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Shareable abstract (@ERSpublications)
Bronchoalveolar lavage can help characterise severe asthma in children. However, it can be poorly tolerated and, in most cases, its impact on the patient's management remains limited.
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Abstract

Background Although bronchoscopy can be part of the exploration of severe asthma in children, the benefit of bronchoalveolar lavage (BAL) is unknown. The present study aimed to decipher whether systematic BAL during a flexible bronchoscopy procedure could better specify the characteristics of severe asthma and improve asthma management.

Material and methods The study took place in two departments of a university hospital in Paris. Children who underwent flexible bronchoscopy for the exploration of severe asthma between April 2017 and September 2019 were retrospectively included.

Results In total, 203 children were included, among whom 107 had a BAL. BAL cell count was normal in most cases, with an increasing number of eosinophils with age, independently from the atopic status of the patients. Compared with bronchial aspiration only, BAL increased the rate of identified bacterial infection by 1.5. Nonatopic patients had more bacterial infections ($p<0.001$). BAL induced a therapeutic modification only for azithromycin and omalizumab prescriptions. The practice of a BAL decreased bronchoscopy tolerance ($p=0.037$), especially in the presence of tracheobronchial malacia ($p<0.01$) and when performed in a symptomatic patient ($p=0.019$).

Discussion and conclusion Although BAL may provide interesting information in characterising severe asthma, in most cases its impact on the patient's management remains limited. Moreover, BAL can be poorly tolerated and should be avoided in the case of tracheobronchial malacia or current asthma symptoms.

Introduction

Asthma is the most frequent chronic disease in childhood, with 8% to 11% prevalence in school- and preschool-aged children, respectively. The disease is poorly controlled in more than a third of the cases [1, 2]. In severe and poorly controlled asthma, bronchoscopy can guide therapeutic management and optimise asthma control: bronchoscopy may estimate the magnitude of inflammation of the lower airway respiratory tract and allow microbiological analyses of bronchial aspirations. Bronchoscopy can be complemented by bronchoalveolar lavage (BAL). A BAL fluid analysis includes cell count, specific staining and distal airway microbiological analyses. Cell count allows a precise description of the type of predominant cells, *i.e.* eosinophils or neutrophils, to better describe the asthma phenotype [3, 4]. However, even when a bronchoscopy is done, BAL is not systematically performed in asthma exploration and its usefulness and safety remains to be ascertained [5]. In our specialised paediatric hospital, two departments deal with severe asthma but with different habits regarding BAL. Whereas bronchoscopy is performed in both

departments, when necessary, a systematic BAL is performed in one of them but not the other. Based on these heterogeneous practices, the current study aimed to evaluate the benefit of a systematic BAL during a flexible bronchoscopy procedure in comparable populations of children with paediatric asthma. The main objective was to determine if a BAL fluid analysis improved asthma evaluation. The secondary objective was to evaluate its impact on flexible bronchoscopy's morbidity.

Material and methods

The study took place in two departments (paediatric pulmonology and paediatric allergology) at the University Armand Trousseau Hospital in Paris. The patients (when possible) and their parents received information about the study and gave their consent to the study. The study was approved by the Institutional Review Board of the French Society for Respiratory Medicine (Société de Pneumologie de Langue Française, # CEPRO_2020-005) and by the local ethics committee of our institution (MR004-2216637).

Patients

Asthmatic patients older than 3 months of age who underwent flexible bronchoscopy between April 2017 and September 2019 were included from two departments of a single paediatric hospital. Asthma diagnosis and severity were assessed following the Global Initiative for Asthma (GINA). We also considered as severe asthma the patients treated with high doses of corticosteroids or medium-dose corticosteroids plus another treatment and an incomplete asthma control. The usual local procedure for flexible bronchoscopy is conscious sedation. To avoid any overinterpretation of the neutrophil cell count and of the procedure morbidity, patients who had bronchoscopy under general anaesthesia were excluded [6]. Other exclusion criteria were patients with another underlying disease, such as haemopathy, immune deficiency, congenital cardiopathy, neuromuscular disease or respiratory disease other than asthma (cystic fibrosis, primary ciliary dyskinesia, *etc.*).

