Comparison of Induced Sputum with Bronchoalveolar Lavage Samples for Pulmonary Tuberculosis diagnosis in sputum scarce Patients

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MA AM MJ conceived idea, MA AM MWA drafted the study, MWF SP collected data, AM MIS did statistical analysis and interpretation of data, MA AM critical review manuscript, All approved final version to be published.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

Abstract

Background: One of the most common infections in the world is Tuberculosis (TB), mostly in those countries which are under development. As the initial approach to the diagnosis of pulmonary TB (PTB), the detection of acid-fast bacilli (AFB) in respiratory specimens is recommended by the World Health Organization (WHO). But, sensitivity of this method is found to be low especially in patients who are unable to produce sputum spontaneously

Objective: Present study was conducted with the aim to compare diagnostic performance of induced sputum with bronchoalveolar lavage for pulmonary tuberculosis diagnosis in sputum scarce patients.

Methodology: The present study was conducted at Pulmonology department of Nishtar Medical University and Hospital, Multan, from February 2016 until September 2018. A total of 108 patients were recruited in the study. One hour before performing bronchoscopy, nebulization with hypertonic saline solution was given to the patients to obtain induced sputum. Then bronchoscopy was performed and BAL samples were collected. Gene expert MTB/Rif was performed in both specimens and sensitivity, specificity, accuracy, positive predictive value and negative predictive values were calculated.

Results: Sensitivity, specificity, positive predictive value and negative predictive value of induced sputum for AFB smear was 70.6%, 78.8%, 88.3%, and 54.1%, respectively. Sensitivity, specificity, positive predictive value and negative predictive value of induced sputum for gene expert was 68.6%, 54.5%, 65.7, 85.5% and 30.8%, respectively.

Conclusion: Examination of sputum induced sample is a safe, cheap and noninvasive alternative to bronchoalveolar lavage and provided good sensitivity and specificity with lesser side effects for the diagnosis of pulmonary tuberculosis in patients with no sputum production.

Key words: Bronchoalveolar lavage (BAL); Induced Sputum, Pulmonary tuberculosis

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Introduction

One of the most common infections in the world is Tuberculosis (TB), mostly in those countries which are under development. In twenty two countries, which are high tuberculosis burden, Pakistan's number is five.[1] As the initial approach to the diagnosis of pulmonary TB (PTB), the detection of acid-fast bacilli (AFB) in respiratory specimens is recommended by the World Health Organization

(WHO).[2] But, sensitivity of this method is found to be low especially in patients who are unable to produce sputum spontaneously.[3,4] The most effective strategy to control TB is early diagnosis of infection. Nevertheless, in children, the isolation of Mycobacterium-tuberculosis is found to be comparatively difficult. It is followed that for the epidemic control, the bacteriologic confirmation of PTB improving strategies through optimization of sputum collection are much important.[5]

For the diagnosis of PTB, Mycobacterial culture has got some limitations because of duration it takes, while it is considered to be gold standard and a fundamental tool. In persons with paucibacillary TB, gastric lavage and fiberoptic bronchoscopy (FOB) are founded to be useful diagnostic procedures. But, these methods are considered as relatively invasive and not always accessible in under developed countries.[5] With a high diagnostic yield and a high agreement with results of FOB for the diagnosis of PTB, sputum induction is considered as safe procedure. For the diagnosis of sputum scarce PTB, sputum induction includes an additional or alternative approach in those areas, where FOB is not readily available.[6] Currently, TB infects one-third of the world's population and kills about 1.7 million people every year.[7] Acid Fast Bacilli (AFB) smear test is most rapid, highly specific (98% to 99%) and with low cost but its sensitivity is poor (30% to 70%).[8,9] Mycobacterial cultures require 3 weeks to 8 weeks, but these are more sensitive than AFB smears (80-85%).[10] In spite of all its ups and downs, culture examination is still considered to be the gold standard for the diagnosing of pulmonary TB. But it might remain smear negative for AFB for about 30% of pulmonary TB new cases. About 70% of these patients may jump to active TB in next 12 months, in case they are not treated properly.[11]

