bronchoscopy, rapid diagnosis, suspected tuberculosis


(Received 26 February 2009 – Accepted 23 October 2009)

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Introduction
Tuberculosis (TB) causes approximately two million deaths per year, 98% of which occur in low-income countries [1]. India has the highest TB burden of any country in the world [2,3]. The widespread implementation of the internationally recommended Directly Observed Treatment, Short-course (DOTS) strategy has proved to be an effective tool in controlling TB on a mass basis and is being practiced in over 180 countries [4-6].

Sputum microscopy continues to be the best tool for detection of infectious TB [7] in patients with a compatible clinical picture; however, sputum smears do not reveal acid-fast bacilli (AFB) in all patients, and a “smear-negative/culture-positive” state has been observed in 22% to 61% of the cases [8-10]. The DOTS approach has provided access to standardised, quality assured microscopy [11].

However, sputum smear-negative pulmonary tuberculosis (SSN-PTB) still remains a common problem. This is particularly true in immunosuppressed patients, such as those with acquired immunodeficiency syndrome (AIDS) in whom SSN-PTB is quite common. Various methods have been employed to ascertain active TB disease in patients with suspected SSN-PTB, including mathematical modelling for predicting active disease [12,13]. Of these, bronchoscopic procedures have been studied in some detail.

Flexible bronchoscopy has proven to be a useful technique in the evaluation of suspected cases of pulmonary tuberculosis that are sputum smear-negative [14,15]. The present study tested the sensitivity of bronchial wash for rapid diagnosis of tuberculosis in sputum smear-negative suspected tubercular patients. The study further aimed to assess the diagnostic yield of flexible bronchoscopy in
patients, suspected to have tuberculosis, whose sputum smears were negative.

**Materials and methods**

**Study Settings**

This study was conducted at a 909-bed tertiary care teaching hospital, Wardha of Datta Meghe Institute of Medical Sciences University (National Assessment of Accreditation Council Accredited Grade A). The hospital provides health care to the nearby area, mainly from the rural area of Wardha district and other parts of Central India. This hospital has a DOTS center and designated microscopy center which implements quality assurance protocol and provides quality assured laboratory services. An built-in routine system has been designed for sputum microscopy External Quality Assessment (EQA) and for the supervision and monitoring of the diagnostic systems from the Revised National TB Control Programme (RNTCP) by the chest and tuberculosis specialist in the Department of Chest Disease. The program is run per the guidelines of RNTCP. Sputum microscopy is examined by a trained technician under the supervision of the senior Tuberculosis Laboratory supervisor.

**Study Design**

This study is a hospital-based, cross-sectional study.

**Study period of recruitment**

The study period of recruitment was between 1 February 2007 and 30 March 2008.

**Ethical Issues**

The study protocol was approved by the institutional ethical committee.

**Method of Selection**

Recruitment was done by using consecutive sampling in which the patients were chosen on a strict "first come, first chosen" basis to the Department of Chest Disease. All individuals who were eligible were included as they were seen.

**Eligibility Criteria**

The eligible individuals were the adult patients suspected of having pulmonary tuberculosis who presented negative sputum smears (in at least three samples), and who were registered under RNTCP (already taking DOTS). The suspected tuberculosis patients were the individuals in whom sputum smears were smear-negative and who showed symptoms of cough for more than three weeks, evening rise of temperature, and loss of weight. The diagnosis of sputum smear-negative pulmonary tuberculosis was based on the following criteria: at least three negative sputum smears (including at least one early-morning specimen); chest radiography findings consistent with tuberculosis; and lack of response to a trial of broad-spectrum antimicrobial agents. Because the fluoroquinolones are active against *M. tuberculosis* and thus may cause transient improvement in persons with tuberculosis, they were avoided. In persons with known or suspected HIV infection, the diagnostic evaluation was expedited. Patients younger than 18 years were excluded from the study.

**Data Collection**

In 13 months, 144 patients in the DOTS centre were diagnosed with smear-negative pulmonary tuberculosis. Every third patient was eligible for inclusion in the study; therefore, a total of 48 patients were eligible but only 42 participants gave consent and were subsequently included in the study. The response rate was 88%.

The purpose of the study was explained to the patients and those who consented to participate were included. Others, who left the interview and examination prematurely for various reasons, were excluded from the study. Rapport was developed with the participants and data was collected using a structured interview schedule and examination by a trained and experienced chest physician. Patients suspected of having pulmonary tuberculosis and presenting negative sputum smears (in at least 3 samples) were evaluated using flexible bronchoscopy. Participants were evaluated according to a pre-designed protocol. The clinical profile and radiological lesions in these patients were consistent with the diagnosis of pulmonary tuberculosis but three consecutive occasions produced specimens of sputum that were negative for AFB.

Forty-two patients who were suspected to have pulmonary tuberculosis with sputum smear-negative were enrolled in the study. Flexible bronchoscopy and selective bronchial washings were performed on all patients. Flexible bronchoscopy was conducted trans-nasally.

Prior to the procedure, the patients were given pre-medication with sedatives, opiates and atropine.
Not more than 30 ml of 4% topical Xylocaine and no vasoconstrictors were administered during the exam. After inspection of the airways, the bronchoscope was wedged in areas of maximal involvement, as evident on chest roentgenogram. The bronchoalveolar lavage (BAL) consisted of five or six ml aliquots of normal saline solution; fluid was aspirated using mechanical suction.

