DOI: 10.14260/jemds/2015/249

ORIGINAL ARTICLE

ROLE OF BRONCHOALVEOLAR LAVAGE IN DIAGNOSIS OF PULMONARY DISEASES: EXPERIENCE AT A NORTH INDIAN HOSPITAL

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HOW TO CITE THIS ARTICLE:
Nirmal Chand, Bharat Bhushan, Ajay Gupta, Nadia Kajal, Heena Bharti. "Role of Bronchoalveolar Lavage in Diagnosis of Pulmonary Diseases: Experience at a North Indian Hospital". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 11, February 05; Page: 1738-1748, DOI: 10.14260/jemds/2015/249

ABSTRACT: INTRODUCTION: Fiberoptic bronchoscopy, a semi-invasive procedure, is an important entity in the armamentarium of procedures listed in diagnosis of respiratory problems. Bronchoalveolar lavage (BAL) involves introduction of fluid to the terminal bronchioles and its recollection for analysis to examine cells, inhaled particles, infectious organisms or fluid constituents. First introduced into clinical practice in early 1980s, BAL is an important diagnostic tool. **MATERIAL AND METHODS:** Current prospective study was carried out on 100 patients, presenting with cough, hemoptysis, fever, chest pain or having pulmonary radiological lesions, at a north Indian hospital. **RESULTS:** Diagnostic yield of BAL fluid examination was 59%, with lung cancer in 22% patients being the commonest diagnosis. 37% patients were diagnosed to have pulmonary infections on BALF examination with pulmonary tuberculosis detected in 17% patients, whereas bronchial brush smear identified only 13% cases.. Combining all the bronchoscopic diagnostic modalities namely BAL, bronchial brushings and bronchoscopic biopsy, 70% yield was achieved in our study, indicating a far superior yield than either of the modality used alone. Bronchial brushings gave higher yield of malignancy cases (27%), showing its superiority over BAL (22%) in diagnosing lung cancers. **CONCLUSION:** The procedure can be easily performed in varied situations with diagnostic puzzle, does not require general anaesthesia, has better patient tolerance and very low incidence of complication rate which are rarely life-threatening..The biggest deterrents to the modality being its cost, expertise required and its semi-invasive nature; apprehending the patient at times.

KEYWORDS: Bronchoalveolar lavage, diagnosis, pulmonary diseases, fiberoptic bronchoscopy.

INTRODUCTION: A resting human adult inhales an estimated 12, 000 litres of air per day, which can be doubled or tripled even with mild physical activity,[1] thus exposing the lungs continuously to the external environment and mixtures of complex antigens through the air, making them vulnerable to various insults.

Various lung conditions like lung malignancy, tuberculosis, bacterial and fungal infections may present both clinically and radiologically in a similar manner. Therefore, the diagnosis of these conditions remains a challenge to the physicians throughout the world. Routine diagnostic methods including chest radiography to advanced tools such as computed tomography and other imaging modalities, at times fail in the task of finding the exact etiology and reaching a definitive diagnosis with resultant delay in appropriate treatment.

Fiberoptic bronchoscopy is an important entity in the armamentarium of procedures listed in diagnosis of respiratory problems. Since the development of the fiberoptic bronchoscopy and various accessory instruments that can be inserted via the working channel, bronchoscopic exploration to the lung periphery has been facilitated. The instrument permits careful inspection of the bronchial tree

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for endo-bronchial lesion and foreign body and also helps in recovery of deep respiratory secretions, brushing and biopsy which is useful in the diagnosis of uncommon infections, neoplasm and other noninfectious causes.[2]

Bronchoalveolar lavage (BAL) is a diagnostic procedure where lavage fluid is introduced to the terminal bronchioles and then recollected for analysis to examine cells, inhaled particles, infectious organisms or fluid constituents. This semi-invasive procedure is to be performed prior to biopsy or brushing procedures to avoid contamination with blood. The successive instillation of lavage fluid (100 - 300 ml for adults) into the target area is done to ensure that sufficient aspirate is available for analysis. The highest aspiration rates of fluid have been identified from the right middle lobe. In diffuse lung diseases, the middle lobe or lingula are the standard sites for BAL. In patients with radiographic heterogeneity, fluid can be instilled into two or three different regions, to reach a higher representation of the entire lung.

