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ROLE OF BRONCHOSCOPIC ASSISTED PROCEDURES IN DIAGNOSING SPUTUM SMEAR NEGATIVE PULMONARY TUBERCULOSIS

General Medicine

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ABSTRACT

Background: Why we do an invasive and time-consuming procedure like bronchoscopy in diagnosing pulmonary tuberculosis. **Aims:** To find the role of bronchoscopic assisted procedures in Diagnosing sputum smear negative pulmonary tuberculosis. **Materials and Methods:** The study was carried out in the Post Graduate Department of Medicine, S.N. Medical College and Hospital, Agra and Post Graduate department of Pathology, S.N. Medical College and Hospital, Agra. A total sample of 50 patients were included in this study and these patients had clinical suspicion of pulmonary tuberculosis. They had either dry cough or three negative sputum smear examination for AFB, which is the requirement for study. **Results:** A final diagnosis of sputum smear-negative pulmonary tuberculosis was made in 50 patients by various methods. BAL fluid smear/culture for acid-fast bacilli (AFB) was positive in 21/50(42%) patients while smear/ culture of bronchial brushing was positive in 13/31(41.93%) patients, post bronchoscopy sputum (PBS) smear/culture yield total 12/50(24%) as a positive result and trans bronchial lung biopsy (TBLS) smear/culture also positive in 3/10 (30%) patients. During our study, we are able to diagnose 23 case cases out of 50 cases (46%) by combining all the bronchoscopic aided procedures and using either smear for AFB and culture for AFB as the end result of our study. **Conclusion:** The study concludes that flexible fiberoptic bronchoscopy is a useful tool in early diagnosis of pulmonary tuberculosis in sputum smear negative patients.

KEYWORDS

INTRODUCTION

Pulmonary tuberculosis (PTB) is one of the most important problems worldwide.[1] India has more new TB cases annually than any other country.[2]. The WHO also recommends the detection of acid-fast bacilli (AFB) in respiratory specimens as the initial approach in the diagnosis of pulmonary TB.[3] Though AFB smear is the most rapid, highly specific (98- 99%) and low-cost test but has poor sensitivity (30-70%).[4,5] Early diagnosis to reduce the period of infectivity is considered to be one of the most effective TB control strategies. Mycobacterial cultures are more sensitive than AFB smears (80-85%) but cultures require 3-8 weeks.[6,7] Though sputum smear and culture examinations still remain the gold standard in the diagnosis of PTB, but even in advanced disease it may be negative due to immunosuppression, low bacterial yield, poor quality of the sample collection, inadequate preparation, staining or examination of the smear.[8] In 2018, there were about half a million new cases5 of rifampicin-resistant TB (of which 78% had multidrug resistant TB)[9]. Fiberoptic bronchoscopy is a useful procedure for evaluation suspected cases of sputum smear negative PTB. The forceps and brush biopsy specimens, bronchoalveolar lavage (BAL) fluid and post bronchoscopy sputum (PBS) on evaluation aid in the confirmation of diagnosis of sputum smear negative cases of pulmonary tuberculosis [10].

MATERIAL AND METHODS

50 patients of age group 15-65 years, with clinical and radiological suspicion of pulmonary tuberculosis with three sputum smear negatives were included in this study after obtaining an informed consent. Patient with cardiac disease, extrapulmonary TB, history of ATT intake more than 1-month, coagulating disorder, and those with $PaCO2 > 50$ mmHg and dyspnea were excluded from the study. Non-cooperative and immunocompromised patient also excluded from study.

