Research Article

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Comparison of bronchoalveolar lavage and protected mini- bronchoalveolar lavage in diagnosis of pneumonia in intensive care unit

Abstract

Aim: The aim is to compare microbiological examination of samples, which were taken by fiberoptic BAL and protected mini-BAL methods from patients with diagnosis of pneumonia in the intensive care unit.

Methods: Study population included all adult critically ill mechanically ventilated patients, who were admitted to Intensive Care Units of Cerrahpaşa Medical School between July 2013 and November 2014, and diagnosed as pneumonia either on admission or during their stay. Patients were assessed by APACHE II, SOFA and CPIS. The patients were randomly allocated in to two groups using computer generated random numbers. In the first group FOB and BAL was applied first followed by protected mini-BAL, in the second group protected mini-BAL was the first sampling method. The samples were then transferred to the microbiology laboratory for microbiologic examination. The materials were evaluated by gram-staining and quantitative cultures. The compability of fiberoptic BAL and protected mini-BAL results for all cases was evaluated with kappa statistics. A two tailed p value of <0.05 was considered statistically significant.

Results: Sixty-six patients were included in to the study. Fiberoptic BAL followed by protected mini-BAL was performed in 32 (48.5%) patients, protected mini-BAL followed by fiberoptic BAL in 34 (51.5%) patients. No significant difference was found between two groups about demographic features, severity scores, laboratory values, use of antibiotics, comorbidities and prognosis. When the types of pathogens were compared between two groups no significant differences were found. When the results of samples were evaluated for compatibility all together, the Kappa coefficient was found as 0.476 (p=0.0001), which is not high value, and this kappa coefficient is considered to be moderate value.

Conclusion: Protected mini-BAL procedure is effective, less invasive and easier to apply compared to FOB. But it cannot be used as an alternative to fiberoptic BAL to determine the causative organism of pneumonia in ICU patients according to this study results.

Keywords: pneumonia, BAL, FOB, protected mini-BAL, intensive care unit, VAP

Atasoy Gurlevik, Seval Urkmez, Tughan Utku, Yalim Dikmen
Department of Anaesthesiology and Reanimation, Cerrahpaşa Medical School, Istanbul University, Turkey

Correspondence: Seval Urkmez, Department of Anaesthesiology and Reanimation, Cerrahpasa Medical School, Istanbul University, Kocamustafapasa 34098 Fatih, Istanbul, Turkey, Tel 0090532 441 8451, Fax +90212 414 3588, Email sevalurkmez@yahoo.com

Introduction

Pneumonia is a common respiratory problem, which involves infection of the alveoli, inflamation and consolidation of the lung tissue.[1] Pneumonia is common in intensive care (ICU) patients, and caries a risk of high mortality in the affected patients. Pneumonia is identified by using a combination of imaging, clinical and laboratory criteria.[2-5] Timely diagnosis and treatment with antibiotics is life saving however, there is no gold standart for the diagnosis of pneumonia. One of the criteria of pneumonia established by Centers for Disease Control and Prevention (CDC) is getting semi-quantitative or non-quantitative cultures of sputum obtained by deep cough, induction, aspiration or lavage.[6]

Procedure, which used to obtain samples from airways is important because of the contamination risk from upper airways, which makes defining the causative organism difficult, and leads to use inappropriate antibiotics. To prevent this contamination from upper airways, the use flexible fiberoptic bronchoscopy (FOB) is suggested. But use of FOB is complex and needs expertise. Protected mini-broncoalveolar lavage (protected mini-BAL) can also be used instead of FOB. This procedure is not as difficult and complicated as FOB and does not take much time as in FOB, but there is still doubt about the accuracy of culture results in protected mini-BAL.

The aim of this study is to evaluate compatibility of the quantitative cultures in microbiological specimens taken with FOB and protected mini-BAL from ICU patients who are diagnosed as pneumonia.

Material and method

The study was approved by the Clinical Research Ethics Committee of Istanbul University Cerrahpaşa Medical School (Date: 18.12.2012, number: 36051). Study population included adult, intubated and mechanically ventilated critically ill patients, who were admitted to Intensive Care Units of Cerrahpaşa Medical School between July 2013 and November 2014, and diagnosed as pneumonia either on admission or during their stay. The only exclusion criterion was the contraindication for FOB. Informed consent for the study was obtained from the patients' next of kin.