Non infectious	Infectious
Sarcoidosis	(Ventilator-associated) pneumonia
Hypersensitivity Pneumonitis	Pneumocystis pneumonia
Idiopatic lung fibrosis	Mycobacterial infection
Connective tissue disorders	Aspergillus fumigatus infection
Langerhans cell histiocytosis	Viral pneumonia
Malignancies	Toxoplasma pneumonia
Alveolar hemorrhage	Legionella infection
Alveolar proteinosis	Mycoplasma pneumoniae pneumonia
Eosinophilic pneumonia	Chlamydia pneumoniae pneumonia
Bronchiolitis obliterans with organizing pneumonia	Cryptococcal infection
Asbestosis	Histoplasma infection
Silicosis	Strongyloides infection

Table 1. Pulmonary diseases where BALF can be used for diagnosis [3,4,5]

Possible uses of BAL in diagnostics are summarized in Table 1.BAL provides a very useful tool for diagnosing lower respiratory tract infections in both immunocompetant and immunocompromised patients. To detect and quantitate common bacterial respiratory pathogens, an uncentrifuged BAL fluid specimen can be sent for quantitative bacterial culture. Newer tools that utilize immunofluorescent staining with antibodies and nucleic acid analysis via polymerase chain reaction (PCR) methods are increasingly available for the detection of these pathogens and can facilitate more rapid diagnosis than culture techniques currently allow.[6,7,8]

Another useful application of BAL combined with PCR is for the diagnosis of pulmonary tuberculosis in smear-negative patients [9]. BAL is helpful in the evaluation of pulmonary infiltrates in immunocompromised patients, who generally do not produce sputum facilitating a noninvasive diagnosis. Furthermore, BAL can be performed safely even when significant renal failure or

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coagulopathies are present[7, 10-16.] The diagnostic yield may be increased when BAL is combined with transbronchial lung biopsy (TBLB), but these patients are often at significant risk for hemorrhage when endoscopic lung biopsy is performed in the presence of coagulopathies.

BAL has also been used to diagnose ventilator associated pneumonia (VAP). Various sampling methods have been used to detect and quantify bacterial pathogens in patients suspected of having VAP, including endotracheal aspirate, blind bronchial sampling, protected specimen brush and BAL.[17,18,19]

AIM:

1. To evaluate the utility of bronchoalveolar lavage to find out the etiology of various lung conditions.
2. To ascertain complications before, during and after the procedure of obtaining bronchoalveolar lavage.
3. To compare diagnostic yield of BAL and other investigative modalities for various conditions.

MATERIAL AND METHODS: The present prospective study was designed to be carried out on patients attending the outpatient department and/or admitted in Chest & Tuberculosis hospital, Govt. Medical College, Amritsar, starting December, 2012, after taking informed consent from them. The enrollment was closed in August 2014 after including 100 patients in the study. Patients presenting with cough, hemoptysis, fever, chest pain or having pulmonary radiological lesions were considered for the study. Ethics committee approval was taken as per the protocol.

Inclusion Criteria:

1. Patients having clinically / radiologically demonstrable lung lesions.
2. Patients having sputum smear negative for acid fast bacilli (AFB).
3. Suspected cases of interstitial lung disease.
4. Patients aged between 18 – 65 years.

Exclusion Criteria:

1. Sputum smear positive for AFB.
2. $PaO_2 < 60$ mm Hg or $SaO_2 < 89\%$ inspite of O_2 therapy.
3. $FEV_1 < 1L$, hypercapnia ($PaCO_2 > 45$mm Hg).
4. Myocardial infarction in the past six weeks.
5. Serious cardiac arrhythmias.
6. Hemodynamic instability.
7. Uncorrected bleeding diathesis.

A detailed clinical history, through physical examination and routine radiological and laboratory investigations were done on all these patients. Fujinon's fiberoptic video bronchoscope (5.8 mm external diameter) was used for bronchoscopy. Appropriate sedation and pre-procedural medication were given to the patient prior to bronchoscopy.

Monitoring of pulse rate, respiratory rate, blood pressure and oxygen saturation was done during the procedure. Oxygen was administered throughout the procedure to maintain saturation. Both sides of tracheobronchial tree were inspected systematically. Collection trap was attached to the

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bronchoscope and 20 ml of saline was infused with a syringe, observing the flow of saline at the distal tip of the bronchoscope. Maintaining wedged position, gentle suction (50-80mmHg) was applied, collecting the lavage specimen in the collection trap. Above steps were repeated, up to 5-6 times as needed (Total 100-120 ml), to obtain an adequate BAL specimen. Depending on the lesion detected, other appropriate samples such as bronchial washings, bronchial brushings and biopsy were also obtained. Samples were subjected to cytology, histopathology, Gram staining for bacterial infections, potassium hydroxide staining for fungal infections and Ziehl-Neelsen staining for suspected cases of pulmonary tuberculosis.