The following data were collected: age at asthma onset (defined as the age at the first wheezing episode) and the treatments for asthma prescribed 2 months before bronchoscopy (oral and/or inhaled corticosteroid; long- and short-acting β-agonist, anticholinergic, montelukast, azithromycin, biologic therapy and antibiotics). Atopic asthma was defined when one or more commonly inhaled allergens had been identified by one of the following tests: prick test, multiallergic blood test (Phadiatop, Phadia; Thermo Fisher Scientific, Uppsala, Sweden) or specific immunoglobulin (Ig)E dosage (Phadia; Thermo Fisher Scientific) [7]. Tests for asthma severity and control were carried out before the bronchoscopy and during the following visit, 1 to 5 months after the bronchoscopy using an asthma control questionnaire before the age of 4 years and the Asthma Control Test (ACT) in patients over 4 years. Absence or presence of respiratory symptoms beyond 24 h was noted. Severe asthma was defined as uncontrolled asthma despite well-conducted strong therapy (high-dose inhaled corticosteroid therapy in children under 6 years of age, in combination with another treatment in the elderly).

The bronchoscopy was performed under conscious sedation using atropine and midazolam premedication (supplementary Table 1). After local anaesthesia of the nostril and the pharynx with lidocaine, a flexible fibrescope was introduced in the right nostril (or in the mouth in case of nostril obstruction). Macroscopic evaluation of the tracheobronchial anatomy, kinesis (absence or presence of a significant malacia (>70%)) and inflammation (absent, mild, moderate, severe) was first realised, followed by bilateral bronchial aspiration for microbiological analysis. Inflammation was assessed using the following criteria, as described by Thompson *et al.* [8]: erythema, oedema, friability of the mucosa and presence of secretions.

BAL was usually performed in a segmental bronchus of the middle lobe. A total volume of 10% of the functional respiratory capacity of saline solution was distributed in six syringes (plus 2 mL per syringe corresponding to the fibrescope channel volume). Each syringe's fluid was instilled in the same distal bronchus and sucked up. The first 2 mL was retrieved, whereas the following fluid captures of each suction were pooled for cytology, pathology and microbiological analyses. BAL fluid cytology was considered normal when the total cell count was below 500 000 cells·mL^{-1} with 80% to 95% macrophages, 10% to 15% lymphocytes, 1% to 5% neutrophils and <0.2% (or 500/mm^3) eosinophils [9]. A microbiological analysis was also carried out on the BAL fluid. A lower airway bacterial infection was defined by the identification of a bacterial charge over 10^4 colony-forming units (CFU)/mL [10]. Bronchoscopy complications such as bronchospasm, fever and oxygen or hospitalisation requirements were collected.

Statistical analyses

Patients with and without BAL were compared. Quantitative variables were expressed as mean±SD. Chi-squared or exact Fisher tests were applied when the expected values were below 5. The grouped

quantitative variables were compared with t-test or Mann–Whitney test. Univariate and multivariate logistic regressions were carried out for the qualitative variables. The Spearman correlation coefficient was used to measure the relationship between the quantitative variables. Excel and R software were used for the statistical analyses. A $p<0.05$ was considered significant.

Results

Patients' characteristics

From the 515 patients who underwent a bronchoscopy for the exploration of severe asthma during the 29-month period of inclusion, 203 were included in the study: 96 without BAL (non-BAL group) and 107 with BAL (BAL group) (figure 1). The clinical characteristics of the patients and their current treatments are provided in tables 1 and 2, respectively. At the time of the bronchoscopy, compared with the non-BAL group, the patients in the BAL group were older ($p<0.001$), had a later asthma onset ($p<0.01$) and were more often atopic ($p<0.001$). Both groups displayed similar proportions with severe asthma: 60 (63%) patients in the non-BAL group *versus* 78 (75%) in the BAL group ($p=0.07$). Asthma control was comparable in both groups in the different age classes (<3 years, 3–6 years, >6 years).