Detailed clinical history and thorough physical examination was done. Hemogram, ESR, other routine investigations and chest roentgenogram were performed, to assess the fitness of patients for bronchoscopic procedure. Written consent was obtained from all the patients undergoing bronchoscopy. All patients were fasting for at least 4 hours prior to bronchoscopy and Role of bronchoscopic assisted procedures in diagnosing sputum smear negative Pulmonary Tuberculosis premedicated 30 to 45 min before the procedure with intramuscular injection of 0.6 mg Atropine and 10 mg of Diazepam orally. Local anesthesia to upper respiratory tract was given using 4% XYLOCAINE through nebulizer, just before the procedure. Bronchoscopy was done with patient in supine position with operator standing at the head end of the patient. Before the procedure was carried out, the bronchoscope was cleaned and immersed in 2% glutaraldehyde for an hour. After lubricating the shaft of the bronchoscope with 2% lignocaine gel, it was inserted through one of the anaesthetized nostrils. Largest passage was the inferior meatus, below the inferior turbinate along the floor of the nose, on reaching the nasopharynx, the tip was moved caudally to pass into the space behind the tongue. The pharynx, epiglottis and the vocal cords were inspected for any abnormality and movements were observed. On reaching up to carina 2 ml of 2% xylocaine solution was instilled into main bronchi very gently. Thorough examination of the bronchial tree was carried out. The bronchoscope was then wedged into the segmental and sub-segmental bronchi and bronchoalveolar lavage was taken from the involved area. For BAL fluid, sterilized buffered normal saline at body temperature was used. A 20 ml of this was instilled through the bronchoscope and promptly aspirated using a low-pressure suction. Total of 8-10 aliquots (150- 200 ml) were instilled. Lavage fluid was collected in to a non-siliconized sterilized container. After the collection of BAL fluid, bronchoscopic brush was introduced via Fiberoptic bronchoscope and brushings were taken from the target pathological site. The brush along with adhered cells was smeared on glass slides & fixed immediately in 95% propranolol and stained with Papanicolaou stain after fixation. Biopsy was taken out from the pathological site with the help of biopsy forceps after instillation of 1:200000 epinephrine solution to avoid risk of serious bleeding. The biopsy material was then sent for histopathological examination. After the procedure, the patient was observed for development of pneumothorax, hemorrhage, infection and cardiac arrhythmias for 24-48 hours. The sputum samples for next 3 days after bronchoscopy (post-bronchoscopic sputum) were collected and sent for staining & culture along with bronchial washings. The BAL fluid, bronchial brushings and endobronchial and trans bronchial lung biopsy specimens were then sent for Z-N staining and culture for mycobacteria using RADIOMETRIC BACTEC method.

OBSERVATION AND RESULTS

Through fiberoptic bronchoscope, brushings and BAL were collected and smeared for ZN staining for AFB. BAL was done in all 50 cases where as brushings were taken from the affected segment in 31 cases. Bronchial biopsies were done only in 10 out of 50 patients, where bronchoscopy revealed some pathology and biopsies were feasible.

This was taken from the affected segment of the lung and aspirate sent for cytological examination. After bronchoscopy, post bronchoscopy sputum was also taken on next 3 occasions (one immediately after bronchoscopy and other two on next 2 days.)

In our study group of 50 patients, tuberculosis was confirmed by smear examination for AFB by BAL fluid in 18 cases (36%), by bronchial brushings in 12 cases (38.70%), by post bronchoscopy sputum in 11 cases (24%) and by TBLB in 3 cases (30%).

Table -1 Bronchial Specimens Smear Results (n=50)

BRONCHOSCIPIC SPECIMENS	POSITIVE RESULTS N (%)
BRONCHOALVEOLAR FLUID (BAL)	18/50(36%)
BRONCHIAL BRUSHING	12/31 (38.70%)
POST BRONCHOSCOPY SPUTUM (PBS)	11/50 (22%)
TRANS BRONCHIAL LUNG BIOPSY (TBLB)	3/10 (30%)

All specimens collected through fiberoptic bronchoscopy were cultured for mycobacteria using RADIOMETRIC BACTEC method. BAL culture for M. tuberculosis was positive in 21 patients whereas Bronchial brushings culture was positive in 13 cases, PBS culture was positive in 12 patients and TBLB culture was positive in 3 cases. Two specimens of BAL culture were exclusively positive whereas one Bronchial brushings culture and one bronchial biopsy culture were exclusively positive. No PBS culture was exclusively positive.

