Bronchoalveolar lavage usefulness in the pediatric population

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ABSTRACT

Objective. To analyze bronchoalveolar lavage diagnostic effectiveness and impact on therapeutic management in pediatric patients.

Materials and methods. Retrospective study of patients undergoing bronchoalveolar lavage at the pediatric surgery department from 2009 to 2019. The sample was divided into two groups: hemato-oncological patients and non-hemato-oncological patients. Demographic variables, bronchoalveolar lavage result, and subsequent therapeutic attitude were collected.

Results. 45 bronchoalveolar lavages were carried out in 38 patients. The hemato-oncological group consisted of 25 bronchoalveolar lavages. Patient mean age was 9.99 ± 2.34 years. 80% of patients had received anti-infective treatment prior to bronchoalveolar lavage. Bronchoalveolar lavage culture was positive in 52% of cases. Bronchoalveolar lavage results translated into therapeutic management change in 24% of cases (6/25). 3 postoperative complications were recorded, all mild. In the non-hemato-oncological group (n = 20), mean age was 6.70 ± 5.17 years. Bronchoalveolar lavage was positive in 25% of cases, and translated into management change in 5% of patients. Complication rate in this group was 30%. 2 patients required mechanical ventilation.

Conclusions. According to our results, bronchoalveolar lavage in hemato-oncological patients helps achieve microbiological diagnosis in infectious respiratory conditions and is relatively well-tolerated. In non-hemato-oncological patients, diagnostic and therapeutic usefulness is low, and complication rate is not negligible. The risk-benefit balance should be individually considered in each patient.

KEY WORDS: Bronchoalveolar lavage; Bronchoscopy; Opportunistic infection; Diagnostic usefulness.

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RENTABILIDAD DEL LAVADO BRONCOALVEOLAR EN LA POBLACIÓN PEDIÁTRICA

RESUMEN

Objetivos. Analizar la eficacia diagnóstica del lavado broncoalveolar y su impacto en el manejo terapéutico en pacientes pediátricos.

Material y métodos. Estudio retrospectivo incluyendo a los pacientes a los que se les realizó un lavado broncoalveolar por parte del Servicio de Cirugía Pediátrica entre 2009 y 2019. Se ha dividido la muestra en dos grupos: pacientes hemato-oncológicos y no hemato-oncológicos. Se han recogido variables demográficas, el resultado del lavado broncoalveolar y la actitud terapéutica posterior.

Resultados. Se realizaron 45 lavados broncoalveolares en 38 pacientes. El grupo hemato-oncológico constaba de 25 lavados broncoalveolares. Los pacientes tenían una edad media de 9,99 ± 2,34 años. El 80% de los pacientes tenían tratamiento antiinfeccioso previo al lavado broncoalveolar. El cultivo del lavado broncoalveolar fue positivo en el 52% de los casos. El resultado del lavado broncoalveolar influyó en un cambio de manejo terapéutico en un 24% (6/25). Se produjeron 3 complicaciones postoperatorias, todas leves. En el grupo no hemato-oncológico (n = 20) la edad media era de 6,70 ± 5,17 años. El lavado broncoalveolar fue positivo en el 25% y supuso un cambio de manejo en un 5% de los pacientes. Este grupo tuvo una tasa de complicación del 30%, 2 pacientes requirieron ventilación mecánica.

Conclusiones. Según nuestros resultados, el lavado broncoalveolar en los pacientes hemato-oncológicos ayuda al diagnóstico microbiológico en procesos respiratorios infecciosos y es relativamente bien tolerado. En los no hemato-oncológicos, tiene una baja rentabilidad diagnóstico-terapéutica con una tasa de complicaciones no desdeñable. Sería necesario individualizar el balance beneficio-riesgo en cada paciente.

PALABRAS CLAVE: Lavado broncoalveolar; Broncoscopia; Infección oportunista; Rentabilidad diagnóstica.