Macroscopic bronchoscopy findings

Compared with the BAL group, the non-BAL group had less bronchial inflammation (50% *versus* 93%, respectively, $p<0.001$) and more frequent bronchial anatomical disorders, such as bronchial atresia or unusual bronchial segmentation (53% *versus* 28%, respectively, $p<0.001$) (supplementary Table 2).

BAL cytology analysis

The mean BAL fluid cell count was inversely correlated with the child's age, with a Spearman correlation coefficient between age and total cell count of −0.44 ($p<0.001$). Lymphocyte cell count was higher in the 3- to 6-year-old patients, whereas eosinophil cell count was higher in the patients over 6 years old (table 3).

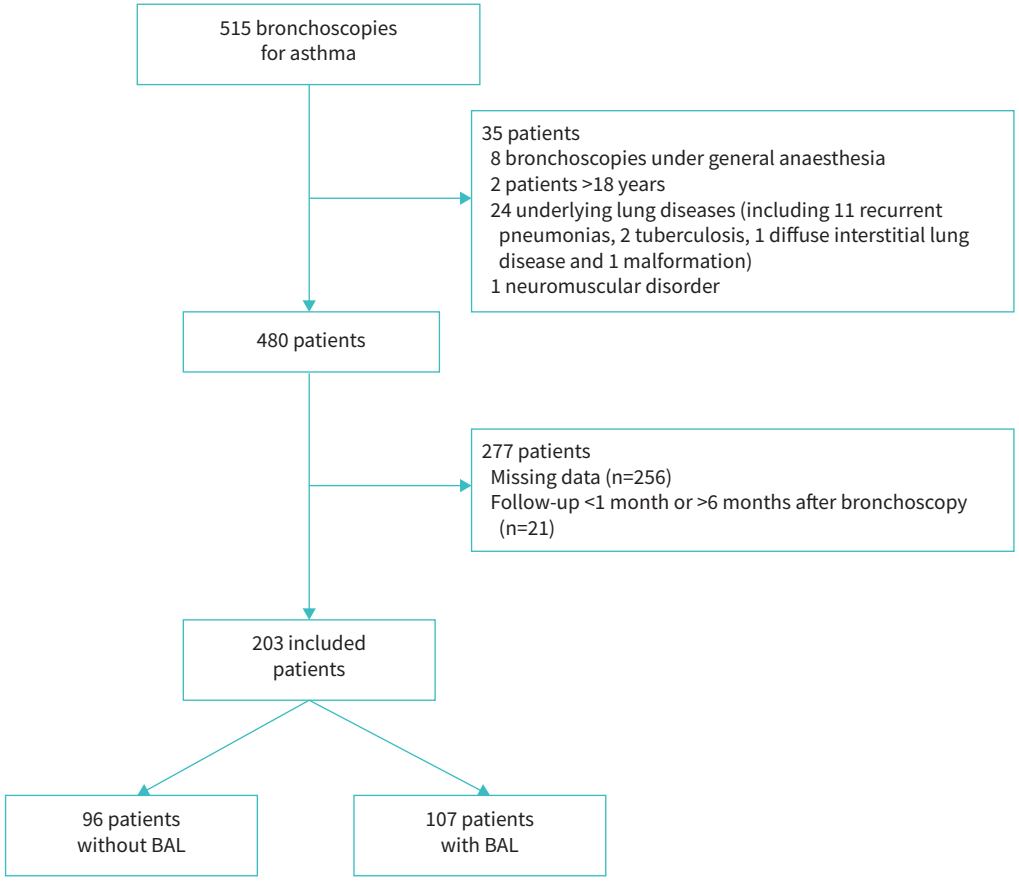

FIGURE 1 Flow-chart of the study. Between April 15, 2017 and September 30, 2019, 480 flexible bronchoscopies were performed under conscious sedation in Armand Trousseau Hospital for uncontrolled asthma in children. A total of 203 patients qualified for inclusion in the study.