Sputum induction and bronchoscopic procedures are appearing to be practical and promising. In suspected pulmonary tuberculosis patients with no sputum production, some of the methods for TB diagnosis are: (i) Using hypertonic saline for sputum induction, (II) Transtracheal needle aspiration, (iii) transthoracic needle aspiration guided radiologically, (iv) Gastric lavage, (v) Bronchoscopic procedures – Bronchial aspirate/BAL, and (vi) Post Bronchoscopy sputum.

In countries which are resource-limited, where feasibility of FOB in every case of suspected PTB with no sputum is not possible, alternative approach for diagnosing such cases, an alternative approach is offered by sputum induction. Aiming this, the current study was considered to be undertaken for comparing efficacy of sputum induction against bronchoalveolar lavage (BAL) in the diagnosis of clinically and radiological suspected cases of PTB having no or scanty sputum production.

Methodology:

This prospective observational study was conducted in Pulmonology department of Nishtar Medical University and Hospital, Multan, this study was conducted starting from February 1st 2016 until September 31st 2018. With clinical and radiological evidence of PTB but with negative sputum production, 108 patients were admitted. Patient with

Table 1. Distribution of cases according to Gene Xpert (Detected/ Not detected), Rifampicin Resistance and Smear result (Positive/ Negative)

Variable		Value
Age, years		32.54 ± 6.8
Weight, kg		39.68 ± 7.3
Gender		**N (%)**
Male		57 (53)
Female		51 (47)
Smoking status		**N (%)**
Active smokers	Male	32 (30)
	Female	16 (15)
Ex-smokers	Male	29 (27)
	Female	9 (8)
Residence		**N (%)**
Urban		40 (37)
Rural		68 (63)

Data entered as mean ± S.D or mentioned otherwise.

ischemic heart disease, sputum smear positive for AFB and interstitial lung disease were excluded from the study.

The registered patients went through to a procedure, which included thorough history concerning types of onset, period of disease, history of drug consumption and radiological proof of PTB. Age, weight, gender, smoking history and area of residence were documented for all the patients. One hour before performing bronchoscopy, 5 ml of hypertonic saline solution by nebulizer was inhaled by all patients. After that, they were asked to cough. Collection of specimens attained by this method (induced-sputum) was done. All patients were refrained from eating for at least four hours prior to bronchoscopy and pre-medicated 30 to 45 minutes before the procedure with intra-muscular injection of atropine 0.6 mg and 10 mg of diazepam directed orally. 4% xylocaine through a nebulizer was used to administrate local anesthesia to upper respiratory tract, just before starting the procedure. The bronchial tree was examined thoroughly. The bronchoscope was then impacted into the segmental and sub-segmental bronchi and the involved area was used for BAL. At body temperature, sterilized buffered normal saline was used for BAL fluid; low pressure suction was used for instilling 20 ml of this through the bronchoscope and sharply articulated. A non-siliconised sterilized container collected lavage fluid. Examination of all samples of induced sputum by hypertonic saline and BAL fluid was done for gene expert to detect Mycobacterium tuberculosis. The study was approved by the hospital review board.

Data was entered in SPSS version 23 and analyzed. Induced sputum results were plotted against BAL examination results in 2x2 table. Sensitivity, specificity, positive predictive value and negative predictive values of AFB smear, and Expert MTB/Rif were calculated in both induced sputum and BAL.

Results

Mean age of all the patients was 32.54±6.8 years with an average weight of 39.68±7.3 kg. Among all the patients, 57 (53%) were males and 51 (47%) females. History of current smoking was present in 45% of the patients which included 32 males and 16 females. History of smoking in the past was present in 35% of the patients which included 29 males and 9 females. Study population included 40 (37%) urban residents and 68 (63%) residents of rural area (Table 1).