RESULTS: The ratio of males to females (M: F) was 2.2 : 1 with 68 males, 31 females and one transgender in our study. Majority of patients i.e. 64 were non-smokers, 24 smokers and 12 were found to be reformed smokers. On comparing these groups of patients, it was found that the incidence of disease confirmed by bronchoscopy was more in smokers (83.3%), followed by reformed smokers (75%) and non-smokers (64.1%).

Common symptoms observed in this series were in following order of frequency: cough with expectoration (56%), fever (52%), breathlessness (45%), weight loss (42%), dry cough (26%), anorexia (8.0%), hemoptysis (6%), chest pain (5.0%) and facial swelling (4%). Many of the patients presented with more than one symptom.

The indications for performing broncoscopy in patients were presence of mass lesion in 42 subjects, suspected sputum smear negative pulmonary tuberculosis in 35, consolidation in 12, nodular opacities in 5, atelectasis in 4, lung abscess in 1 and bronchiectasis in one patient. Although there were patients having more than one presentation on chest imaging, the dominant lesion present amongst them has been mentioned (Table 2).

SL. No.	Indications for bronchoscopy (Dominant lesion)	Number of cases (n=100)
1.	Mass lesion	42
2.	Smear negative suspected cases of pulmonary tuberculosis	35
3.	Consolidation	12
4.	Nodular opacities	5
5.	Atelectasis	4
6.	Lung abscess	1
7.	Bronchiectasis	1

Table 2: Indications for performing bronchoscopy

Mucosal congestion was seen in 28%, bronchial narrowing in 21%, and presence of visible secretions in 18% patients. Active bleeding was seen in 9%, although mild in majority of them. Growth was visible in the airway lumen in 8% patients. Unilateral vocal cord immobility/ paralysis was observed in 5% whereas mucosal ulceration was observed in 2 patients (Table 3). No abnormality was visualized in 23 patients on bronchoscopic examination.

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Post-procedure minor adverse events in the form of mild hemoptysis were present in 4 patients, which were controlled with treatment. Hemoptysis was less than 50 ml in all these patients. Two patients had persistent cough after the procedure which also responded to symptomatic medication. No major complication in the form of chest pain, fever, arrhythmias or death, was encountered.

Sl. No.	Bronchoscopic appearances	Percentage
1.	Mucosal congestion	28.0
2.	Narrowing of bronchus	21.0
3.	Pus or secretions	18.0
4.	Hemorrhage/ blood streak	9.0
6.	Growth	8.0
7.	Vocal cord paralysis	5.0
8.	Mucosal ulceration	2.0
10.	Normal appearance	23.0

Table 3: Bronchoscopic appearances (n=100)

In the present study, diagnostic yield of BAL fluid examination was 59%, with lung cancer in 22% patients being the commonest diagnosis. Pulmonary tuberculosis was detected in 17%, bacterial pneumonia in 12%, bronchiectasis in 4%, fungal pneumonia in 3% and pyogenic lung abscess in 1% of patients. Accordingly, 37% patients were diagnosed to have pulmonary infections with the aid of BALF examination, whereas it was non-conclusive in 41% patients (Fig 1).

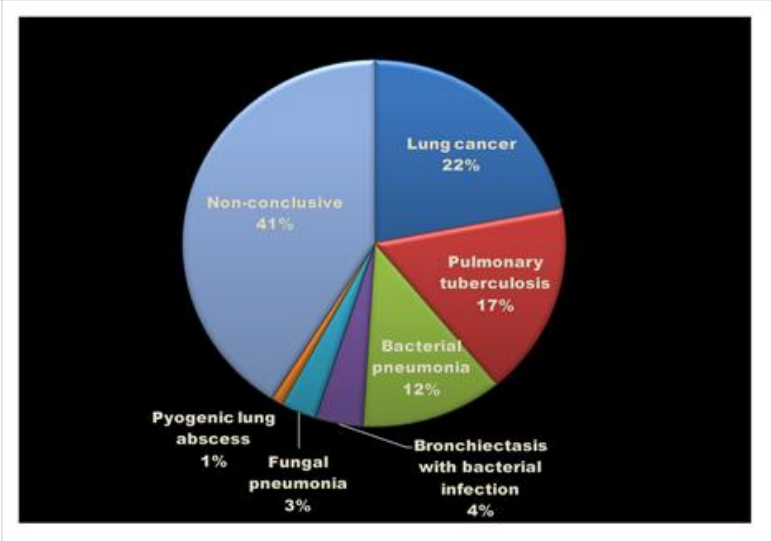

Fig. 1: Diagnosis in patients with BAL fluid examination

Bronchial brush (BB) smears were prepared from all the cases (n=100) and yielded diagnosis in 40 amongst them. Lung cancer was found in 27 patients, pulmonary tuberculosis in 8, bacterial pneumonia in 4 and bronchiectasis in 1 patient with this modality.

