J Vet Intern Med 2005;19:161–167

Bronchodilators in Bronchoscopy-Induced Airflow Limitation in Allergen-Sensitized Cats

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This study investigated the effect of bronchoscopy and bronchoalveolar lavage (BAL) on respiratory function, determined by barometric whole-body plethysmography (BWBP), of healthy and allergen-sensitized cats. Furthermore, the efficacy of inhaled bronchodilators in preventing changes in respiratory function was determined. For test 1, 18 healthy experimental cats were investigated on day 1 by BWBP. On day 2, the cats underwent BWBP after sedation (medetomidine), after anesthesia induction (propofol), and after bronchoscopy and BAL. Enhanced pause (Penh) was significantly increased after bronchoscopy and BAL (1.64 ± 0.17 versus 1.23 ± 0.07, $P < .05$). For test 2, 6 cats were sensitized to ovalbumin (OVA), 6 cats were sensitized to *Ascaris suum* (AS), and 6 cats served as controls. On day 0, OVA- and AS-sensitized cats underwent an inhaled allergen challenge, whereas controls were exposed to saline. On days 1 and 2, the same protocol as described for test 1 was repeated. Post-BAL Penh of the AS-sensitized cats was significantly higher than at test 1 (2.28 ± 0.22 versus 1.69 ± 0.33, $P < .05$) and was correlated with BAL fluid neutrophil count ($r = 0.55$, $P < .05$). During tests 3, 4, and 5, the same protocol as used for test 2 was applied to each cat group, with the animals being randomly treated before sedation with inhaled salbutamol (200 μg), ipratropium bromide (40 μg), or a combination of both (200 + 40 μg). Post-BAL Penh of the AS-sensitized group was significantly decreased after the salbutamol + ipratropium bromide treatment (1.56 ± 0.18 versus 2.28 ± 0.22, $P < .05$). This study suggests that bronchoscopy and BAL induce airflow limitation in cats, which is more severe in the presence of lower airway inflammation. Inhaled salbutamol + ipratropium bromide reduce BAL-induced bronchoconstriction in AS-challenged cats and might be recommended as preventive treatment of asthmatic cats undergoing bronchoscopy.

Key words: Barometric whole-body plethysmography; Bronchoalveolar lavage; Inhaled bronchodilators.

Bronchoscopy and bronchoalveolar lavage (BAL) have become important diagnostic procedures in evaluating lower airway disease in cats.[1–5] In comparison with blind sampling techniques using a catheter, fiberoptic bronchoscopy allows a macroscopic appreciation of the lower airways and a better standardization of BAL fluid collection.[5] Although bronchoscopy and BAL are generally considered as safe investigations, these procedures need to be performed by an experienced clinician.[3,5] Cats with an impaired lung function (eg, cats presenting clinical signs of asthma, such as coughing, wheezing, and dyspnea) must be evaluated with caution to avoid an acute asthma attack during or after bronchoscopy or BAL.

The introduction by Hoffmann and coworkers[6] of barometric whole-body plethysmography (BWBP) as a noninvasive tool that allows detection of airflow limitation in cats possibly has improved the evaluation of lung function in feline patients.[7] Indeed, it has been demonstrated in cats and other species that the enhanced pause (Penh), an index of bronchoconstriction, allows the detection and quantification of obstruction of the lower airways[6,8–10] and the determination of the response to a bronchodilator.[a,10,11]

Bronchoscopy and BAL are routinely performed in human medicine and numerous studies have assessed the safety of bronchoscopy and BAL or biopsies in adults and children by investigating lung function, oxygen saturation of hemoglobin, cardiovascular effects, and other parameters.[12–15] BAL induces a marked but transient fall of the forced expiratory volume expired within 1 second (FEV_1) in healthy and asthmatic humans, and studies have been conducted to evaluate the preventive use of bronchodilators, such as atropine, glycopyrrolate, ipratropium bromide, salbutamol, and fenoterol.[12,15–18] Because atropine, the most frequently used bronchodilator, does not provide a consistent benefit for lung function and often induces adverse effects, including tachychardia, arrhythmia, and mouth dryness, the routine use of bronchodilators before bronchoscopy is not advised.[17,19] However, use of parenteral or inhaled bronchodilators before bronchoscopy is indicated in patients with low FEV_1 that is responsive to bronchodilators or with poorly controlled asthma.[19,20]

Based on the findings in human patients, the aims of the present study were to assess the effect of bronchoscopy and BAL on respiratory function in healthy cats and in experimentally sensitized asthmatic cats by using BWBP and to test whether use of inhaled bronchodilators allows the prevention of BAL-induced airflow limitation.

