Original Article

Comparison of the Results of BAL and ETA Culture in Intubated COVID-19 Patients

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Received: 12-Sep-2023;
Revision: 29-May-2024;
Accepted: 25-Jul-2024;
Published: 26-Aug-2024

Abstract

Background: The isolation of pathogens using bronchoalveolar lavage (BAL) culture or endotracheal aspirate (ETA) culture may enhance the treatment success for secondary pneumonia due to COVID-19, thereby reducing the risk of morbidity and mortality. **Aim:** This study aimed to retrospectively analyze the results of BAL and ETA cultures in intubated COVID-19 patients and to determine whether BAL has an advantage over ETA. **Methods:** We routinely perform BAL culture via bronchoscopy or ETA culture within the first 48 h after intubation. We retrospectively reviewed cases that underwent BAL and ETA. The patients were divided into two groups: Group B (BAL) and Group E (ETA). Various parameters were evaluated and compared between the two groups. **Results:** The demographic data and blood test results were similar between the two groups. However, ICU stay, duration of intubation, and culture positivity were significantly higher in Group B. Although not statistically significant, the mortality rate was higher in Group E. The most commonly isolated microorganisms were *Candida* species. **Conclusion:** The observed mortality rates were consistent with the existing literature. Since the microorganism isolation rate is higher with BAL, leading to more effective antimicrobial treatment, early deaths were prevented, and ICU stay durations were prolonged. Conversely, these durations were shorter in the ETA group due to higher mortality. In intubated COVID-19 patients, a more effective treatment process can be achieved by clearing the airway with fiberoptic bronchoscopy and tailoring the treatment based on BAL culture results. This approach may positively impact prognosis and mortality rates.

Keywords: *Bronchoalveolar lavage, bronchoscopy, COVID-19, critical care, intubation*

Introduction

Since its initial identification, COVID-19 has infected over 519 million people and caused more than 6 million deaths globally.[1] The follow-up and treatment of COVID-19 cases with severe respiratory distress are primarily managed in intensive care units (ICUs). Endotracheal intubation and invasive mechanical ventilation are necessary for patients who do not respond to high-flow oxygen and non-invasive mechanical ventilation. In intubated COVID-19 patients, the occurrence of secondary infections is influenced by immunosuppression caused by the viral load, and the use of steroids and immunosuppressive therapies such as tocilizumab to treat the cytokine storm.[2,3] Secondary pneumonia in these patients can lead to high mortality rates.[4] Studies conducted since the onset of the pandemic have reported mortality rates ranging from 45.6% to 97% in intubated patients.[5-7]

Microbiological culture analysis of bronchoalveolar lavage (BAL) fluid obtained via fiberoptic bronchoscopy, or endotracheal aspirate (ETA) fluid obtained by

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Quick Response Code:

Website: www.njcponline.com

DOI: 10.4103/njcp.njcp_666_23

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How to cite this article: Kilic HH, Gozukucuk R. Comparison of the results of BAL and ETA culture in intubated COVID-19 patients. Niger J Clin Pract 2024;27:945-9.

aspirating tracheal secretions with a catheter, are the methods used to diagnose pneumonia. Early and specific antimicrobial treatment based on culture positivity and antibiogram results can increase the effectiveness of the treatment. Early identification of the infectious agent ensures the timely initiation of effective antimicrobial therapy. Although there may be concerns about increased viral spread during fiberoptic bronchoscopy in COVID-19 cases,[8,9] isolating the microbial agent through BAL culture and targeting the antimicrobial therapy can enhance treatment efficacy.[10-12]

This study aimed to retrospectively analyze and compare the results of BAL and ETA cultures in intubated COVID-19 patients.

