Evaluation of the diagnostic utility of fiberoptic bronchoscopy for smear-negative pulmonary tuberculosis in routine clinical practice*,**

Avaliação da utilidade diagnóstica da fibrobroncoscopia óptica na tuberculose pulmonar BAAR negativa na prática clínica de rotina

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Abstract

We evaluated the diagnostic yield of fiberoptic bronchoscopy for the diagnosis of smear-negative pulmonary tuberculosis in patients treated at a referral hospital in Lima, Peru. Of the 611 patients who underwent the procedure, 140 (23%) were diagnosed with tuberculosis based on the analysis of BAL samples. Being young and being male were significantly associated with positive cultures. In addition, 287 patients underwent post-bronchoscopic sputum smear testing for AFB, the results of which increased the diagnostic yield by 22% over that obtained through the analysis of BAL samples alone. We conclude that the analysis of BAL samples and post-bronchoscopic sputum samples provides a high diagnostic yield in smear-negative patients suspected of having pulmonary tuberculosis.

Keywords: Tuberculosis, pulmonary/diagnosis; Bronchoscopy; Sputum.

Resumo

Avaliamos o rendimento diagnóstico da fibrobroncoscopia óptica no diagnóstico de tuberculose pulmonar BAAR negativa em pacientes atendidos em um hospital de referência em Lima, Peru. Dos 611 pacientes submetidos ao procedimento, 140 (23%) foram diagnosticados com tuberculose com base nas amostras de LBA. Ser mais jovem e do sexo masculino foi associado a culturas positivas. Além disso, 287 pacientes tiveram baciloscopia de escarro após a broncoscopia, e os resultados aumentaram o rendimento diagnóstico em 22% em relação às amostras de lavado. Concluímos que amostras de lavado brônquico e de escarro pós-broncoscopia tiveram um bom rendimento diagnóstico nos pacientes com suspeita de tuberculose pulmonar BAAR negativa.

Descritores: Tuberculose pulmonar/diagnóstico; Broncoscopia; Escarro.

In low- and middle-income countries, fiberoptic bronchoscopy (FBO) is typically indicated as a means of identifying infectious conditions.[1] However, access to the procedure is limited in resource-constrained settings, and it implies some risks; therefore, patient selection should be quite accurate in order to avoid unnecessary risk for the patients and the overburdening of medical staff and laboratories. One common indication for FBO has been the diagnosis of smear-negative pulmonary tuberculosis (SNPT). The decision to perform FBO is usually based on the premise that the bacillary load is higher in samples taken directly from bronchial secretions than in sputum samples. Nevertheless, the evaluation of this particular application of FBO has been limited, and few studies have been conducted in Latin America. In addition, according to guidelines established by the Peruvian National Tuberculosis Control Program,[2] the use of bronchoscopy is not to be included in the diagnostic workup of patients with clinical suspicion of SNPT; the suggested course of action is to wait for sputum culture results before a consultation with an expert, who will decide whether treatment should be initiated or not. The pragmatic evaluation of the

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diagnostic yield of bronchoscopy is therefore a key element of generating evidence-based recommendations for the use of the procedure in cases of SNPT. The objective of our study was to evaluate the diagnostic value of FBO in patients with two negative sputum smears and clinical suspicion of pulmonary tuberculosis in routine clinical practice.

The study was carried out at the *Hospital Nacional Hipólito Unanue*, a referral hospital in Lima, Peru. Within the districts served by the hospital the incidence of tuberculosis is high, being up to 300/100,000 population in some areas.[3] The study was approved by the Research Ethics Committee of *Hospital Nacional Hipólito Unanue*.

We reviewed the results of AFB smears and mycobacterial cultures from bronchial aspirates of adult patients who underwent FBO between January of 2008 and December of 2009 due to clinical suspicion of tuberculosis and who had at least two negative AFB smears. The procedures were performed by trained pulmonologists. Samples obtained by BAL were decontaminated, stained with Ziehl-Neelsen, and cultured in Ogawa medium in accordance with national guidelines.[2] Pulmonary tuberculosis was defined as a positive AFB smear or a positive culture for *M. tuberculosis* in the BAL or sputum samples obtained within two weeks before or after the procedure. A secondary analysis was carried out in order to compare the BAL results with the results of the pre-procedure sputum culture (if available) and the post-bronchoscopic sputum sample analysis. The incremental diagnostic yield was defined as the number of additional diagnoses divided by the number of cases diagnosed times 100, and it was calculated for all three procedures.

During the study period, 632 patients underwent FBO. Of those, 21 patients were excluded: 6 because their sputum smears tested positive prior to the procedure, 6 because the samples were contaminated, and 9 because data were missing. Therefore, 611 patients were included in the analysis. The mean age of the patients was 41.98 ± 17.09 years. Most of the patients were male (56.5%). Pulmonary tuberculosis was diagnosed in 140 patients (22.9%). In comparison with the other patients, those diagnosed with tuberculosis were younger (31.8 vs. 45.2 years; $p < 0.001$) and more often male (65% vs. 54%; $p = 0.02$).

The AFB smears of BAL samples were positive in 68 (49%) of the tuberculosis patients (Table 1). Positive cultures provided the diagnosis in 72 additional cases, giving an incremental diagnostic yield over AFB smears of BAL samples of 106%.