Of all the patients, 75 were TB positive on BAL AFB smear while 33 were negative. When induced sputum specimen was examined for gene expert for AFB, 60 samples were found to be positive with 48 results being true positive, while 39 samples were found to be negative with 26 results being true negative. Sensitivity, specificity, positive predictive value and negative predictive value of induced sputum for AFB smear was 70.6%, 78.8%, 88.3%, and 54.1%, respectively (Table 2)

Of all the patients, 86 were TB positive on BAL gene expert while 22 were negative. When induced sputum specimen was examined for gene expert for AFB, 69 samples were found to be positive with 59 results being true positive, while 39 samples were found to be negative with 12 results being true negative. Sensitivity, specificity, positive predictive value and negative predictive value of induced sputum for gene expert was 68.6%, 54.5%, 65.7, 85.5% and 30.8%, respectively (Table 3).

Discussion

Sensitivity, specificity, positive predictive value and negative predictive value of induced sputum for AFB smear was 70.6%, 78.8%, 88.3%, and 54.1%, respectively. Sensitivity, specificity, positive

Table 2. Cross tabulation for AFB smear against sputum and BAL

Induced Sputum		BAL AFB smear		
		Positive	Negative	Total
AFB smear	Positive	53	7	60
	Negative	22	26	48
Total		75	33	108

Table 3. Cross tabulation between sputum and BAL for Gen Xpert

Induced Sputum		BAL AFB smear		
		Positive	Negative	Total
AFB smear	Positive	59	10	69
	Negative	27	12	39
Total		86	22	108

predictive value and negative predictive value of induced sputum for gene expert was 68.6%, 54.5%, 65.7, 85.5% and 30.8%, respectively. The results were more promising in case of AFB smear examination as compared to gene expert.

A study was performed in Brazil, 6 which describes the effectiveness of induced sputum and FOB in sample of patients with HIV infection and negative sputum; 34 % was the sensitivity of AFB smears of specimens through inducted sputum and 38% was measured by using BAL fluid. According to conclusion of authors, safe and reliable diagnostic tool is induced-sputum.[6]

A study from New Zealand, by Mc Williams et al[12] which is based on comparison between induced-sputum and bronchoscopy sampling with radiologic findings is also considerable. Author concludes in spite of the fact that induced-sputum is one-six times expensive than bronchoscopy, patients with radiologic pattern of active TB have positive induced-sputum sampling with higher prevalence. Schoch and fellows[13] depicts that for TB diagnosis, clinical signs and radiologic findings are not sensitive enough. According to them, induced-sputum technique is less accurate than bronchoscopy.[13]

Al Zahrani and associates, in Canada[14] were able to find out that specificity of induced-sputum technique can be increased from 64% to 97% by intermittent repeating this technique for up to three times. This process will also augment the culture sensitivity from 70% to 99%.[14] Results of their study are in accordance with those observed in current study.

In Bangladesh, Gangulyet al[15] assessed the sensitivity of AFB-smears in samples from sputum induction as 74% and BAL as 58%, in the study including 52 sputum smear-negative cases. In another study[16], 80% and 87% were reported sensitivity of smear and culture of induced-sputum. Another study[1] also described almost same results with 90% sensitivity (on AFB smear examination) of sputum induction and 83.3% for BAL. AFB culture had also showed a sensitivity for sputum induction and BAL to be 85.7% and 77.1% respectively.

In another study, the positive yield of FOB for tuberculosis was found to be 65%,[17] which was analogous with the formerly stated studies.[18] Moreover, in new cases (32%), the positive yield was significantly higher if compared with retreatment cases (16%) of PTB using FOB. Hence, in new patients ofsuspected PTB, FOB is more helpful.[17]

Conclusion

Examination of sputum induced sample is a safe, cheap and noninvasive alternative to bronchoalveolar lavage and provided good sensitivity and specificity with lesser side effects for the diagnosis of pulmonary tuberculosis in sputum scarce patients.

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