Materials and Methods

After obtaining approval from the Hisar Intercontinental Hospital Ethics Committee (approval number 22/5-5), the data of patients who were intubated due to COVID-19 in our ICU between January and December 2021 and underwent BAL or ETA analysis were retrospectively reviewed using the hospital information management system and patient files. Our clinical trial registry number is NCT05403489, registered on clinicaltrials.gov. This is an observational study. The study analyzed demographic parameters, comorbidities, ICU stay duration, intubation duration, mortality rates, culture positivity, types of microorganisms grown, and laboratory test results including C-reactive protein (CRP), procalcitonin, leukocyte, neutrophil, lymphocyte, and immature granulocyte counts. For a culture result to be considered positive, the microbial agent detected had to be $\geq 10^4$ CFU/ml in BAL culture and $\geq 10^5$ CFU/mL in ETA culture.[13]

We routinely perform BAL culture via bronchoscopy within the first 48 h after intubation in ICU cases approved for the procedure. If bronchoscopy is not approved by the patient or their relatives, we perform ETA culture within 48 h instead of BAL. If any microorganism grows in both BAL and ETA cultures, an antibiogram test is conducted to determine which antimicrobial agents the microorganism is resistant to and sensitive to, thereby enabling more accurate antimicrobial treatment.

With the necessary patient consent, fiberoptic bronchoscopy was performed. BAL was conducted by entering the bronchi and bronchioles that the bronchoscope could reach on both sides, administering saline, and aspirating the fluid for microbiological analysis without delay. In cases where informed consent for fiberoptic bronchoscopy could not be obtained, fluid (ETA) was obtained by aspirating tracheal secretions through a sterile aspiration catheter inserted via the endotracheal tube, and this fluid was directly analyzed microbiologically. Figure 1 shows an example of BAL aspiration and bronchiole view, while Figure 2 depicts the removal of mucus plugs encountered during bronchoscopy.

The patients were divided into two groups: Group B (BAL) with 24 patients and Group E (ETA) with 43 patients. The evaluated parameters were compared between the two groups.

Inclusion criteria

Patients diagnosed with COVID-19 and followed up as intubated in the ICU between January and December 2021 were included in the study.

Exclusion criteria

Patients who were not followed up as intubated despite being diagnosed with COVID-19 and patients under the age of 18 were excluded from the study.

Statistical analysis

All analyses were performed using SPSS 25.0 (Statistical Package for Social Sciences, Chicago, USA). Categorical data were presented as counts and percentages, while quantitative data were expressed as means and standard deviations (SD). Differences between patient group data were analyzed using the Student's *t*-test. The Chi-Square test was used to analyze whether there was a statistically significant difference in mortality and culture growth percentages between COVID-19 cases with BAL and ETA. A P value of <0.05 was considered statistically significant.

Results

The study included 24 cases in Group B (BAL) and 43 cases in Group E (ETA). The demographic data were similar between the two groups, with no statistically significant differences. Both groups had a predominance of male patients. The gender ratio, mean body mass index (BMI) and mean age values for both groups are presented in Table 1. Additionally, there were no

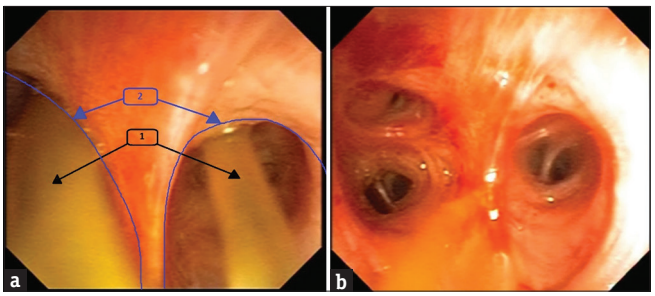

Figure 1: (a) Bronchoalveolar lavage aspiration. 1: Bronchoalveolar fluid (during suction) 2: Bronchioles. (b) View of the bronchioles after aspiration

significant differences in comorbidity rates between the groups, as shown in Table 1. The mean values of laboratory test results, including leukocytes, lymphocytes, neutrophils, platelets, CRP, procalcitonin, and immature granulocytes, also did not show statistically significant differences between the groups [Table 1].

When analyzing the durations, Group B cases had significantly longer ICU stays, which was highly statistically significant ($P < 0.001$). Similarly, the intubation duration was also longer in Group B, with this result being highly statistically significant ($P < 0.001$). The duration data and comparisons are detailed in Table 1.

Regarding mortality rates, although higher in Group E, the difference was not statistically significant. The number of survivors and non-survivors is illustrated in Figure 3, and detailed data on mortality and group comparisons are provided in Table 1.