Demographic features, comorbid diseases, prior use of antibiotics, full blood count, C reactive protein (CRP), blood and urine cultures, chest x-ray findings, Acute Physiology and Chronic Health Evaluation (APACHE II), Sequential Organ Failure Assessment Score (SOFA) were recorded.

For diagnosis of pneumonia CDC 2013 criteria[7] and CPIS[8] were used (Tables 1 & 2). Patients with more than 6 points in CPIS were diagnosed as pneumonia. The patients were randomly allocated in

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to two groups using computer generated random numbers. In the first group (32 patients) fiberoptic BAL was applied first, and then followed by protected mini-BAL, in the second group (34 patients) protected mini-BAL was the first sampling method.

For fiberoptic bronchoscopy, a fiberoscope (Pentax, Orangeburg, New York, USA) was inserted through the endotracheal tube and advanced to the affected area, where consolidations were seen on the chest x-ray, and wedged to the distal bronchi. Then 20 mL aliquots of sterile saline solution was instilled though the working lumen of the fiberoscope then aspirated in to a sterile container. This was performed five times. Protected mini-BAL samples was obtained through a sterile catheter (Combicath Plastimed, Saint-Leu-La-Foret, France). This catheter has a telescoping longer second catheter inserted within the first one, and is protected by a polietilen glikol plug, which plugs the distal orifice of the first lumen to prevent contamination of the second catheter. This catheter is placed in the airways by advancing through the endotracheal tube until the patient caughs or it cannot be advanced

further. When it is in place the second catheter is pushed further, for 15-20 mm to remove the plug and expose its tip. To obtain mini-BAL samples 40 mL of sterile saline was instilled followed by aspiration in to a sterile syringe. This generally yielded an aspirate of 2-3 mL. The samples were then transferred to the microbiology laboratory for microbiologic examination. The materials were evaluated by gram-staining and quantitative cultures. The bacteria in white blood cells were searched under light microscopy in gram-stains. The samples were vortexed for 60 seconds, diluted with salin to 1/10, 2/10, 3/10 ratios and inoculated 0.01 cc to blood agar, chocolate agar and MacConkey agar. Cultures were incubated at 37° Celcius for 24 hours and than bacteria were evaluated quantitatively. The cut-off values for bacterial colony counts was taken as 104 colony forming units (CFU)/cc. When different types of bacteria were seen, colony count was done separately for all types. Microbial identification and antimicrobial susceptibility testing were done with Vitek 2 system (BioMerieux, USA).

Table 1 Algorithm for Clinically-Defined Pneumonia (CDC 2013 guideline)

Radiology	Signs/Symptoms/ Laboratory
Two or more serial chest radiographs with at least one of the following: 1. New or progressive and persistent infiltrate	At least one of the following:
2. Consalidation	
3. Cavitation	1. >Fever (38°C or >100.4 °F)
Note: In patients without underlying pulmonary or cardiac disease, one definitive radiograph is acceptable.	2. Leukopenia (<4000 WBC/mm3) or leukocytosis (≥12.000 WBC/mm3)
	3. For adults ≥70 years old, altered mental status with no other recognized cause
	and At least two of the following:
	1. New onset of purulent sputum, or change in character of sputum, or increased respiratory secretions, or increased suctioning requirements
	2. New onset or worsening cough, or dyspnea or tachypnea
	3. Rales or bronchial breath sounds
	4. Worsening gas exchange (e.g., O2 desaturations (e.g., PaO2/FiO2 ≤ 240), increased oxygen requirements, or increased ventilator demand)

WBC: White Blood Cell; PaO_2/FiO_2: The Ratio of the Arterial Tension (PaO_2) to the Inspiratory Fraction of Oxygen (FiO_2)

Table 2 Clinical Pulmonary İnfection Score (CPIS)

CPIS Points	0	1	2
Tracheal secretions	Rare	Abundant	Abundant+purulent
Chest X-ray infiltrates	No infiltrate	Diffused	Localized
Temperature, °C	≥36.5 and ≤38.4	≥38.5 and ≤38.9	≥39 or ≤36
Leukocytes count, per mm3	≥4.000 and ≤11.000	<4.000 or >11.000	<4.000 or >11.000 + band forms ≥ 500
PaO2/FiO2 , mmHg	>240 or ARDS		≤240 and no evidence of ARDS
Microbiology	Negative		Positive

ARDS: Acute respiratory distress syndrome; PaO_2/FiO_2: The Ratio of the Arterial Tension (PaO_2) to the Inspiratory Fraction of Oxygen (FiO_2).