TABLE 1 Clinical characteristics of the included patients

	Non-BAL group	BAL group	n	p-value
Subjects n	96	107		
Male	63 (66)	61 (57)	124	0.21
Prematurity <35 WG	16 (17)	18 (17)	34	0.98
Age years (mean±SD)	2.24±2.12	5.53±4.13	203	**<0.001**
<3 years	72 (75)	42 (39)	114	**<0.001**
3–6 years	18 (19)	26 (24)	44	0.34
>6 years	6 (6.2)	39 (36)	45	**<0.001**
Age at onset months (mean±SD)	6.15±8.98	12.5±21.6	200	**<0.01**
Atopy				
Patient[#]	34 (47)	83 (84)	117	**<0.001**
Family[#]	70 (80)	90 (87)	160	0.14
Passive smoking[#]	29 (35)	37 (35)	66	0.99
Hospitalisation[#]	79 (84)	72 (68)	151	**<0.01**
Hospitalisation (mean±SD)	2.42±1.41	2.86±1.87	151	0.11
ICU hospitalisation[#]	22 (24)	16 (15)	38	0.12
Current asthma symptoms	29 (30)	4 (3.7)	33	**<0.001**
High-dose inhaled corticosteroids associated with another controller therapy[#]	24 (25)	70 (68)	94	**<0.001**
Uncontrolled or partially controlled asthma	72 (75)	85 (79)	157	0.45
Systematised alveolar opacities on chest radiography[#]	7 (8.1)	5 (5.4)	12	0.46
Elevated eosinophils >500 per mm^3[#]	9 (13)	19 (19)	28	0.27
Lung function tests	3 (3.1)	36 (33.6)	39	**<0.001**
Normal	3 (100)	26 (72)	29	0.56

Data are presented as n (%) unless otherwise stated. High-dose inhaled corticosteroids: according to GINA, inhaled fluticasone >200 µg·day^{-1} for children under 6 years old and >500 µg·day^{-1} over 6 years of age, inhaled budesonide >400 µg·day^{-1} under 12 years old and >800 µg·day^{-1} over 12 years old; nebulised budesonide >1000 µg·day^{-1} for all children. BAL: bronchoalveolar lavage; WG: weeks of gestation; ICU: intensive care unit. [#]: based on 171 to 200 patients. Significant p-values appear in bold.

Blood eosinophil count was correlated to BAL eosinophil count in number and percentage (p<0.01), with a respective correlation coefficient of 0.266 (p=0.032) and 0.248 (p=0.047). In atopic patients, the mean eosinophil cell count was positively correlated with age: 0.3±1.12% in the 3- to 6-year-old patients *versus*

TABLE 2 Basal treatment of the included patients

	Non-BAL group	BAL group	Total	p-value
Subjects n	96	107	203	
Controller steroid treatment				
No corticosteroids	4 (4.2)	1 (0.97)	0 (0)	0.19
Low-dose inhaled corticosteroids	3 (3.2)	6 (5.8)	4 (3.9)	0.5
Medium dose inhaled corticosteroids	15 (16)	14 (14)	15 (15)	0.66
High-dose inhaled corticosteroids	73 (77)	82 (80)	84 (82)	0.64
Oral corticosteroids	37 (39)	17 (16)	54 (26)	<0.001
Bronchodilators				
Long-acting β-agonist	5 (5.2)	17 (16)	18 (17)	0.015
Short-acting β-agonist	47 (49)	83 (78)	87 (81)	<0.001
Anticholinergic	13 (14)	75 (70)	76 (71)	<0.001
Other				
Montelukast	15 (16)	22 (21)	16 (15)	0.36
Omalizumab	0 (0)	2 (1.9)	8 (7.5)	0.5
Antibiotics				
Azithromycin	2 (2.1)	5 (4.7)	31 (29)	0.45
Long-term antibiotics	1 (1)	3 (2.8)	14 (13)	0.62
Short-term antibiotics	8 (8.3)	1 (0.93)	48 (45)	0.014

Data are presented as n (%) unless otherwise stated.

