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Diagnostic Value of Bronchoscopic Procedures and Postbronchoscopic Sputum in Suspected Pulmonary Tuberculosis; A Pilot Study

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Abstract: *In patients, suspected to have pulmonary tuberculosis (PTB) on clinical and radiological grounds, but who have negative sputum results for Acid-Fast Bacilli (AFB) or who do not expectorate adequate sputum for testing fiberoptic bronchoscopy (FOB) is a useful method for overcoming definitive diagnostic difficulties. This study has aimed at comparing the diagnostic value of the data acquired by the sampling procedures applied with FOB and the diagnostic value of the post bronchoscopy sputum samples. The study included 31 patients. Using FOB, bronchoalveolar lavage, catheter mediated aspiration, bronchial brush biopsy andtransbronchial biopsy were performed. Samples of secretion aspiration were taken before terminating the procedure. Sputum samples were taken in the first 24 hours after FOB. On all the samples obtained AFB direct spread microscopy and AFB culture seeding were carried out. The transbronchial biopsy samples were investigated histologically.: Confirmatory PTB diagnoses were made in 14 (46.6%) patients within 1-2 days by the FOB assisted procedures performed . When bronchoalveolar lavage and catheter mediated aspiration were performed, definitive PTB diagnoses were made in 25 (83.3%) patients. When the results on one of the 3 post FOB sputum samples were also included, 26 (86.6%) patients were diagnosed with PTB.*
Among the FOB assisted procedures, bronchoalveolar lavage and catheter mediated aspiration have been found especially useful. Inclusion of the post FOB sputum sample results leads to faster diagnoses and diagnostic confirmation.

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I. Introduction

Tuberculosis is still one of the 10 diseases that cause most deaths in the world, such that approximately 1.4 million HIV-free humans died from tuberculosis in 2015 and approximately 10.4 million had contracted the infection [1]. Early diagnosis of active pulmonary tuberculosis (PTB) and treatment is effective in the prevention of the disease spread and reduction of mortality. The basic diagnostic approach has been the detection of positive Acid-Fast Bacilli (AFB) staining in sputum samples. However, sputum samples of about 50% of patients with active (PTB) can be AFB-negative [2]. Thus, patients suspected for PTB but presenting with negative sputum smear or unable to expectorate sputum can be investigated with fiberoptic bronchoscopy (FOB) as a useful diagnostic aid for PTB confirmation [3]. Using FOB, bronchoalveolar lavage, bronchial brush biopsy, bronchial forceps biopsy, needle aspiration and biopsy and bronchoscopic aspiration procedures can be carried out [4].
The aim of this study was to compare the diagnostic values of bronchoscopic procedures and post bronchoscopic sputum samples in suspected pulmonary tuberculosis that could not be diagnosed by sputum sampling.

II. Material And Methods

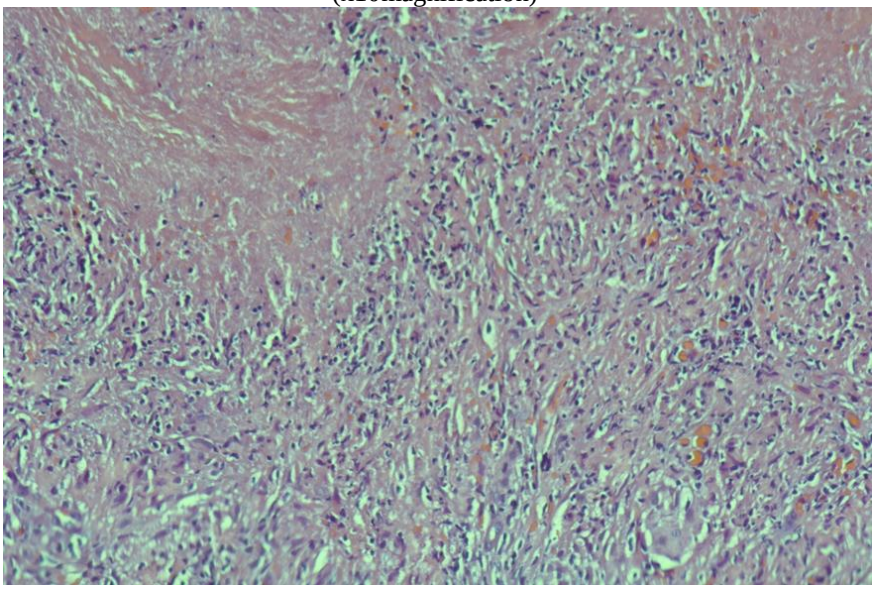
This study was a pilot study and prospective single blind study.