The results of post-bronchoscopic sputum AFB smears were available for 278 patients. The comparison between AFB smears of post-bronchoscopic sputum samples and those of BAL samples is shown in Table 2. The incremental diagnostic yield of AFB testing of post-bronchoscopic sputum smears over that of BAL smears was 19%. Cultures of post-bronchoscopic samples were obtained for 30 patients. Of those 30 cultures, 11 were positive in both post-bronchoscopy sputum and BAL samples, 3 were positive only in post-bronchoscopy sputum samples, and 2 were positive only in BAL samples.

Sputum cultures performed before the procedure were available for comparison in 56 patients. Of those 56 patients, 14 were diagnosed with pulmonary tuberculosis, the diagnosis being based only on positive BAL samples in 8 and only on pre-procedure sputum cultures in 3. In the 3 remaining patients, BAL and pre-procedure sputum cultures were both positive.

Our results show that, in patients suspected of having SNPT, the diagnostic yield of AFB

Table 1 - Comparison between the diagnostic yield of AFB and that of culture in BAL samples in patients suspected of having smear-negative pulmonary tuberculosis. Lima, Peru, 2008-2009.

Method		Culture		
Method		Positive	Negative	Total
AFB	Positive	61	7	68
	Negative	72	471	543
	Total	133	478	611

Table 2 - Comparison of the diagnostic yield of direct testing for AFB in BAL samples and in post-bronchoscopic sputum samples in patients suspected of having smear-negative pulmonary tuberculosis. Lima, Peru, 2008-2009.

Sample type		Post-bronchoscopy sputum		
Sample type		Positive	Negative	Total
BAL	Positive	15	16	31
	Negative	6	241	247
	Total	21	257	278

smears and cultures from BAL samples is high, having the potential to diagnose tuberculosis in 1 out of 4 patients undergoing FBO. This might even be an underestimation, considering that we used only solid culture media, which have low sensitivity in comparison with other media.[4,5] Another Latin American study in an HIV-prevalent setting also reported a good diagnostic yield from the procedure.[6] Nevertheless, the procedure is not included in the diagnostic workup of SNPT by the Peruvian Tuberculosis Control Program[2] or by the World Health Organization.[4]

One remarkable finding of the present study was the high frequency of tuberculosis among young male patients. This probably does not mean that the procedure is better for this age group but might rather reflect the higher prevalence of tuberculosis among such individuals.

Another interesting result was the high positivity of post-bronchoscopic sputum samples, which increased the diagnostic yield by approximately 20%. Although the analysis of post-bronchoscopy sputum samples has already been shown to have a good diagnostic yield in settings other than Latin America, the increase in diagnostic yield in previous studies was found to be close to 7%.[7] It is also of note that post-bronchoscopy sputum samples are currently sent for AFB smears but not for culture. In the few patients for whom cultures were performed in post-bronchoscopy samples, the cultures appeared to increase the diagnostic yield. However, because of the small size of our study sample, we could not explore this hypothesis further. Other limitations of our study are the retrospective nature of data collection, which might generate bias due to missing data, and the relatively short follow-up period (which might preclude the diagnosis of additional SNPT cases among those with negative AFB and culture results from BAL samples). In addition, we were not able to perform transbronchial biopsies, which have been shown to increase the sensitivity of the procedure from 25% to 40%.[8,9] Unless contraindicated, we believe that transbronchial biopsies should be performed in all patients who undergo FBO for the diagnosis of tuberculosis.

It is worrisome that, in routine clinical practice—despite the recommendations of the Peruvian National Tuberculosis Control Program, which stipulate that, after two negative sputum samples, a culture should be performed—a very low proportion of patients undergo sputum culture before undergoing FBO. This could be due to the lack of rapid sputum sample testing methods and the belief that BAL samples are superior to sputum samples. In addition, other methods for optimizing the yield of smear microscopy are not currently performed in routine clinical practice in Peru. In particular, sputum induction has been shown to be an effective method for the diagnosis of tuberculosis, with a high rate of agreement with bronchoscopy,[6] and this can avoid a significant number of procedures. However, this method has not been yet implemented.

Given the very low proportion of patients for whom sputum cultures were performed, either prior to or immediately after FBO, we cannot draw definitive conclusions regarding their utility. However, our results suggest that both types of cultures add value to BAL testing. We believe that pre-bronchoscopy sputum, BAL, and post-bronchoscopy sputum samples should all be cultured, although the utility of this approach has not been formally validated, and, from an operational point of view, this could overburden laboratories. In fact, laboratory facilities typically do not perform more than one culture per patient. However, considering that few patients undergo FBO and that the diagnostic yield of such an invasive procedure should be maximized, we believe that it is worthwhile to culture those samples. Further research on the value of these types of samples should be done under operational conditions in order to evaluate their true contribution. In addition, the use of liquid media and molecular methods, which can improve the sensitivity of bronchoscopic sample analysis, should also be investigated.[10]

In summary, FBO is a procedure with a good diagnostic yield in patients suspected of having SNPT in a high incidence setting, such as ours. It is reasonable to perform at least one post-bronchoscopy sputum smear test in addition to BAL testing. The routine culture of pre-bronchoscopy sputum samples (including induced sputum samples) and post-bronchoscopy sputum samples seems to be useful and should be the object of future studies.

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