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Bronchial biopsy was performed in 7 patients, in whom lesion could be visualized in the tracheobronchial tree, whereas transbronchial lung biopsy (TBLB) was performed in single patient. Lung cancer was diagnosed in 6/8 patients (75%), sarcoidosis in 1/8 (12.5%), whereas diagnosis remained non-conclusive in another patient.

The diagnostic yield of BALF examination, bronchial brush smear examination and bronchoscopic biopsy thus was found to be 59%, 40% and 87.5% respectively. While BAL fluid and bronchial brush smear examination was performed in all the patients, biopsy was taken in 8 patients. Streptococcus pneumoniae growth was reported in 7 (41.2%), Staphylococcus in 4 (23.5%), Pseudomonas in 3 (17.6%), Klebsiella in 2 (11.8%) and Citrobacter in 1 (5.9%) patient, indicating that Streptococcus pneumoniae was the commonest organism causing bacterial infections in the study.

Thus, combining all these bronchoscopic diagnostic modalities, 70% yield was achieved in our study, indicating a far superior yield than either of the modality used alone (Table 4).

Bronchoscopic modality	No. of patients	AFB positivity	Malignancy	Gram staining results for bacteria	Positive KOH stain for fungus	Other (s)	Diagnostic yield (%)
Bronchoalveolar Lavage	100	17	22	17	3	-	59.0
Bronchial Brushings	100	8	27	5	-	-	40
Bronchial/ trans bronchial lung biopsy	8	-	6	-	-	1 (Sarcoidosis)	87.5
Total diagnostic yield from bronchoscopy	100	17	32	17	3	1	70

Table 4: Diagnostic yield from bronchoscopic modalities

DISCUSSION: With the advent of flexible fiberoptic bronchoscope, respiratory diagnostics took a new turn as samples like bronchial washings, bronchial brushings, broncho-alveolar lavage and trans-bronchial needle aspirations could be collected from the respiratory tract, yielding significant amount of cytological material and causative agent(s).[20] When BAL was first introduced into clinical practice in the early 1980s, expectations were high from it as a diagnostic tool and outstripped its eventual utility.[2] Even if not diagnostic at times, BAL can provide findings that are inconsistent with suspected diagnoses and thus help focus attention on pursuing alternative diagnoses.

In the present study, the most common bronchoscopic finding was mucosal congestion found in 28 cases. Amongst those diagnosed with malignancy, majority were found to have growth or narrowing of bronchus during bronchoscopy. Tubercular patients predominantly had mucosal congestion or irregularity of bronchial wall, patients having bronchiectasis clinico-radiologically had dilatation of involved bronchus flooded with secretions, whereas congestion of the bronchial mucosa of the involved lobe/ segment was seen in cases of pneumonia.

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Trans-nasal fiberoptic bronchoscopy is very safe procedure which is tolerated well by almost all patients. Trans-nasal introduction offers the added advantage of viewing nasal fossae, naso-pharynx and larynx which at times may have pathology. The only contraindication to this route is a complete nasal obstruction by either trauma or disease. No major complication occurred during/after the procedure in the present study subjects. However, minor adverse events in the form of mild hemoptysis (4%) and persistent cough (2%) occurred in the post-procedure period, which were resolved with symptomatic treatment.

No case with more than 50 ml bleeding was seen, whereas Herf et al[21] in a survey of 5, 450 cases reported 68 cases (1.2%) of more than 50 ml bleeding and Hanson et al reported 1.8% cases. None of the patients reported fever after bronchoscopy. Gaude et al[22] reported minor adverse events in 18.8% patients including fever (8.6%), persistent cough (6.3%), bronchospasm (2.8%) and mild hemoptysis (1.1%).

Bronchoscopy currently remains the primary means for diagnosis of pulmonary malignancies. With the advent of bronchoscopy, the emphasis shifted from diagnosis of malignancy in operable patients and confirmation of metastases, to the use of cytology as a first line diagnostic procedure on which crucial management decisions could be based.[2,20,23-26] Whereas lung cancer yied from BAL was 22% in the current study, it had been found to be 30.27% by Khara et al,[27] 65% by Vigg et al[28] and 53%[29] reporting from still another study. Worth mentioning, that these studies with higher result yield were carried out exclusively in suspected lung cancer patients.