INTRODUCTION

Lower airway infectious pathology is frequent at pediatric age and is associated with high morbidity and mortality in immunosuppressed patients. Etiologic diagnosis is achieved in 30-60% of cases only[1], and by means of

an airway sample culture, which is not an easy task in children. Even in collaborative patients, sample quality is typically insufficient and reflects upper respiratory tract flora only. In respiratory conditions with unfavorable progression, this can be addressed by resorting to fibrobronchoscopy with bronchoalveolar lavage (BAL) for sample collection purposes.

This is an invasive technique, which means it requires a specialized cross-disciplinary team, and it is not exempt from complications, so usefulness in children has been called into question. The objective of our study was to analyze diagnostic effectiveness of BAL in the pediatric population and the impact of BAL results in patient therapeutic management.

MATERIALS AND METHODS

A retrospective study of all patients undergoing fibrobronchoscopy at the pediatric surgery department of our healthcare facility from 2009 to 2019 was carried out.

The sample was subsequently divided into two groups –hemato-oncological (HO) patients and non-hemato-oncological (non-HO) patients– as a result of etiology and management differences. Demographic variables, baseline pathology and diagnostic suspicion, presence or absence of neutropenia, thoracic CT-scan, time from empirical treatment initiation to BAL, microbiological results, complications (in the following 48 hours), and subsequent therapeutic attitude were collected in all patients. Management change was defined as drug addition or discontinuation as a direct consequence of microbiological results, excluding modifications stemming from clinical signs or radiological imaging. This information was gathered from patient clinical history records.

The procedure was conducted at the operating room or at the pediatric ICU. All BALs were performed by the same cross-disciplinary team, made up of pediatric surgeons and anesthesiologists or pediatric intensivists. It was carried out under general anesthesia using a laryngeal mask or an endotracheal tube with a fibrobronchoscope adapted to patient size. Three 1 ml/kg 0.9% saline solution doses were instilled inside the most affected pulmonary lobes according to imaging tests, or bilaterally in diffuse cases. At least two samples per patient were collected to ensure sufficient material was available for microbiological studies.

Samples were analyzed using general bacteriological culture and Gram and auramine staining in all cases. In all HO patients, and according to suspicion in non-HO patients, culture and tests were performed to detect the presence of fungi, viruses, and other opportunistic pathogens.

Statistical analysis was carried out using SPSS Statistics software, version 22. Chi square tests (with Fisher's correction if necessary) and T of Student were used. Time to any given event was analyzed using Kaplan-Meier descriptive statistics and log-rank test. Statistical significance was established at $p \leq 0.05$.

RESULTS

In the 10-year period, a total of 45 BALs were carried out in 38 patients. In all patients, sample collection was sufficient for analysis purposes. Mean age was 8.53 ± 1.78 years (range: 24 days-19.89 years). 55.6% of patients were male.

HO group

HO group consisted of 19 patients undergoing 25 BALs. Mean age was 9.99 ± 2.34, with 65% of patients being male. Baseline diagnoses included acute myeloblastic leukemia (3), B (3) and T (2) acute lymphoblastic leukemia, Hodgkin lymphoma (1), medullary aplasia (1), sickle cell disease (2), Ewing sarcoma (1), Wilms tumor (1), osteosarcoma (1), and primary immunodeficiency (4). 5 patients were at hematopoietic progenitor transplantation graft period. At BAL, 60% of patients had neutropenia (neutrophils below 100 cells/mm^3). Indication for BAL was defined as persistent respiratory symptoms with fever and pulmonary parenchyma alteration at imaging tests.

96% (24/25) of them had previously undergone CT-scan, which was abnormal in all cases. 70.8% of patients had bilateral alterations, and 79.2% (19/24) had more than one pathological finding (Table 1).

In patients from this group, empiric therapeutic measures were implemented following infectious symptom onset according to our healthcare facility protocols. 80% of BALs were carried out under wide-spectrum anti-infective treatment (always including antibiotics and antifungals). Median time from treatment initiation to BAL was 3 days (1-20 days).

3 patients (12%) had complications: 1 ICU stay for less than 24 hours as a result of respiratory deterioration not requiring mechanical ventilation, 1 fever peak, and 1 episode of self-limited mild hemoptysis.