Materials and Methods

Animals

Eighteen shorthaired cats[b] aged 10–18 months (10 neutered males and 8 intact females; mean weight: 3.9 ± 1.2 kg) were enrolled in the study for 12 months. The animals were housed and cared for according to the national guidelines and the principles advised by the European Council for the care of laboratory animals. They were housed in appropriate rooms where they were allowed to move freely and were fed twice daily with commercially available food. The animals underwent regularly clinical examination and lung auscultation. The study was approved by the Ethical Committee of the University of Liège.

Study Design

Three groups of cats were randomly formed, including 1 control group (n = 6; 2 males and 4 females), 1 group undergoing ovalbumin

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Submitted April 16, 2004; Revised September 30, 2004; Accepted October 26, 2004.

0891-6640/05/1902-0003/$3.00/0

(OVA) sensitization (n = 6; 4 males and 2 females), and 1 group undergoing *Ascaris suum* (AS) sensitization (n = 6; 3 males and 3 females). Before starting placebo or allergen sensitization, test 1 was performed, where all cats were investigated by the following protocol. On day 1, a chest radiography followed by BWBP measurements was performed. On day 2, the cats underwent sedation and anesthesia in order to undergo a BAL by bronchoscopy. BWBP measurements were performed after sedation, after anesthesia induction, and immediately after bronchoscopy and BAL. The same procedure was repeated 10 weeks later (test 2) after OVA and AS sensitization, but on day 0 (24 hours before chest radiography), the cats underwent an inhalation challenge (controls: 0.9% NaCl; OVA-sensitized cats: 0.05% ovalbumin; AS-sensitized cats: 0.01% *A suum*). Tests 3, 4, and 5 took place 10 weeks apart; the cats were challenged with placebo or allergens as for test 2, but were treated immediately before sedation with an inhaled bronchodilator. Three bronchodilator treatments were tested in a random order (see *Preventive Bronchodilator Administration*).

Barometric Whole-body Plethysmography

The system of BWBP for cats as previously described was used.[6,9,21] The cats were placed in the transparent plexiglas chamber of a barometric whole-body plethysmograph[c] (height: 25 cm, length: 51 cm, width: 30 cm) that was ventilated by continuous bias flow[d] of 4 L/min, which was adjustable by a flowmeter.[e] The air inlet was via a screen pneumotachograph (35-mm diameter) positioned on 1 wall of the main chamber, whereas the air outlet was at the opposite end through a 30-mm outlet in the chamber's cover. One pole of a differential pressure transducer[f] was open to the main chamber, whereas the other pole was open to a reference chamber equilibrated with atmospheric pressure by a small channel (1.5 mm). Transduced signals were amplified,[g] digitized, and sampled at 100 Hz by use of the IOX software version 1.569,[h] which provided a breath-by-breath analysis of waveforms. The following respiratory variables were recorded: respiratory rate (RR), calculated from inspiratory time (Ti [milliseconds]) and expiratory time (Te [milliseconds]); peak inspiratory pressure (PIF) and expiratory pressure (PEF), expressed as pseudoflows (mL/s); estimated tidal volume (V_T [mL]); and Penh = (Te − RT)/RT × PEF/PIF, where RT is the relaxation time (ie, the time from the beginning of expiration to the point where 65% of V_T is expired, in milliseconds) and (Te − RT)/RT is the Pause. Penh is a unitless variable or index that increases during bronchoconstriction in mice,[8] cats,[6,9] and pigs.[10] Waveforms disturbed by movements and sniffing were automatically eliminated when V_T was smaller than 10 mL (5 mL when sedated or anesthetized) and Ti was less than 150 milliseconds or greater than 10,000 milliseconds or when the difference between inspiratory and expiratory volume exceeded 20%. The chamber pressure signal was calibrated by dynamic injection of 50 mL of room air via a syringe into the main chamber of the plethysmograph.

Allergen Sensitization and Exposure

Ovalbumin[i] and AS antigen[j] sensitization was achieved by 2 intramuscular injections of a freshly prepared adjuvant-allergen[k] emulsion that were administered 2 weeks apart.[21,22] The cats were examined daily for 4 days after each injection and no adverse reactions were observed. Two to 4 weeks after the 2nd injection, the OVA-sensitized group was exposed for 15 minutes to an aerosol[l] containing 0.05% of OVA, whereas the AS-sensitized group underwent a 5-minute challenge with an aerosol containing 0.01% of AS. The control cats underwent a 5-minute placebo challenge by inhaling sterile saline (NaCl 0.9%). Nebulizations were performed on day 0 of each test.