Statistics

Statistical analysis of the data was performed using SPSS 22.0 package program (SPSS, IBM Ltd, Chicago, USA). Results are expressed in frequency, percentage or mean and standart deviation when appropriate. Parametric data was compared using Mann-Whitney U test, Pearson's chi-square and Fisher Exact tests were used for non-parametric data. The compability of fiberoptic BAL and protected mini-BAL results for all cases was evaluated with kappa

statistics. A two tailed p value of <0.05 was considered statistically significant.

Results

Sixty-six patients were included in to the study, demogrophic features are given in Table 3. Fiberoptic BAL followed by protected mini-BAL was performed in 32 (48.5%) patients, protected mini-BAL followed by fiberoptic BAL in 34 (51.5%) patients. No significant differences were found in the demographic features of two groups.

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Of the patients 22 (33.3%) of 66 had Community Acquired Pneumonia (CAP), 25 (37.9%) had Ventilator Associated Pneumonia (VAP) and 19 (28.8%) had Hospital Acquired Pneumonia (HAP). Fifty-eight (87%) patients had comorbidities, which increase the mortality risk such as diabetes, hypertension, congestive heart failure and chronic obstructive lung disease.

In 83.3 % of patients (55/66) antimicrobial therapy was started prior to pneumonia diagnosis for prophylaxis or treatment of an infection in other parts of the body. Mortality in this patients population was 77.27%. No significant difference was found between two groups about severity scores, laboratory values, use of antibiotics, comorbidities and prognosis (Table 3). When the types of pathogens were compared between two groups no significant differences were found. The types are listed in Table 4. When the types of bacteria obtained from two techniques regardless of group allocation (timing of procedure) were compared no statistically significant difference was observed (Table 5). The compatibility of cultures obtained by fiberoptic BAL and protected mini-BAL in patients, who were diagnosed as pneumonia were 81.81% in CAP (18/22), 73.68% in HAP (14/19) and 64% in VAP(16/25). When the results of samples were evaluated for compatibility all together, the Kappa coefficient was found as 0.476 (p=0.0001).

Table 3 Demographic features and patients' condition

Patient's features		First group (FOB-BAL) n (%)	Second group (Protected mini-BAL) n (%)	p
Gender (F/M)		9/23 (28.1)/(71.9)	18/16 (52.9)/(47.1)	0.04
Use of antibiotics	No	3 (9.4)	8 (23.5)	0.123
	Yes	29 (90.6)	26 (76.5)	
Comorbidities	No	3 (9.4)	5 (14.7)	0.39
	Yes	29 (90.6)	29 (85.3)	
Prognosis	Exitus	24 (75.0)	27 (79.4)	0.669
		Mean (Sd)	Mean (Sd)	
Age		68.7 (14.9)	61.2 (17.6)	0.061
ICU length of stay		34.4 (27.9)	38.4 (42.6)	0.944
APACHE II		23.6 (5.7)	21.8 (6.2)	0.313
SOFA		8.6 (3.1)	8.6 (3.2)	0.637
CPIS		6.5 (1.2)	6.6 (1.1)	0.403
White Blood Cells count, per mm3		12.404 (6.578)	15.460 (14.927)	0.404
CRP		167.0 (129.6)	190.3 (119.6)	0.281

*Sd: Standart Deviation; APACHE: Acute Physiology, Assessment and Chronic Health Evaluation; SOFA: Sequential Organ Failure Assessment; CPIS: Clinical Pulmonary Infection Score; CRP: C Reaktive Protein