Patients: The study was initiated after the written informed consent of the patients and was carried out by the World Health Organization on the basis of the Helsinki Declaration. The study included a total of 31 patients consulting our center within a period of 6 months, given preliminary PTB diagnoses on clinical and radiological evidence that could not be confirmed bacteriologically by detection of AFB in the sputum samples or by lack of an adequate quantity of expectorated sputum. One of the patients was excluded from the study on grounds of non-small cell lung cancer (NSCLC). All patients underwent FOB for bronchoalveolar lavage, catheter mediated aspiration, transbronchial biopsy, the procedure being terminated after obtaining aspirated secreted samples. In the first 24 hours after FOB, sputum samples were collected and used for AFB direct spread microscopy and AFB culture seeding. Postbronchoscopic sputum samples of 24 patients were evaluated because 6 patients could not give sputum samples after FOB. In 1 (3.3%) of the patients transbronchial biopsy could not be performed due to minimal haemorrhage occurrence. The transbronchial biopsy samples (n=29) were handed to the pathology laboratory for investigation.

FiberopticBronchoscopy: The patients, fasted for at least 8 hours, were premedicated with 0.5 mg atropine (AtropinSülfat 0,50 mg/1 ml; Biofarma) (sc) and 10 mg diazepam(Diazem 10 mg; Deva Holding) (IM) 30 min before FOB. Topical anaesthesia was achieved with 2-3 ml 4% lidocaineXylocaine 10mg Anaesthetic Spray; Astra Zeneca). While the patient was in a sitting position, the fiberopticbronchscope (OlympusBF Type P 30) was used via the trans-nasal route. After the inspection of the bronchial tree, the bronchscope was wedged into the bronchus of the lung segment containing the radiographically observed lesion, 20 cc of sterile physiological serum was used for lavage and the aspirate was placed in sterile tube. Also catheter (MillRose MW:138, bronchial lavage catheter/Liver fitting) mediated aspirations were made from the subsegments in the same area. Bronchial brush biopsy was taken using the MillRoseLab 129R, Lot 12359-233. Transbronchial biopsy was made (MillRose 18100-1 Rite bite biopsy forceps). Lastly, secretions in the investigated area were aspirated before terminating the FOB procedure.

Microbiological Investigation: To each of the samples obtained from bronchoalveolar lavage, catheter mediated aspiration, bronchial brush and post FOB sputum sampling equal volume of 4% NaOH was added and the sample was homogenized by shaking. After keeping at 37°C for 15 minutes the samples were centrifuged for 20 minutes at 3000 Revolutions per minute (rpm). The pellets at the bottom of the tubes were dispersed with physiological serum, small aliquots of which were transferred to glass microscopy slides and stained with the Ziehl-Neelsen technique to be examined by direct microscopy. Also, small aliquots were placed in Lowenstein-Jensen microbiological growth medium and placed in the incubator at 37°C for 8 weeks. The transbronchial biopsy samples were fixed with 10% formaldehyde, washed and dehydrated in alcohol and acetone. Paraffin blocks were prepared to obtain 5 µ thick sections which were stained with haematoxyline-eosine and examined histologically by microscopy (Figure 1).

Figure no 1: Granulomatous inflammation with caseified necrosis by transbronchial biopsy sample. (x10magnification)



Statistical analysis

Data was analyzed using SPSS version 23 (SPSS Inc., Chicago, IL). The numerical data were expressed in terms of the median and the minimum-maximum levels; and the categorical data were expressed in percentage values. Cochran Q Test was used to compare the positive outcome rates of bronchoscopic procedures. The level $P < 0.05$ was considered as the cutoff value or significance.

III. Result

The patients consisted of 4 (13.3%) females and 26 (86.7%) males. The median age of the patients was 27 years (min:17 years, max:75 years); PTB lesions were detected in the right hemithorax of 16 (53,3%) patients, in the left hemithorax of 6 (20%) patients and bilaterally in 8 (26.6%) of the patients; and, radiologically, 15 (50%) of the patients had consolidation, 14 (46.6%) had cavitation lesion and consolidation and 1 (3.3%) patient had cavitation, consolidation and paratracheal opacity. While 6 patients (20%) could not give spontaneous sputum sample, all 3 sputum samples of the remaining 25 patients (83.3%) were negative for AFB. In 25 patients (83.3%) normal endobronchial appearance was observed; while mucosal hyperemia was observed in 2 (6.6%), haemorrhagic secretion in 2 (6.6%) and mucosal granuloma in 1 (3.3%).