Thoracic Radiography

All cats underwent chest radiography on day 1. A ventrodorsal and a lateral view were performed. A scoring system to evaluate bronchial (0: absent, 1: light, 2: moderate, 3: severe), interstitial (0: absent, 1: light, 2: moderate, 3: severe), and alveolar pattern (0: absent, 1: light, 2: moderate, 3: severe) was applied to each pair of views by a radiologist (FS) blinded to the animals' histories.

Preventive Bronchodilator Administration

For tests 3, 4, and 5, salbutamol[m] (100 μg, 2 puffs), ipratropium bromide[n] (20 μg, 2 puffs), or a combination of salbutamol + ipratropium bromide[o] (120 μg + 20 μg, 2 puffs) was administrated to the conscious cat before sedation by use of a pressurized metered dose inhaler (pMDI) and a spacing chamber connected through an inspiratory valve to a facemask.[p] The facemask was carefully placed on the cat's nose and mouth and the pMDI was activated once. The cat took 4–5 breaths before the 2nd puff was administrated. Three different spacing chambers and facemasks were used for aerosol administration to avoid cross-contamination.

Bronchoscopy and BAL

The cats were sedated by intramuscular injection of medetomidine[q] (100 μg/kg). When sufficient sedation was achieved (minimum 5 minutes), BWBP data were acquired for a 3-minute period. The cats were equipped with an antebrachial intravenous catheter and anesthesia was induced and maintained by intravenous administration of propofol[r] (1–2 mg/kg). A further 3-minute BWBP record preceded bronchoscopy and BAL. After topical laryngeal anesthesia,[s] a preoxygenation period of 60 seconds preceded bronchoscopy. A pediatric 4.8-mm-diameter video-endoscope[t] was introduced through the oral cavity and the trachea into the right main bronchus, allowing a macroscopic evaluation of the trachea and the large airways. A bronchoscopy score taking into account the mucosal aspect (0: normal, 1: moderate mucosal reddening and edematous appearance, 2: severe reddening and edematous appearance), the presence of mucus (0: absent, 1: moderate, 2: abundant), and the airway reactivity (ie, coughing, and tracheal and bronchial mobility or collapse: 0: absent, 1: moderate, 2: severe) was attributed by the same person (NK). When the bronchoscope was wedged, 10 mL of preheated (37°C) sterile saline (NaCl 0.9%) was instilled into the right main bronchus and recovered by gentle suction. The same procedure was repeated in the left main bronchus. Recovery rate of BAL fluid ranged between 50 and 65%. After extraction of the bronchoscope, the cats were oxygenated for 3 minutes by spontaneously breathing oxygen-enriched air. A score to evaluate bronchoscopy-induced dyspnea during and immediately after bronchoscopy was attributed (0: absent, 1: moderate, 2: severe). A last 3-minute BWBP record was performed and anesthesia was reversed by intravenous administration of atipamezole[u] (250 μg/kg).

The recovered BAL fluid was kept on ice until being processed within 1 hour of collection. Cytology and total nucleated cell count were performed by light microscopy after Cytospin[v] centrifugation followed by Giemsa staining and after Türck coloration and use of a Thomas cell, respectively. A semiquantitative bacteriologic analysis of BAL fluid was systematically performed and was negative in all cases ($<1.7 \times 10^3$ colonies/mL).[23]

Statistical Analysis

Barometric whole-body plethysmography variables and BAL fluid cytology variables were normally distributed and are shown as mean values ± SD, whereas radiography and bronchoscopy scores are shown as medians with ranges. Normally distributed data were analyzed by analysis of variance (ANOVA) for repeated measures for within-group comparisons, and a 2-way ANOVA followed by post hoc analyses (Fisher protected least significant difference tests) was used for between-group comparisons. Nonparametric data were analyzed by Kruskall-Wallis (between groups) and Friedman (within groups) tests, followed by Mann-Whitney and Wilcoxon tests (Statview, version 5[w]). Correlation analyses were performed by linear regressions. A *P*-value lower than .05 was considered to be significant.

Table 1. Respiratory variables recorded by whole-body barometric plethysmography 24 hours before sedation (PRE), after medetomidine-induced sedation (SED), after propofol-induced anesthesia (AN), and immediately after bronchoscopy and bronchoalveolar lavage (BAL) in healthy cats (n = 18). Data are shown as mean ± SD.