In terms of test performance, 52% (13/25) of BALs had microbiological results (Table 2). No differences in BAL performance were found between neutropenic and non-neutropenic patients (37.5% *vs.* 41.4%, $p = 0.799$). Regarding the influence of the previous anti-infective treatment on culture results, no differences were found: 60% (3/5) of positives in patients without treatment *vs.* 50% (10/20) of positives in patients with treatment, $p > 0.05$. Mean treatment duration in positive culture patients was 2.55 vs. 5.33 days in negative culture patients ($p = 0.187$). No significant differences in terms of usefulness were found among patients who had been under treatment for more than 4 days ($p = 0.65$).

Table 1. CT-scan radiological findings.

	Cohort	*HO*	*Non-HO*	*p*
Abnormal CT-scan	94.4% (34/36)	100% (24/24)	83.3% (10/12)	0.105
More than 1 finding	69.4% (25/36)	79.2% (19/24)	50% (6/12)	0.395
Consolidation	47.2% (17/36)	58.3% (14/24)	25% (3/12)	0.059
Focal or diffuse nodule(s) or mass	38.9% (14/36)	45.8% (11/24)	25% (3/12)	0.292
Ground glass opacity	30.6% (11/36)	33.3% (8/24)	25% (3/12)	0.715
Pathological lymph nodes	25% (9/36)	29.2% (7/24)	16.7% (2/12)	0.685
Atelectasis	19.4% (7/36)	20.8% (5/24)	16.7% (2/12)	1
Tree-in-bud pattern	13.9% (5/36)	16.7% (4/24)	8.3% (1/12)	0.646
Bronchiectasis	13.9% (5/36)	12.5% (3/24)	16.7% (2/12)	1
Pleural effusion	5.5% (2/36)	8.3% (2/24)	–	
Calcified granuloma	5.5% (2/36)	8.3% (2/24)	–	
Abscess formation areas	2.7% (1/36)	4.1% (1/24)	–	
Fluid overload	2.7% (1/36)	4.1% (1/24)	–	
Air leak areas	2.7% (1/36)	–	8.3% (1/12)	
Main bronchus stenosis	2.7% (1/36)	–	8.3% (1/12)	

Table 2. Microbiological results.

HO group		
Age	*Baseline pathology*	*Microbiology*
10 months	Acute myeloblastic leukemia	*P. jiroveci* (PCR)
10 months	Acute myeloblastic leukemia	Coagulase-negative staphylococcus
18 months	Severe combined immunodeficiency	*S. viridans* *Enterovirus*
5 months	Chronic granulomatous disease	*Aspergillus* (PCR)
5 months	Chronic granulomatous disease	*A. fumigatus, A. niger* *Beauveria bassiana*
8 months	Medullary aplasia	*Aspergillus* (antigen)
9 months	Acute myeloblastic leukemia	*Aspergillus* (PCR)
10 months	Ewing sarcoma	*M. tuberculosis* *Influenza B*
11 years	B acute lymphoblastic leukemia	*Rhinovirus*
12 years	Hodgkin lymphoma	*Parainfluenza*
14 years	Femoral osteosarcoma	*Myringyales*
18 years	B acute lymphoblastic leukemia	*Cryptococcus neoformans*
19 years	Hematopoietic progenitor transplantation	*Influenza B*
Non-HO group		
Edad	*Indication for BAL*	*Microbiología*
24 days	Acute bronchopneumonia refractory to empirical treatment	*H. influenzae* *M. catarrhalis* *Neisseria* sp
3 months	Suspected interstitial pulmonary disease	*S. aureus* *C. pseudodiphtheriticum* *P. jiroveci*
10 months	Persistent atelectasis	*H. influenzae*
11 years	Hematemesis	*S. pneumoniae* *Cladosporium*
15 years	Chronic cough	*C. albicans* *Cladosporium*

BAL results entailed patient management change in 6 patients (24%) – 4 positive culture patients (4/13, 30.8%) and 2 negative culture patients (2/12, 16.7%) (p = 0.645).