Table no1:AFB Direct Smear positivity rates in FOB samples, post-FOB sputum specimens and transbronchial biopsy were shown in Table 1. In this study, 14 patients (46.6%) were diagnosed with PTB within 1 to 2 days after FOB with AFB direct smear examination of all samples. There was statistically significant difference between FOB procedures in terms of direct smear microscopy AFB positivity (p=0.004). There was no statistically significant difference between procedures except for postbronchoscopic sputum (p = 0.221).

Table no 1:AFB direct smear positive patient counts.

	Patient counts	%
Bronchoalveolar Lavage	4/30	13.3
Cathater-mediated Aspiration	3/30	10
Bronchial Brush Biopsy	1/30	3.3
Transbronchial Biopsy	1/29	3.4
Secretion Aspiration	1/30	3.3
Post-FOB* sputum	7/24	28.7
Histological Assessments	5/29	17

*Post-FOB: Post-fiberoptic bronchoscopy, %: Percentage

Table no2: Positive culture data on the samples obtained by all of the FOB assisted procedures are shown in Table 2. In 27 (90%) of the cases PTB diagnosis was confirmed using the data acquired through FOB assisted sampling procedures and the post FOB sputum sample analyses. In the remaining 3 patients, only 1 (3.3%) patient was confirmed with PTB diagnosis using the pre-FOB sputum sampling. The other 2 (6.6%) of these patients were taken under anti-tuberculosis therapy on the bases of clinical examination with AFB-negative results of direct smear microscopy; and both were clinically and radiologically cured. There was no statistically significant difference between FOB procedures in terms of AFB culture positivity (p=0.085).

Table no2: Patient counts of AFB cultures positive.

	Patient Counts	%
Pre-FOB* sputum	14/24	58
Bronchoalveolar Lavage	21/30	70
Cathater-mediated Aspiration	17/30	56.6
Bronchial Brush Biopsy	16/30	53.3
Transbronchial Biopsy	8/29	27.5
Secretion Aspiration	15/30	50
Post-FOB** sputum	10/24	41.6

Pre-FOB: Pre-fiberoptic bronchoscopy, Post-FOB**: Post-fiberoptic bronchoscopy, %: percentage

Table no3: Bronchoalveolar lavage and catheter mediated aspiration data confirmed PTB diagnosis in 25 (83.3%) of the patients, and when the results on the bronchial brush biopsy and secretion aspiration samples or the post FOB sputum samples were also used, PTB diagnosis was confirmed in 26 (86.6%) of the patients.

Table no3:AFB- positivity determined by various combinations.

	Counts	%
Bronchoalveolar Lavage + Cathater-mediated Aspiration	25/30	83.3
Bronchoalveolar Lavage + Bronchial Brush Biopsy	24/30	80
Bronchoalveolar Lavage + Secretion Aspiration	24/30	80
Bronchoalveolar Lavage +post-FOB* sputum	22/30	73.3
Bronchoalveolar Lavage + Cathater-mediated Aspiration +post-FOB sputum	26/30	86.6
Bronchoalveolar Lavage + Bronchial Brush Biopsy +post-FOB sputum	24/30	80
Bronchoalveolar Lavage + Secretion Aspiration +post-FOB sputum	25/30	83.3
Bronchoalveolar Lavage + Cathater-mediated Aspiration + Bronchial Brush Biopsy	26/30	86.6
Bronchial Lavage+ Cathater-mediated Aspiration +Secretion Aspiration	26/30	86.6
Bronchial Lavage+ Histology on Transbronchial Biopsy + post-FOB sputum	23/30	76.6

*Post-FOB: Post-fiberoptic bronchoscopy, %: percentage

With respect to the complications of flexible tube FOB, in 1 (3.3%) of the patients transbronchial biopsy could not be performed due to minimal haemorrhage occurrence. In 1 3.4%) of the 29 patients who had completed transbronchial biopsy pneumothorax occurred requiring closed tube drainage.

IV. Discussion

There was no statistically significant difference between procedures in our study. No other study comparing all of the procedures in our study was found. However, bronchial aspirate, bronchoalveolar lavage, postbronchoscopic sputum and transbronchial needle aspiration were performed by Quaiser et al. They also found that the diagnostic values of the procedures were close to each other [5].