Table 4 The types of pathogens were compared between two groups

Procedure	Pathogens	First group		Second group		P value
		n	%	n	%	
Fiberoptic BAL	Acinetobacter baumanii	3	9.40%	2	5.90%	0.552
	Pseudomonas aeruginosa	1	3.10%	1	2.90%	0.5
	Corinobacterium species	1	3.10%	0	0.00%	0.449
	Staphilococcus aureus (MSSA and MRSA)	0	0.00%	1	2.90%	-
	Stenotrophomonas species	2	6.20%	0	0.00%	0.551
	Streptococcus pneumoniae	0	0.00%	1	2.90%	-
	Klebsiella species	1	3.10%	0	0.00%	-
	Gram pozitif difteroid rods	1	3.10%	0	0.00%	0.5
	Candida species	3	9.40%	6	17.60%	0.552
	No pathogen	4	12.50%	2	5.90%	0.159
	Multiple pathogens	16	50.00%	21	61.80%	0.748
Protected Mini-BAL	Acinetobacter baumanii	2	6.20%	1	2.90%	0.549
	Pseudomonas aeruginosa	0	0.00%	2	5.90%	0.451
	Corinobacterium türleri	1	3.10%	0	0.00%	-
	Staphilococcus aureus (MSSA and MRSA)	2	6.20%	1	2.90%	0.5
	Stenotrophomonas species	1	3.10%	1	2.90%	0.5
	Streptococcus pneumoniae	0	0.00%	1	2.90%	-
	Gram pozitif difteroid rods	1	3.10%	0	0.00%	-
	Candida species	2	6.20%	5	14.70%	0.553
	No pathogen	11	34.40%	5	14.70%	0.35
	Multiple pathogens	12	37.50%	18	52.90%	0.711

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Table 5 Total number of pathogens regardless the priority of the procedure

Pathogens	Fiberoptic BAL		Protected Mini-BAL		p
	n	%	n	%	
Acinetobacter baumanii	5	7.6	3	4.5	0.571
Pseudomonas aeruginosa	2	3	2	3	0.5
Corinobacterium species	I	1.5	I	1.5	0.5
Staphilococcus aureus (MSSA ve MRSA)	I	1.5	3	4.5	0.43
Stenotrophomonas species	2	3	2	3	0.5
Streptococcus pneumoniae	I	1.5	I	1.5	0.5
Klebsiella species	I	1.5	0	0	-
Gram pozitif difteroid rods	I	1.5	I	1.5	0.5
Candida species	9	13.6	7	10.6	0.574
No pathogens	6	9.1	I6	24.2	0.17
Multiple pathogens	37	56.1	30	45.5	0.807

Discussion

Pneumonia, either community acquired or health care associated is a serious problem. Main threatment option is antibiotics. It has been shown that when treatment with appropriate antibiotics is initiated promptly the mortality is low.[9] Choosing the appropriate antibiotic is problematic due to difficulties in finding the causative organisms. Because of this difficulty broad spectrum antibiotics are generally used, at least initially until microbiological evaluations are performed.

In intensive care patients samples obtained by endotracheal suctioning may give erroneous results due to contamination from colonized upper airways.[10] That's why clinicians need to obtain dependable lower respiratory tract samples, which are not contaminated. Microbiological evaluation of the specimens obtained with broncoschopy is considered as the specific diagnostic approach to determine the causative microorganism in pneumonia.[11,12] However bronchoscopy is invasive, requires expertise, expensive, needs longer time to perform, disturb oxygenation, respiratory mechanics and hemodynamics during the procedure in intensive care patients.[13-16] Therefore an easier to perform technique is needed. Protected mini-BAL is easier to perform, needs less expertise, takes less time and have lesser effects on oxygenation or hemodynamics, and is cheaper.[17] Sensitivity and specifity of protected mini-BAL was found to be %63-100 and %66-96 in different studies.[18,19] These results are compatable with fiberoptic broncoscopic BAL. Broncoscopy is not indicated as a routine diagnostic test for some certain group of pneumonias like CAP, and should restricted to selected individuals with severe forms or unresponded to initial therapy and require additional investigations of pneumonia.[20] It has been published that patients with progressive pneumonia acceptable as non-responding to traditional diagnostic procedures could be improved clinically by using broncoscopic investigations.[21] In present study, severe CAP cases were included (22 cases; 33.3% of all cases) primarily according to their clinicall severity, and applied FOB as a diagnostic tool.