The culture positivity rates were significantly higher in Group B compared to Group E ($P < 0.01$). The values and comparisons of these rates are shown in Table 1.

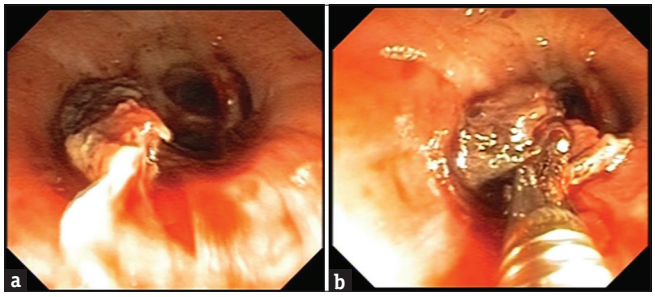

Figure 2: (a) The mucus plug blocking the bronchiole. (b) Removal of the plug

The most commonly isolated microorganism in both groups was Candida species. In Group B, 25% (5) of the microorganisms were *Candida albicans* and 20% (4) were *Candida non-albicans*. In Group E, both subgroups had rates of 27% (6) each. The distribution of the isolated microorganisms is shown in Table 2.

Discussion

BAL culture accompanied by bronchoscopy is highly valuable in detecting pulmonary infections.[10,11] This method helps prevent delays in infection diagnosis and allows for early treatment, reducing the risk of sepsis and septic shock, especially in critical cases. Our study data indicate that BAL facilitated the detection of infectious agents, enabling more effective antimicrobial treatments. Additionally, bronchoscopy-assisted secretion clearance positively contributed to airway and ventilation management.[11] We maintained airway patency by effectively clearing mucus plugs encountered

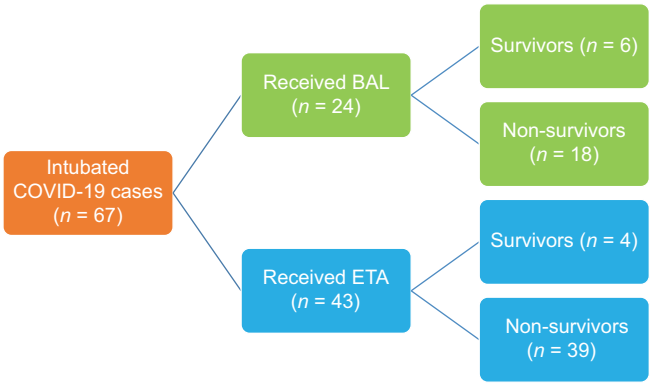

Figure 3: The diagram of survivors and non-survivors

Table 1: Descriptive and laboratory data in COVID-19 cases with BAL and ETA

	Group B, *n*=24 (BAL)	Group E, *n*=43 (ETA)	Test Coefficients	*P*
Age (years)	55.7±14.4	61.9±15.2	*t*=1.632	0.108
Gender (male/female) [% (*n*)]	62.5% (15)/37.5% (9)	65.1% (28)/34.9% (15)	-	-
BMI (kg/m^2)	28.78±3.92	29.07±4.17	*t*=0.283	0.778
Duration of stay in ICU (days)	32.2±19.6	13.8±10.8	*t*=4.956	<0.001*
Duration of intubation (days)	27.3±19.2	9.5±9.9	*t*=5.006	<0.001*
Mortality (%)	75.0% (18)	90.6% (39)	2=2.989	0.084
Culture positivity (%)	83.3% (20)	51.6% (22)	χ^2=6.815	0.009*
DM, Diabetes Mellitus	29.1% (7)	27.9% (12)	χ^2=0.012	0.913
HT, Hypertension	33.3% (8)	53.5% (23)	χ^2=2.517	0.113
CRP, C-Reactive Protein (mg/L)	105.6±95.6	104.9±84.5	*t*=0.032	0.975
PCT, Procalcitonin (ng/mL)	1.43±3.19	1.35±2.61	*t*=0.107	0.916
WBC, White Blood Cell (10^3/µL)	16.2±9.5	14.6±8.9	*t*=0.681	0.498
Neutrophil (10^3/µL)	14.6±8.8	13.2±8.3	*t*=0.632	0.530
Lymphocyte (10^3/µL)	0.78±0.46	0.83±0.96	*t*=0.237	0.813
NLR, Neutrophil Lymphocyte Ratio	22.3±14.2	24.7±18.6	*t*=0.557	0.579
IG, Immature Granulocytes, (10^3/µL)	1.29±2.70	0.39±0.74	*t*=1.441	0.158
PLT, Platelet (10^3/µL)	213.7±106.2	203.5±100.3	*t*=0.388	0.699