TABLE 3 Bronchoalveolar lavage (BAL) cell count according to age

	Total population n (%)	<3 years[#] (mean±SD)	3–6 years[¶] (mean±SD)	> 6 years[+] (mean±SD)	n	p-value
Total cells (10^3 per mL)	255 (175)	341±219	244±109	166±95.8	103	**<0.001**
Macrophages	83.6 (13.9)	82.4±16.3	83.4±10.8	85.1±13.2	105	0.43
Lymphocytes	10.5 (6.47)	10.2±6.12	13.7±7.80	8.57±4.96	105	**<0.01**
Neutrophils	4.48 (12.3)	7.44±16.4	2.19±2.75	2.73±10.4	105	0.0503
Eosinophils	1.00 (3.83)	0.131±0.314	0.269±0.992	2.50±6.16	105	**<0.01**

Data were available for 103 patients. [#]: n=41; [¶]: n=25; [+]: n=37.

2.08±5.38% in the patients over 6 years old (p=0.048). After adjusting for age, atopy, bacterial and viral infection, a higher total cell count remained associated with younger age (<3 years) (supplementary Table 3).

Microbiological analyses

Viral analyses were performed in bronchial aspiration in the non-BAL group and in BAL fluid in the BAL group (figure 2). The most frequently identified virus was *Rhinovirus*, independently of age (table 4 and supplementary Table 4). *Rhinovirus* presence was associated with a higher lymphocyte count in the youngest patients (<3 years old: 11.9±5.71% *versus* 9.32±6.24%, p=0.042). *Adenovirus* was more often found in bronchial aspirations than in BAL and in patients under 6 years old (p<0.05).

Bacterial analyses were performed in bronchial aspiration in both groups, and also in BAL fluid in the BAL group (figure 2). Both the non-BAL and BAL groups presented a similar rate of bacterial infections (29% *versus* 24%, respectively, p=0.47), regardless of the patient's age (figure 2). *Haemophilus influenzae* was the most frequently identified bacteria in both groups (15.7%) but was never found in the six patients treated with long-term azithromycin. The other identified bacteria were mainly *Branhamella catarrhalis*

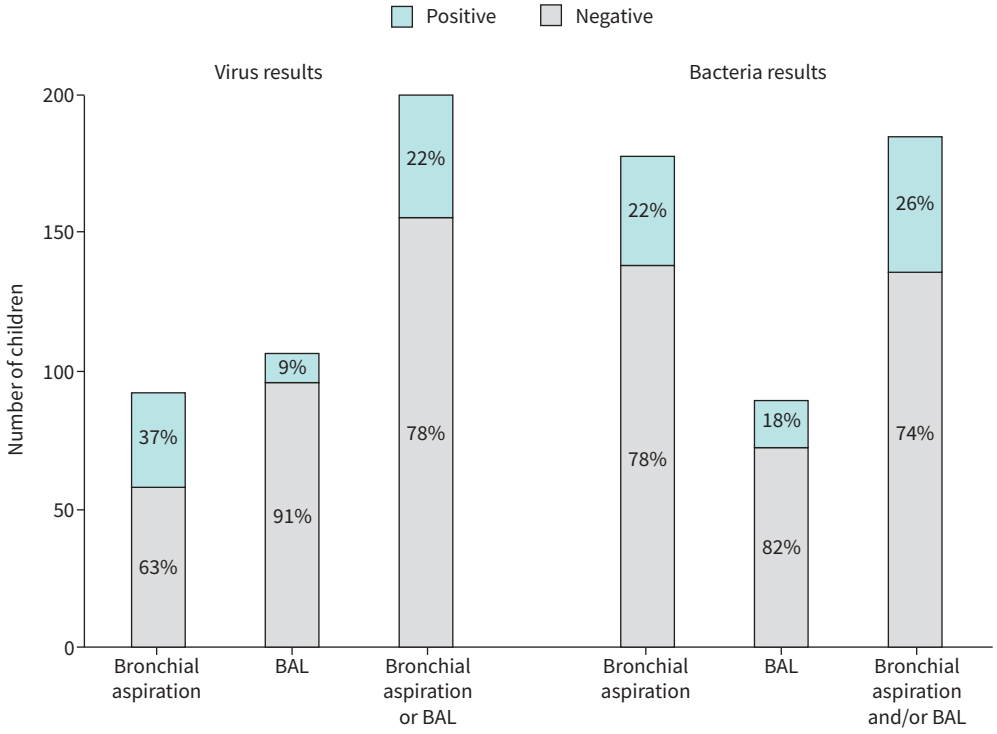

FIGURE 2 Distribution of virus and bacteria findings by sampling method. Results of the microbiological culture/detection were assessed for viruses and bacteria in bronchial aspiration, bronchoalveolar lavage or both.