The most important result of this study is that 14 of the patients (46.6%) received PTB within 1 to 2 days after FOB. Comparable results of 42.5% and 54.5% were given by Quaiser et al. [5] and Zaunidin et al. [6], respectively. The differences in percentages may be attributed to the differences in techniques of the procedures and the type and the quantity of local anesthetics agents used.

Direct smear microscopy should not be overlooked in post FOB sputum. AFB positivity was determined in 7 (28.7%) of the 24 post FOB sputum samples. With the use of post-FOB sputum specimens, the diagnosis rate of PTB was found to be higher than that of FOB-assisted procedures. Studies have shown that the incidence of AFB positivity in post FOB sputum specimens is 17.5%, 16% [respectively, 5,7].

Gopathi et al. [2] determined AFB positivity in 78.3% of their patients by the direct smear microscopy of bronchial lavage samples; which was 13% in our study. However, whereas 50% of the patients in our study had radiological evidence of only consolidation, Gopathi et al.[2] observed consolidation in 8.3% of their patients, nodular infiltration in 22%, cavitation in 53% and the miliary pattern in 12%. Özkaya et al. found that bronchoalveolar lavage samples were 26% AFB positive at direct smear microscopy [9]. This rate was reported as 66.6%, 12% and 47.27% respectively in different studies [respectively, 7,10,11]. These differences can arise from the small differences in the bronchoalveolar lavage technique such as the quantity of fluid used.

In our study, It was determined AFB positivity by direct smear microscopy in 10% of the catheter mediated aspiration samples. This percentage previosly has been given as 0% [12] and 23% [13]. AFB positivity was given at different rates of 67% and 16% in different studies on direct microscopic examination of bronchial brush biopsy specimens [respectively, 11,7]. In our study, there was a positive AFB of 3.3%. Differences in the clinical and radiological evidence of the disease in patients, the institutional differences in FOB application, and variations in the preparative and staining techniques can all be expected to contribute to the reported results.

Using the AFB direct smear microscopy on the transbronchial biopsy samples, the AFB positivity was reported to be 12% [8] and 0% [12], while our result was 3.4%. Differences have been reported on the observation of necrotic granulomatous lesions in transbronchial biopsy samples as 58% [14], 30% [15] and 16% [16] while our result was 17%.

In this study, PTB diagnosis was confirmed in 27 (90%) of our patients by using all of the FOB assisted sampling procedures and the post FOB sputum samples. This incidences was reported as 94% [14]. It was found that, the highest AFB positivity in cultured samples was 70%, obtained in the bronchoalveolar lavage samples, and,

our study supported previous study. [14,17]. This was followed by the 56.6% and 53.3% AFB positivity in the catheter mediated aspiration samples and bronchial brush biopsy samples, respectively. Result of Ozturk et al. on catheter mediated aspiration samples was reported as 20% [12]. Those were 24% [8] and 67.5% [18] in previous studies. In our study, 50% AFB culture positive was found in the secretion samples that were aspirated with FOB. However, we have not been able to find a previous study in this regard. The post FOB sputum sample cultures yielded a result of 41.6% AFB positivity which was in agreement with the results previously [14,15,19].

Bacch et al. [20] have argued that the incidence of AFB positivity in the cultured samples of sputum collected before FOB and in cultured samples of bronchoalveolar lavage fluid were statistically significantly different with a greater diagnostic value indicated for the bronchoalveolar lavage samples. In our study, however, we did not observe a difference in the respective results. We could not find a study to make comparisons on the statistical evaluations.

Definitive PTB diagnosis was achieved in 25 (83.3%) of our patients using the bronchoalveolar lavage and catheter mediated aspiration sampling techniques, which escalated to 26 patients (86.6%) with the inclusion of the results of bronchial brush biopsy and secretion aspiration samples or the post FOB sputum samples. There has been previous report of 95% [7] definitive diagnosis of PTB by others using the bronchoalveolar lavage or the bronchial brush biopsy sample cultures, our results with these techniques being 80%.

The main limitation of our work is the small sample size. In addition, AFB direct smear and culture results were not compared with the polymerase chain reaction results.

V. Conclusion

There is no statistically significant difference between diagnostic values of FOB procedures in patients with suspected PTB. However, the rate of diagnosis was relatively high with bronchoalveolar lavage and catheter mediated aspiration procedures. Adding brushing biopsy or secretion aspiration specimens to these procedures increases diagnostic yield. Postbronchoscopic sputum sampling is also a method that should not be forgotten in the definite diagnosis of these patients.

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