Bronchial washings were obtained from the affected parts. Mucosal biopsies were done in patients where endobronchial abnormalities were noted. Transbronchial biopsies were performed in selected patients from the radiological localizations. Ziehl-Nielsen staining and culture in Lowenstein-Jensen medium were the microbiological studies. Aliquots of BAL fluid were sent for staining of the cell pellet in the cytology laboratory.

To prevent cross-contamination, guidelines such as those issued by the British Thoracic Society regarding bronchoscopy and infection control [16] and the American College of Chest Physicians and the American Association of Bronchology [17] were followed.

**Results**

Among the 42 patients, 28 (66.7%) were males. The average age was 38.4 ± 15.3 years. Table 1 shows that only 15 patients (35.7%) out of 42 patients had tuberculosis. Twenty-seven (64.2%) patients were confirmed with diagnoses other than tuberculosis. The diagnoses were community-acquired pneumonia (CAP) in 18 patients (42.9%), foreign body in five patients (11.9%), bronchial carcinoma in three patients (7.2%) allergic bronchopulmonary aspergillosis in one patient (2.4%).

**Table 1. Bronchoscopy involved in diagnosis**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary Tuberculosis</td>
<td>15 (35.7)</td>
</tr>
<tr>
<td>Community Acquired Pneumonia</td>
<td>18 (42.9)</td>
</tr>
<tr>
<td>Foreign Body</td>
<td>5 (11.9)</td>
</tr>
<tr>
<td>Bronchial Carcinoma</td>
<td>3 (7.2)</td>
</tr>
<tr>
<td>Allergic bronchopulmonary aspergilosis</td>
<td>1 (2.3)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>42 (100.0)</strong></td>
</tr>
</tbody>
</table>

**Discussion**

When there is suspicion of active tuberculosis, patients in whom direct examination of sputum is inconclusive represent a diagnostic and therapeutic challenge. Our study confirms this observation since other infectious, neoplastic and foreign bodies (beetel nut which was extracted from all the patients; retrospectively, all patients gave history of beetel nut chewing while going to sleep) were diagnosed in these patients (64%) who were originally thought to be suffering from pulmonary tuberculosis.

Rao [18] has demonstrated the usefulness of bronchoscopy among smear-negative patients in India. Of 55 sputum smear-negative patients, 15 (27.3%) had AFB-positive bronchial washings (cultures were not performed), and bronchial carcinoma was diagnosed in another five patients. In our study it was found that bronchoscopic lavage smears were positive for *M. tuberculosis* in 10 (24%) patients and 15 (36%) patients had positive culture. Similar results were seen in a study conducted by Yuksekol et al. [19], in which Bronchoscopic lavage smears were positive for *M. tuberculosis* in 13 (23%) patients and 28 (50%) patients had positive culture. Using bronchoscopic procedures early in the diagnosis was performed in 27 (48.2%) patients. Bronchoscopic procedures provided overall diagnostic yields in 62.7% (23/39) of the patients. A study conducted by Charoenratanakul et al. [20] shows that bronchoscopic procedures provided overall diagnostic yields in 47.5% (19/40) of the patients. The diagnostic yield of overall bronchoscopic procedures for tuberculosis in this study was 35.7% (15/42) of patients. It consisted of positive BAL smear in 23.8% (10/42) of patients and positive for mycobacterial culture in 35.7% (15/42) of patients. Non-tuberculosis conditions were diagnosed by the bronchoscopic method in 27 patients (64.2%).

In the present study, bronchoscopy was useful not only for the diagnosis of tuberculosis but also for the identification of other pathologies, especially neoplasia (3 cases) and foreign bodies (5 cases), whose delayed diagnosis may exclude the possibility of a surgical cure. Some authors whose objectives were similar to those of our study have also reported diagnosing neoplasia after performing bronchoscopy [21]. Other infectious diseases such as CAP and
aspergillosis were also diagnosed through bronchoscopy during this study.

The limitation in this study was that no investigative method other than bronchoscopy was used for detection of tuberculosis. Therefore, no comparative study was possible. The sensitivity of bronchoscopy for tuberculosis and the determination of the diagnosis of other pathologies (neoplasia, infectious diseases or diseases mediated by the hypersensitivity mechanism) reinforce data in the literature indicating this type of examination when there is suspicion of tuberculosis but no confirmation in the sputum microscopy. This study though cannot be generalized as it was conducted in a tertiary care hospital setup.

High prevalence settings for TB are often resource-limited and thus offer constraints for the use of bronchoscopy. There would be a need for further research on the feasibility and cost-effectiveness of bronchoscopy for TB diagnosis in resource-limited settings before it can be recommended as a useful tool. Involving medical colleges as partners and implementing Public Private Partnership are ways in which big hospitals can cater to the needs of the patients. In such setups, flexible bronchoscopy through the RNTCP can be one approach to prevent needless governmental expenditures on TB diagnosis and loss of disability-adjusted life years (DALY) in patients.

Conclusion

Although spread of TB following bronchoscopy has occasionally been reported, flexible bronchoscopy has an important role in the diagnosis of patients suspected to have tuberculosis, whose sputum smears are negative or who can not produce sputum. This study suggests that in tertiary care hospitals of areas with high TB prevalence, bronchoscopic procedures should be performed in those cases in which other diagnoses such as malignancy, foreign body, etc. must be ruled out.

References


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**Conflict of Interest:** No conflict of interest is declared.