TABLE 4 Viral infections in non-bronchoalveolar lavage (BAL) and BAL groups

	All patients	Non-BAL group (bronchial aspiration)	BAL group	p-value
Subjects n	200	93	107	
⩾1 infection	91 (45.5)	50 (52)	41 (38)	0.029
Adenovirus	21 (10.5)	18 (19)	3 (2.8)	<0.001
Enterovirus	14 (7)	9 (9.7)	5 (4.7)	0.17
***Parainfluenza* virus**	7 (3.3)	5 (5.4)	2 (1.9)	0.25
Metapneumovirus	4 (2)	4 (4.3)	0 (0)	0.045
Influenza virus[#]	8 (4)	6 (8.1)	2 (1.9)	0.067
Respiratory syncytial virus[#]	8 (4)	6 (8.1)	2 (1.9)	0.067
***Rhinovirus*[¶]**	37 (18.5)	12 (52)	25 (24)	<0.01
***Bocavirus*[¶]**	10 (5)	4 (17)	6 (5.7)	0.079
***Coronavirus*[¶]**	10 (5)	2 (8.7)	8 (7.6)	1

Data are presented as n (%) unless otherwise stated. [#]: researched respectively in 74 patients in the non-BAL group and 105 patients in the BAL group; [¶]: researched respectively in 23 patients in the non-BAL group and in 105 patients in the BAL group.

(9.2%) followed by *Streptococcus pneumoniae* (4.3%), *Staphylococcus aureus* (1.1%) and *Mycoplasma pneumoniae* (0.5%). Among the 19 patients for whom bacterial analyses were performed in both bronchial aspiration and BAL fluid, six (31.6%) had positive bacterial cultures in BAL only, increasing the rate of bacterial identification by 1.5 (15.5% to 22.6%). The rate of bacterial infections was not related to the age of the patients in the non-BAL *versus* BAL groups, respectively: 22 (33%) *versus* 17 (44%) in patients under 3 years old; 3 (17%) *versus* 2 (9.1%) in patients between 3 and 6 years old; and 1 (17%) *versus* 4 (12%) in patients over 6 years old. Interestingly, the atopic patients presented with fewer bacterial infections than nonatopic patients (20% *versus* 47%, respectively, p<0.001). A bacterial and viral co-infection was more often identified in the non-BAL group (n=12, 14%) than in the BAL group (n=1, 1.1%); p<0.001. None had a positive PCR for *Pneumocystis jirovecii*.

Bronchoscopy and BAL adverse events

Only two children received hydroxyzine as a premedication. All the other children had been premedicated only with midazolam and atropine, and complications included peri-endoscopic and post-bronchoscopy adverse events (table 5).

The length of sedation and the peri-endoscopic tolerance were similar between the groups (table 5). However, it appeared that when the bronchoscopy was performed in a patient with current asthma symptoms, the overall tolerance of bronchoscopy (at least one complication of the procedure among increased length of sedation, poor per bronchoscopy tolerance (hypoxia, significant cough, problems related to midazolam side-effects), post-bronchoscopy complications including fever, bronchospasm, oxygen requirement, hospitalisation) was poorer (p=0.019) and the length of the sedation was increased (p<0.01) in the BAL group compared to the non-BAL group (supplementary Table 5). Moreover, the

TABLE 5 Adverse events of bronchoscopy and bronchoalveolar lavage (BAL)