Table- 2 Results Of Bronchial Specimens Culture For AFB

BRONCHIAL SPECIMENS	POSITIVE SPECIMENS N (%)
BAL FLUIDS	21/50 (42%)
BRONCHHIAL BRUSHING	13/31 (41.93%)
TBLB	3/10 (30%)
PBS	12/50 (24%)

PBS = POST Bronchoscopy sputum, TBLB = Trans bronchial lung biopsy

In our study, we were able to diagnose 23 cases out of 50 cases (46%) by combining all the bronchoscopic aided procedures and using either smear examination for AFB or culture for AFB as the end result of our study. Out of these 23 cases diagnosed as tuberculosis by either smear examination for AFB or culture for AFB, BAL was the most effective method where diagnosis was clinched in 21 cases (21/23) with a sensitivity of 91.30 % followed by brushings where diagnosis was clinched in 14 cases (13/23) with a sensitivity of 56.52%.

Using post bronchoscopy sputum as the method of diagnosis, we were able to clinch the diagnosis in 12 out of 23 positive patients (12/23) with a sensitivity of 52.17% and TBLB clinched the diagnosis in 3 out of 23 positive patients (3/23) with a sensitivity of 13.04%.

Table- 3 Various Bronchoscopic Methods Sensitivity In Our Study (n=50)

	POSITIVE CASE NO.	TOTAL POSITIVE CASE (by SMEAR/CULTURER)	SENSITIVTY OF DIFFERENT METHODS (%)
BAL FLUIDS	21	23	91.30%
BRONCHIAL BRUSHING	13	23	56.52%
PBS	12	23	52.17%
TBLS	3	23	13.04%

When comparing the yield of the study, which was taken as the percentage of No. Of positive cases by the method undertaken divided by no. of cases performed by that method, it was seen that Bronchial brushings had the highest yield (13/31) of 41.93% followed by BAL (21/50) of 42%. TBLB and PBS had comparable low diagnostic yield of 24% and 30% respectively, in our study.

Table - 4 Total Yield Of Various Bronchoscopic Assisted Methods In Our Study (n=50)

	POSITIVE CASES	TOTAL CASES	TOTAL YIELD (%)
BAL FLUIDS	21	50	42%
BRONCHIAL BRUSHING	13	31	41.93%
PBS	12	50	24%
TBLB	3	10	30%

DISCUSSION

Out of the 50 patients in our study, 47 patients complained of cough (94%), 39 patients (78%) with expectoration, 19 (38%) patients with fever, 7 patients (14%) with hemoptysis and 6 patients (12%) with chest pain. These patients' characteristics were also similar to the study done by D D S Kulpati et al[11] where in the sample size of 33 cases, the patients reported with the clinical presentations which was mainly with cough in 18 cases, expectoration in 17 cases, fever in 17 cases, chest pain in 7 cases and hemoptysis in 5 cases. In our study, 23 cases out of 50 (46%) were active smokers, while 9 of them (18%) quitted smoking for more than one year and 18 of them (36%) had never smoked before. This was higher than the study characteristics of study done by Chang et al[12] where history of smoking amongst allotted cases were 46.5% and non-smokers were 53.5%. This discrepancy in data was due to slightly higher prevalence of smoking in India[13]. Amongst the 50 allotted cases, when evaluated for history of contact with a case of pulmonary tuberculosis, 42 cases (84%) were positive. Of the 8 negative cases, 3 were females and 5 were males. This was higher than the study done by Kwan Hoi Yee et al [14] where contact history was positive in 4.5%. This discrepancy in data was there because mostly studies had been done outside India. In Indian scenario, due to the over diagnosis and under treatment of TB, we had a high prevalence as compared to the western world. Based on whether they had history of tuberculosis or had been taking anti-tubercular drugs in the past, 10 patients (20%) had received whole course of anti-tubercular treatment before, 12 patients (24%) were defaulters, 28 patients (60%) were those without any prior history of anti-tubercular treatment. The previous study done by Chang et al[12] had reported a very low percentage of ATT history of 14% and study done by Kwan Hoi Yee et al[14] reported 5 cases (22.7%) with previous history of ATT. This discrepancy in data was again because mostly studies had been done outside India. In Indian scenario, we had a high prevalence of defaulters as compared to the western world.