t: Student's *t* coefficient, χ^2: Chi-Square Coefficient, *P*: significance value, *P<0.01

Table 2: Distribution of detected microorganisms

Microorganism	Group B		Group E	
	Count	%	Count	%
Acinetobacter baumannii	3	15	4	18.2
Aspergillus			1	4.5
Candida albicans	5	25	6	27.3
Candida non-albicans	4	20	6	27.3
Klebsiella pneumoniae			1	4.5
Pseudomonas aeruginosa	2	10	2	9.1
Staphylococcus epidermidis	2	10		
Stenotrophomonas maltophilia	4	20	2	9.1

during bronchoscopy. Kodaka *et al*.[12] highlighted that bronchoscopy can prevent bronchial and parenchymal damage caused by mucus plugs obstructing the lower airway.

In our study, the ICU stay and intubation duration were longer in the BAL group. This can be attributed to the higher microorganism isolation rate with BAL, which led to more effective antimicrobial treatments. In contrast, the shorter hospitalization and intubation follow-up days in the ETA group may be associated with higher mortality, resulting in shorter durations due to rapidly developing mortality.

The absence of significant differences in demographic data and comorbidities between the groups underscores the importance of differences in mortality and culture positivity. Previous studies have reported mortality rates ranging from 45.6% to 97% in intubated COVID-19 patients.[5-7] Lee *et al*.[13] reported a mortality rate of 50.3% when investigating the relationship between sepsis and COVID-19. In our study, the mortality rate was 75% in the BAL group and 90.6% in the ETA group. Although our mortality rates are consistent with the literature, the difference between the two groups was not statistically significant, likely due to the small sample size.

Our findings showed that BAL culture positivity was significantly higher compared to ETA culture. Visual BAL with fiberoptic bronchoscopy provides better access for isolating the agent, which aids in planning appropriate treatment. While there are studies comparing BAL and ETA cultures in ventilator-associated pneumonia (VAP),[14] Our study is unique in comparing BAL and ETA culture results specifically in COVID-19 patients. Further studies are needed in this area.

Previous studies have shown that the development of VAP increases in patients undergoing invasive mechanical ventilation, especially after 5–9 days.[15] However, in our clinic, we collected culture material within 48 h after intubation, indicating that the infection was secondary to COVID-19 rather than VAP. The use of high-dose steroids and immunosuppressive agents like tocilizumab, intended to manage the cytokine storm, may contribute to this situation. Studies have reported that the risk of superinfection is twice as high in patients not receiving tocilizumab.[3] Secondary infection risks have been demonstrated in cases where such treatments are applied.[16]

Unlike common pneumonia agents like *Streptococcus pneumoniae*, our study isolated microorganisms such as *Candida* species, *Acinetobacter baumannii* and *Stenotrophomonas maltophilia*. Similar findings were reported by Cultrera *et al*.[17] in blood cultures, while Moser *et al*.[18] explained the immunological reasons for the loss of immune response against Candida due to COVID-19.

Our study is limited by the number of cases and the fact that it is not a prospective randomized controlled study.

Conclusion

In conclusion, BAL culture performed with fiberoptic bronchoscopy has a higher microorganism isolation capacity than ETA culture. In intubated COVID-19 patients, fiberoptic bronchoscopy can be safely performed using personal protective equipment.[19] We believe that in critically ill intubated COVID-19 cases, a more effective treatment process can be achieved by clearing airway secretions with fiberoptic bronchoscopy and planning treatment based on reliable BAL culture results. This approach may positively impact prognosis and mortality.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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