	Non-BAL group	BAL group	n	p-value
Subjects n	96	107		
Midazolam dose mg·kg^{-1} (mean±SD)	0.397±0.231	0.264±0.0912	191	**<0.001**
During bronchoscopy				
Length of sedation min (mean±SD)	10.8±3.61	11.4±5.27	203	0.41
Poor bronchoscopy tolerance[#]	7 (7.7)	15 (15)	22	0.1
After bronchoscopy				
Fever	19 (20)	13 (12)	32	0.14
Bronchospasm	13 (14)	8 (7.5)	21	0.16
Oxygen requirement	18 (19)	9 (8.4)	27	**0.03**
⩾1 night hospitalisation	15 (16)	7 (6.5)	22	**0.038**

Data are presented as n (%) unless otherwise stated. [#]: during the bronchoscopy (hypoxia, significant cough, problems related to midazolam adverse side-effects). Significant p-values appear in bold.

observation during bronchoscopy of a tracheobronchial malacia (reduction of >70% of the size of airways on exhalation) was associated with a poorer global tolerance (one or more complications) of bronchoscopy (p=0.016).

After bronchoscopy, a total of 27 (13.3%) patients required additional oxygen therapy, and this was more often observed in the non-BAL group (p=0.03). Consequently, more patients in the non-BAL group required hospitalisation during the following night (p=0.038) (table 5). These hospitalised patients were younger than the ones who could be discharged home on the day of bronchoscopy (2.21±2.81 years *versus* 4.45±3.83 years, respectively, p<0.01).

Post-bronchoscopy management of asthma

A treatment modification was documented in 135 patients after bronchoscopy, with no difference between the non-BAL and BAL groups (71% *versus* 63%, respectively, p=0.22). The only significant change was the addition of a short-term antibiotic treatment in 31 (32%) patients in the non-BAL group and 48 (45%) patients in the BAL group; however, there was no difference between groups. A few therapeutic modifications were different between the non-BAL and BAL groups, such as initiation of long-term azithromycin (4.3% *versus* 25%, respectively, p<0.001) and omalizumab (0% *versus* 5.7%, respectively, p=0.03) (supplementary Table 6).

Improvement of asthma control could only be assessed in 156 patients and ACT in only a quarter of the patients. An improvement in asthma control after bronchoscopy was more often observed in the non-BAL group than in the BAL group (n=54, 75% *versus* n=45 (54%), respectively, p<0.01).

Discussion

In the current study, we documented the benefits and risks of performing a BAL during bronchoscopy when exploring severe asthma in children. Using two groups with a fairly symmetrical distribution of patients who did and did not have BAL, we observed that: 1) BAL improves the identification of bacterial infection compared with bronchial aspiration; 2) BAL cytology alone could not differentiate non-atopic from atopic asthma; and 3) a BAL analysis has a limited impact on therapeutic management. Moreover, BAL was associated with a poorer tolerance of bronchoscopy in the presence of a tracheobronchial malacia, or when the bronchoscopy was performed in a symptomatic patient.

BAL cytology and asthma phenotype

The interest in BAL fluid cytology analysis in defining the asthma phenotype is controversial [11]. As found herein, in asthmatic children, the total cell count is usually normal or slightly increased compared with control individuals [12, 13]. As shown by Just *et al.* [14] in a previous study population, we evidenced an inverse correlation between BAL cell count and age, which could be explained by the fact that the youngest patients present with viral asthma more frequently, whereas the oldest present more frequently with atopic asthma [15]. Conversely, some other authors did not find any correlations between BAL fluid total cell count and age in asthmatic paediatric patients [16–18]. Thus, this parameter is unlikely to help depict the asthma phenotype in a single patient.

In a large study including patients aged 6–17 years, a correlation between the cell profile based on neutrophils and eosinophil repartition and clinical characteristics was suggested [19]. Another study failed to find a correlation between neutrophil cell count and lung function but suggested a link between increased intraepithelial airway neutrophilia and better lung function [20]. Our study population was younger, but we could not find a correlation between the eosinophil count or the neutrophil count and the clinical characteristics of the patients, nor with their lung function tests. An increased neutrophil count was noticed in patients under 3 years of age, which may be related to an increased rate of lower airway infections in the youngest, promoting neutrophil recruitment and, therefore, asthma development [4, 11, 16, 17]. Eosinophil count was increased in patients older than 6 years. This has been previously documented by other authors, especially in polyallergic severe asthma [4, 15, 17]. Interestingly, our study and other research showed no difference in eosinophil counts between atopic and nonatopic patients [12]. The link between eosinophil rates in BAL fluid and the risk of developing persistent asthma remains controversial, arguing for the need for further convincing studies [13, 18, 21, 22].