In current study, bronchial brushings gave higher yield of malignancy cases (27%), showing its superiority over BAL (22%) in diagnosing lung cancers. BB has the advantage that the surface of the suspicious lesion is scraped with the help of a brush passed in through the bronchoscope[2]. This technique manages to 'dislodge' the cells from the surface of those well differentiated malignant lesions too, which otherwise do not exfoliate cells readily. Thus, the chances of getting adequate diagnostic cytological sample by BB greatly increase in comparison to BAL samplings. Moreover, since the surface of the malignant lesion is scraped by the brush, the cells retrieved show better preserved morphological details with BB in comparison to the cells which have already been exfoliated into the bronchial lumen and taken up by BAL. These factors contribute towards the increased diagnostic yield of BB samplings.

Combining all the modalities, malignancy was diagnosed in 32%, which was superior to either BAL (22%) or bronchial brushings (27%) alone. Although diagnostic yield of bronchoscopic biopsy was higher (75%), it could be performed in only 8 patients in which lesion could be visualised with fiberoptic bronchoscope. Hence, diagnostic yield is improved considerably when a combination of various modalities is used. Various workers have tried to combine the two techniques of BB and BAL, in order to improve the yield of diagnostic cytological material. Govert et al[30] reported 85.3% sensitivity on combining these two techniques; while Bedrossian et al[31] reported a higher sensitivity of 92%.

BALF examination revealed pulmonary tuberculosis in 17% patients in the current study, with smear positivity for AFB from their BALF; findings almost similar to a previous study reporting AFB positivity in 18.5% patients.[32] While performing the procedure on all PTB suspects, Gaude et al[22] found BAL showing AFB positivity in 32% cases of smear negative PTB, .The utility of BAL in the diagnosis of pulmonary tuberculosis in the difficult to diagnose cases, has been documented by several workers.[33] Obviously BALF examination can prove valueable to demonstrate AFB on smear

examination in the diagnosis of pulmonary tuberculosis where the routine sputum samples are AFB negative or patients are unable to expectorate.

The best documented clinical application of BAL is for the diagnosis of pulmonary infections. The role of BAL in non-resolving pneumonias has already been established in various studies. In the present study, BAL was helpful to establish the diagnosis in 17 cases with bacterial pulmonary infections. These included 12 patients with bacterial pneumonia, 4 having bronchiectasis with superadded bacterial infections and a patient with lung abscess.

Fungal pneumonia remains one of the causes of non-resolving pneumonia. BALF examination revealed fungal pneumonia in 3% patients in the current study. In a similar study, fungal pneumonia was found in four patients amongst 175 study subjects.[25]

In the cuurent study, BAL resulted into an overall diagnostic yield of 59%., with Khara et al[27] reporting 55.7%, while Gaude et al[22] had 81.8% yield, in the diagnosis of various pulmonary diseases. The current study demonstrates a better utility of BAL to diagnose various pulmonary infections as compared to other modalities. Infections including pulmonary tuberculosis, were detected in 37% patients while utilising BAL, whereas bronchial brush smear identified only 13 such cases.

BAL provides a very useful tool for diagnosing lower respiratory tract infections. The higher yield of BAL in case of pulmonary infections may be due to the fact that BAL is able to extract deep seated secretions and can be subsequently cultured to isolate the suspected organism. Moreover, drug sensitivity testing can also be performed subsequently, which can help to decide optimal management for such patients.

CONCLUSION: The combination of the ease of performance of FOB, combined with the accessibility of material for study by means of BAL, has led to the potential for widespread use of this technique in a variety of clinical settings with means for diagnosis and early treatment. BAL is a very safe, effective, economical, easily performable diagnostic modality, without hazards of general anaesthesia. This investigation has come out with flying colours after being evaluated by physicians from time to time.

The procedure can be easily performed in varied situations with diagnostic puzzle, does not require general anaesthesia, has better patient tolerance and very low incidence of complication rate which are rarely life-threatening. Present study reveals its high diagnostic yield with negligible complications.

No doubt, BAL is a wise innovation with minimal side effects and high output, however it needs expertise with good pre-procedural preparation of the patient. The biggest deterrents to the modality being its cost, especially for developing countries along with non-acceptance to the technique by some patients because of its semi-invasive nature. Bronchoalveolar lavage utilizing fiberoptic bronchoscopy, is having a definite role in finding specific etiology of various lung conditions not responding to routine treatment.

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DOI: 10.14260/jemds/2015/249

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Date of Submission: 17/12/2014.
Date of Peer Review: 18/12/2014.
Date of Acceptance: 22/01/2015.
Date of Publishing: 03/02/2015.