In our study, the BAL fluid smears were taken in all 50 cases and were positive for AFB in 18 (36%) patients. In previous studies, it varied from 7.5% in S Charoenratanakul et al[15] to 57.1% in Malekmohammad M et al[16]. BAL culture yielded M. tuberculosis in 42% patients in our study (21 cases out of 50) which was comparable to the 48% positivity (24 cases out of 50) by Wongthim et al[17]. Thus the data generated in our study is comparable to previous studies. In our study, bronchial brush smears were done in 31 patients in whom bronchoscopy revealed some visible pathology. Bronchial brushings were positive for acid fast bacilli in 38.70% (12/31) patients; all of these were confirmed by positive culture. Bronchial brushings when subjected to culture yielded 41.93% in our study. This was also comparable to the studies done by Willcox et al[5] where brushings were positive in 35 cases out of 83 cases (42%), and Wongthim et al [17] where bronchial brushings were positive in 33 of the 65 (51%). In our study, Post bronchoscopy sputum samples were collected on 3 occasions and subjected to both smear for AFB and culture, yielding 22 % (11/50) and 24% (12/50) respectively. This was comparable to the 23% positivity (7 out of 30 cases) in post bronchoscopy sputum studied by Wongthim et al[17]. Also in previous studies, 25% positivity (5 out of 20 cases) by PBS culture was noted by Kulpati et al.[8] and 26% AFB smear positivity (13 cases out of 50) by Purohit et al[18]. Thus the data generated in our study is comparable to previous studies. In our study, transbronchial lung biopsies were taken in areas of suspicion in 10 cases, where bronchoscopy revealed some pathology. In these cases, the positivity on smear was 30% (3 cases out of 10) and on biopsy was 30% (3 0cases out of 12). Previous literature showed similar results with A.K.Jaiswal et al[19] reported bronchoscopic guided biopsy for diagnosis of sputum negative tuberculosis to be 10% (2 out of 20 cases) in their study and D.D. Kulpati and H.S.Heera et al[8] reported 20 % (4 cases out of 20) in their study. Thus the data generated in our study is comparable to previous studies.

During our study, we were able to diagnose 23 cases out of 50 cases (46%) by combining all the bronchoscopic aided procedures and using either smear examination for AFB or culture for AFB as the end result of our study. Out of these 23 cases diagnosed as tuberculosis by either smear examination for AFB or culture for AFB, BAL was the most effective method where diagnosis was clinched in 21 cases (21/23) with a sensitivity of 91.30 % which was comparable to the study by de Gracia et al[20] where BAL had a sensitivity of 88% (15/17). Using

brushings, diagnosis was clinched in 14 cases (14/23) with a sensitivity of 56.52%. This was comparable to the previous studies by A.A Bachh, R Gupta et al [21] where brushings had sensitivity of 48.33% cases and Chawla et al[22] where brushings had sensitivity of 62% (28/45). Using post bronchoscopy sputum as the method of diagnosis, we were able to clinch the diagnosis in 12 out of 23 positive patients (12/24) with a sensitivity of 52.17% which was comparable to the study by Panda et al[23] where PBS had a sensitivity of 48.5% (17/35). TBLB clinched the diagnosis in 3 out of 23 positive patients (3/23) with a sensitivity of 13.04% which was comparable to the study by S.Y.So et al [24] where the sensitivity was 12% (7/57). When comparing the yield of fiberoptic bronchoscopy to aid the dia432gnosis of sputum negative TB, BAL had a yield of 42% which was comparable to the 48% diagnostic yield by Wongthim et al[23]. Brushings had a diagnostic yield of 41.93%. This was also comparable to the studies done by Willcox et al[5] where brushings were diagnostic in 42% and Wongthim et al [23] where bronchial brushings were diagnostic in 51 %. Post bronchoscopy sputum had a yield of 24%. This was comparable to 23% by Wongthim et al[23], 25% by Kulpati et al.[8] and 26% by Purohit et al[18]. TBLB had a yield of 30% which was comparable to D.D. Kulpati and H.S. Heera et al[8] of 20 % in their study. BAL culture was exclusively positive in two cases; bronchial brush culture in one patient and trans bronchial lung biopsy had one patient exclusively positive.

CONCLUSION

The study concludes that flexible fiberoptic bronchoscopy is a useful tool in early diagnosis of pulmonary tuberculosis in sputum smear negative patients. Bronchoscopy reveals a higher bacteriological confirmation of diagnosis in patients with strong clinical and radiological evidence suggestive of pulmonary tuberculosis and those having more risk factors.

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