Microbiology

BAL allows for a culture of distal airway samples along with bronchial aspiration analyses. With a 26% documented bacterial infection rate, the present study is below others that report up to 40% infection using similar thresholds ($>10^4$ CFU·mL^{-1}), despite a low rate of antibiotic treatment prior to bronchoscopy (a total of 20 (9.8%) patients, including four (1.9%) on long-term antibiotics and seven (3.4%) on long-term

azithromycin treatments) [18, 21]. This could be related to the older study population than in other studies [21, 22]. Among the 19 patients who benefitted from bacterial analyses in both bronchial aspiration and BAL, six bacterial infections were documented exclusively in the BAL fluid, increasing the rate of bacterial detection by 1.5. Even though an association between viral asthma and bacterial infections could be expected, surprisingly, atopic patients also displayed elevated rates of bacterial infections. This result encourages the practice of BAL for bacteriological purposes in the case of uncontrolled asthma in children, whatever the atopic status.

Therapeutic modifications

BAL did not seem to be associated with significant changes in asthma management. Indeed, only azithromycin and omalizumab introductions were significantly more common in the BAL group. However, it is important to question the true impact of BAL in the decision for biologic therapy prescription in these children, for whom the treatment's indication could be based on the lack of asthma control associated with an elevated total IgE level.

Complications

The overall tolerance of the sedated–conscious bronchoscopy without or with an additional practice of BAL was good. BAL was associated with a poorer tolerance of bronchoscopy when performed in a symptomatic patient (increased length of sedation and increased rate of complications) and when tracheobronchial malacia was diagnosed. These results suggest two recommendations: postpone bronchoscopy as much as possible when asthma symptoms are present and re-evaluate the benefit of performing BAL when a tracheobronchial malacia is observed during bronchoscopy.

Conversely, the need of additional oxygen therapy was more often observed in the non-BAL group, probably because premedication with nebulised salbutamol was much less frequent ($p<0.001$) in this group, as well as a long-term controller treatment with anticholinergics (the effect of which lasts for up to 6 h). Moreover, the younger age and more frequent tracheobronchial malacia in the non-BAL group may be another explanation [23, 24].

Strengths and limits

The major strength of the current study is that all of the patients included were from a single centre, allowing a high comparability of the procedures and comparable cytological and microbiological analyses. Furthermore, this study draws from a large cohort of children with a fairly symmetrical distribution of those who did and did not have BAL. Another strength is the differential analysis of bronchoscopy and BAL complications in the case of concomitant asthma symptoms. Finally, the study of the cellularity of the BAL fluid in subgroups according to age and the presence or lack of an atopy is an original and informative approach. However, even if the BAL were mainly performed in stable state (96.3%), the treatment effect may be confounding the cytological evaluation and also safety assessment, especially for corticosteroids (26% of the patients in the month before the BAL), which could impact eosinophil and neutrophil count [19]. Cytokine profile could also have been an interesting way to phenotype the BAL and could be discussed in future studies as part of the systematic BAL analysis [25]. Another limitation of the study is the fact of it being retrospective, which resulted in data loss, especially in the evaluation of asthma control (ACT tests documented only for a quarter of the patients).

Conclusion

The present study has highlighted the limited benefit of performing BAL during bronchoscopy for the exploration of severe asthma in children. BAL seems to improve the detection of bacterial infections, and this study encourages the practice of BAL for bacteriological purposes in the case of uncontrolled asthma in children, whatever the atopic status. Moreover, BAL led to limited therapeutic modifications. In clinical practice, it seems cautious to avoid BAL when a tracheobronchial malacia is known or suspected or in a patient with current asthma symptoms, two conditions associated with a poor tolerance of the BAL. Finally, the impact of cytology and inflammatory marker analyses of BAL fluid on predicting the asthma phenotype remains to be evaluated.

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