Non-HO group

The non-HO group consisted of 19 patients undergoing 20 BALs. Mean age was 6.70 ± 5.17 years, with 48% of patients being male. Indication for BAL included repeated pneumonia (5), acute pneumonia with unfavorable progression (3), persistent atelectasis (3), suspected interstitial pulmonary disease (3), suspected tuberculosis (1), fever without a focus after travelling (1), hemoptysis (2), hematemesis (1), and chronic tough (1). 60% of them underwent BAL as part of a fibrobronchoscopy aimed at detecting airway abnormalities. 1 patient (5%) had neutropenia at BAL – the patient was under immunosuppressive treatment following heart transplantation and had repeated pneumonia.

60% (12/20) of patients had previously undergone CT-scan, which was abnormal in 83.3% (10/12) of cases. 33.3% of patients had bilateral alterations, and 50% (6/12) had more than one pathological finding (Table 1).

5 patients (20%) were under previous anti-infective treatment. Median time from treatment initiation to BAL was 7 days (2-38 days).

6 patients (30%) had complications. There were 4 ICU admissions as a result of respiratory deterioration requiring mechanical ventilation, 2 fever peaks, and 2 episodes of self-limited mild hemoptysis.

In terms of test performance, 25% (5/20) of BALs had microbiological results. Microorganism growth was found in most cases (Table 2).

Macroscopic abnormalities at fibrobronchoscopy were noted in one patient (5%), a 1-year-old boy with persistent atelectasis. Thoracic CT-scan demonstrated left main bronchus stenosis. At fibrobronchoscopy, a granuloma was identified in the bronchus and cauterized. BAL results were negative.

Regarding the influence of the previous anti-infective treatment on culture results, no significant differences were found: 26.7% (4/15) of positives in patients without treatment vs. 20% (1/5) of positives in patients with treatment (p > 0.05).

BAL results entailed patient management change in 1 (5%) positive culture patient.

DISCUSSION

BAL is an invasive technique used in patients with already decreased respiratory function. However, it is considered not to entail any more severe risks apart from fibrobronchoscopy itself[2], and it is well-tolerated even in patients with respiratory insufficiency[3]. Fever peaks associated with pulmonary infiltrates (with rates of up to 58%[4,5]), often transitory and without pathological signification, represent the main adverse effect[6]. Other complications reported include transitory and self-limited hypoxemia and hemoptysis. Severe complications have been described in few articles, with an incidence below 0.6%[7]. Apart from those, bronchoscopy-associated complications –cough, laryngospasm, bronchospasm, pneumothorax, and infection– are also to be considered[6,8-11]. In HO patients, various authors have reported heterogeneous complication rates of 1-52%[3,7,8,10-12], mostly mild. Of the few patients requiring ICU stay, most are admitted for monitoring purposes. In our series, 3% of the HO group required ICU stay without invasive mechanical ventilation.

Mortality in oncologic patients developing diffuse pulmonary infiltrates during treatment is 55-90%[8]. Fungi are one of the most dreaded etiologic agents, since they may cause invasive fungal disease. In these patients, early diagnosis has a significant impact on prognosis[11,13]. Diagnostic confirmation (and treatment implementation) less than 5 days following clinical sign onset can reduce mortality from 51% down to 32% (p = 0.024)[10]. Hence, BAL stands as a crucial diagnostic tool.

However, recent papers have called BAL sensitivity and practical usefulness into question by arguing that it rarely changes therapeutic attitude. On the basis of their results, Batra et al.[8] and Rossoff et al.[14] proposed a strategy based on the serial use of CT-scan in these patients, stating that it would provide with higher diagnostic effectiveness and efficiency. However, radiological patterns are considered not to be microorganism-specific[11]. In our cohort, the presence of more than one finding per patient (mean: 2.14) and the small sample size per finding, as well as the fact patients had other pathologies related to their oncologic status potentially causing radiological alterations[11,13], prevented us from analyzing the radiological pattern-microorganism association. On the other hand, the potential risk of exposing particularly sensitive patients (pediatric patients with multiple control imaging, secondary neoplastic risk, and chemotherapy and radiotherapy toxicity) to higher radiation doses should also be considered. Therefore, according to the ALARA principle[15], this is seemingly not the best diagnostic strategy.