The mortality rates varies according to patients score of illness, already taken antibiotics, advanced age, comorbidities and failing to initial therapies including non-invasive mechanical ventilation and need to further MV therapy.[22] On the basis of this approach it has been reported a wide variety of mortality rate between 28-85%.[23,24,22] The mortality rate presented in this study is thought higher then expected (77.27%). Our explanation for such a higher rate while actual APACHE II score was 23.6 and predicted mortality rate was 48.2%; in enrolled patients, it had been already prescribed and failed multi antibiotics, have high co-morbidity rates, all suffered severe respiratory failure with hypoxemia during admission to ICU. Furthermore, length of stay in ICU was long (38.4 days) and organ dysfunctions during that time of long period realized (SOFA: 8.6) and, cultured multiple pathogens. We argue that all these particular factors during the period stay in ICU contributed to high mortality rate.

Rouby et al. used protected mini-BAL in hospital acquired pneumonia patients. Protected mini-BAL was %74 compatable with the pathologic evaluation of postmortem lung tissue in terms of microbiological accuracy. They suggested that protected mini-BAL could be used instead of bronchoscopy.[25] In a different study endotracheal aspirates (ETA) and protected mini-BAL were compared in 82 VAP patients and protected mini-BAL was found to be more sensitive. [26] Khilnani et al. evaluated bronchoscopic and nonbronchoscopic techniques for diagnosis of VAP and calculated sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for this techniques, taking CPIS of $\geq$ 6 as reference standart.[27] Sensitivity, specificity, PPV and NPV for nonbronchoscopic BAL were found similar to bronchoscopic BAL and there were good microbiologic concordance among this procedure. Ost et al. compared the effectiveness of ETA, fiberoptic BAL and protected mini-BAL in the diagnosis and management of ventilator associated pneumonia. They found no difference in mortality but protected mini-BAL had lowered costs and antibiotic use.[28]

Early ventilator associated pneumonia diagnosis requires to reduce VAP mortality and to delay emergence of multidrug-resistant microorganisms. The commonest organisms isolated in VAP are *Staphylococcus aureus, Pseudomonas aeruginosa,* and *Acinetobacter baumannii* i intensive care unit.[29] However, causative organisms vary between intensive care. Artuk et al. studied protected mini-BAL vs endotracheal aspirates (ETA) in VAP patients: *Acinetobacter baumanii, Pseudomonas aeruginosa* and *Staphylococcus aureus* rates were %53, %20, %20 in protected mini-BAL ,%10, %20, %20 in ETA.[30] In our study BAL and miniBAL were compared and in both procedures mostly multiple types of pathogens were found and when evaluated one by one, mostly gram negative microorganisms were the reason of VAP. Tasbakan et al. compared fiberoptic BAL and protected mini-BAL in immuncompromised patients in the ICU and found no significant difference in two methods. They have found 12 patients with Candida albicans with both procedures.[31] In this study Candida species were found in 9 BAL and 7 protected mini-BAL samples.

When we compared the microbiological results between two groups with kappa score, Kappa ratio 0.476 (p=0.0001), which is not high value, and this kappa coefficient is considered to be moderate value. However, we were not able to compare keppa scores between

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CAP, VAP and HAP subgroups because of the inadequate number of cases.

THe priority of the procedure was changed in two groups (half of the patients BAL was applied first and protected mini-BAL was first in the other half). The aim of this change was to see if the priority makes a difference in microbiologic results. Especially we wanted to see if 100 cc of 0.9% saline effect the results of protected mini-BAL because of dilution. Four of the 32 patients who were applied BAL in the first line had no pathogens in BAL cultures and 11 of 32 had no pathogens in protected mini-BAL. This seems to make a big difference but statistically there was no significant difference between two groups.

Conclusion

Protected mini-BAL procedure is effective, less invasive and easier to apply compared to FOB. But it cannot be used as an alternative to fiberoptic BAL to determine the causative organism of pneumonia in ICU patients.

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Conflicts of interest

None.

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