In our HO cohort, BAL diagnostic usefulness was 52% (13/25), consistent with previous articles (25-69%)[3,7,8,10,12,13,16-18]. According to some studies, neutropenia could reduce BAL diagnostic effectiveness[7,13]. However, our results, as well as those from other papers[8], suggest neutropenia is an independent parameter. Anti-infective treatment can also play a role in this. Reinwald et al.[19] observed that BAL sensitivity decreased with the addition of antifungals, especially more than two. In our population, there were only 5 patients without previous treatment *vs.* 20 patients with previous treatment, which prevented significant results on treatment influence from being achieved. In addition, time from treatment initiation has also been suggested to be a potential key factor. Batra

et al.[8] observed that all positive results in their series were patients who had initiated treatment less than 5 days before. Shannon et al.[7] described a 2.5-fold higher likelihood ($p < 0.0001$) of finding positive results if BAL was performed before the 4th treatment day. Even though they were not statistically significant, our results reflected a trend towards shorter previous treatment in patients with positive results.

BAL requires an anesthetic and surgical team which could not be available 24/7. Therefore, considering respiratory infection morbidity in oncologic patients and the good usefulness results described in the 4-5 first treatment days, BAL could be regarded as a non-urgent but preferential procedure following anti-infective therapy initiation.

In HO patients, BAL changes treatment in 8-63% of cases[3,7,8,10,12,17]. Most of our patients had started with wide-spectrum anti-infective treatment, which means the drug was already being administered, so positive results did not change treatment that often (30.8%). When they did, it was mostly due to the presence of viruses or parasites, which are not properly covered by regular prophylaxis. However, finding fungi at BAL did not change treatment in any case, as it had been reported in previous studies[16,17]. Therefore, even though indication for BAL is often aimed at isolating potential fungal infections, its true usefulness lies in the fact it allows the presence of other uncovered pathogens (viruses and parasites) to be ruled out. On the other hand, negative results changed management in 16.7% of cases, which allowed treatment to be optimized, since these patients already receive multiple drugs with significant toxicity.

In non-HO patients, 25% of BALs had microbiological results, *vs.* 30-52% reported in previous studies[20,21]. Only 1 patient (5%) had their treatment modified as a result of BAL findings. Other studies describe treatment change rates of 18.5-38.7%[20-22]. Such a low therapeutic usefulness probably stems from the fact that, in most cases, BAL was carried out as an additional procedure within the context of diagnostic fibrobronchoscopy to rule out macroscopic airway abnormalities. Even though there was only 1 case in our cohort, other studies report macroscopic diagnosis in up to 31% of patients[20].

Although the literature supports BAL is a safe technique with few complications associated (around 11%[20,21]), complication rate in our immunocompetent patient cohort was 30%. 4 complications were mild, but 2 patients required ICU stay. The complications observed are probably those typically associated with fibrobronchoscopy, which means the increase in morbidity cannot be attributed to BAL. And given that indication for bronchoscopy was correct in these patients, we believe that BAL does not excessively increase risks, even if it provides with limited results.

The main limitation of our study was the fact it was a retrospective one, which restricted data collection. In addition, the small sample size played a major role as it prevented statistically significant results from being achieved. Our results were mostly consistent with those previously described in the literature. However, multicenter prospective studies with a larger patient cohort are required to adequately define this.

CONCLUSIONS

According to our results, BAL in HO patients helps achieve microbiological diagnosis in infectious respiratory conditions, which allows antimicrobial treatment to be optimized. In spite of the general and respiratory deterioration of these patients, fibrobronchoscopy with BAL is relatively well tolerated.

In immunocompetent patients, BAL diagnostic and therapeutic usefulness is low, and complication rate is not negligible. However, BAL is often carried out as part of a fibrobronchoscopy aimed at detecting macroscopic airway abnormalities. Therefore, the risk-benefit balance should be individually considered in each patient.

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