Variable (unit)	PRE	SED	AN	BAL
RR (cycles/min)	51 ± 3[a]	50 ± 2[a]	49 ± 2[a]	37 ± 1[b]
Ti (milliseconds)	582 ± 31[a]	497 ± 18[b]	510 ± 17[b]	652 ± 19[c]
Te (milliseconds)	682 ± 50[a]	742 ± 31[a]	756 ± 43[a]	1,023 ± 43[b]
V_T (mL)	30.8 ± 2.8[a]	20.6 ± 0.8[b]	15.9 ± 0.7[c]	19.8 ± 1.1[b]
PIF (mL/s)	89.7 ± 9.5[a]	69.8 ± 2.7[b]	57.0 ± 2.4[c]	56.7 ± 2.5[bc]
PEF (mL/s)	91.2 ± 8.5[a]	50.5 ± 2.7[b]	48.8 ± 2.1[b]	61.6 ± 3.7[c]
Pause (—)	1.15 ± 0.11[a]	0.91 ± 0.07[a]	1.17 ± 0.7[ab]	1.39 ± 0.09[c]
Penh (—)	1.23 ± 0.07[a]	0.76 ± 0.15[b]	1.02 ± 0.07[ab]	1.64 ± 0.17[c]

RR, respiratory rate; Ti, inspiratory time; Te, expiratory time; V_T, estimated tidal volume; PIF, peak inspiratory pseudoflow; PEF, peak expiratory pseudoflow; Pause, (Te − RT)/RT, where RT is relaxation time; Penh, enhanced pause.

[a,b,c] Within-line comparisons with different superscripts are significantly different ($P < .05$).

Results

Effect of Bronchoscopy and BAL

Sedation induced a significant increase of Ti and a significant decrease of estimated V_T, PIF, PEF, and Penh (Table 1). Anesthesia further decreased V_T and PIF, whereas the other variables remained unchanged or became similar to values recorded on day 1. Bronchoscopy and BAL induced a significant decrease in RR, which was due to a significant increase in both Ti and Te. V_T and PEF remained significantly decreased, but were higher than during anesthesia. Pause and Penh were both significantly increased.

Effect of a Placebo and Allergen Challenge

Records 24 hours after the 1st inhalation challenge (postexposure) in control, OVA-sensitized, and AS-sensitized cats are shown in comparison with values recorded during test 1 (pre-exposure) (Fig 1A). No significant differences were found between pre- and postexposure values and between groups. BWBP variables recorded on day 2 under sedation and after anesthesia induction did not differ significantly between groups (data not shown). Post-BAL Penh was significantly increased in AS-sensitized cats after an allergen challenge, whereas control and OVA-sensitized cats had similar values when compared with pre-exposure values (Fig 1B).

Differential cell count of BAL fluid collected before and after exposure is shown in Figure 1C. The inhalation challenge induced a significant increase of neutrophils and eosinophils in the AS-sensitized group, whereas placebo or OVA challenge did not induce significant changes.

Effect of a Preventive Bronchodilator Treatment

The effect of 3 different preventive bronchodilator treatments was not significant on BWBP variables recorded after sedation and anesthesia induction (data not shown), but the combined salbutamol + ipratropium treatment significantly decreased post-BAL Penh in AS-sensitized cats (Fig 2). Differential cell count of BAL fluid of each cat group at tests 3, 4, and 5 was similar to that shown in test 2 (data not shown).

Each allergen challenge induced a significant increase of the radiography and bronchoscopy score in the OVA- and AS-sensitized groups (Table 2). The dyspnea score was significantly increased in OVA- and AS-sensitized cats after the allergen challenge without treatment; this increase was no longer evident after the preventive use of a bronchodilator.

Correlation between Post-BAL Penh, Respiratory Variables, Scores and BAL Fluid Cytology

Given that bronchoscopy and BAL-induced bronchoconstriction appeared to be related to the inhalation challenges and subsequent lower airway inflammation, a correlation analysis between post-BAL Penh, BAL fluid cytology, and respiratory variables, which might be assessed before bronchoscopy, was performed at each treatment (pre-exposure, postexposure, salbutamol, ipratropium, and salbutamol + ipratropium; Table 3). Afer exposure, post-BAL Penh was positively correlated with the bronchoscopy and dyspnea score, as well as with BAL fluid neutrophil count. After different bronchodilator treatments, these correlations were no longer significant.

Discussion

Bronchoscopy and BAL induce airflow limitation, detected by BWBP, in healthy and allergen-sensitized cats. Inhaled salbutmol + ipratropium is useful in preventing airflow limitation in cats with lower airway inflammation.

Sedation by medetomidine induced a significant depression of the respiratory system, as shown by the decrease of V_T, PIF, PEF, Pause, and Penh. The decrease of Penh resulted from a decrease of the PEF to PIF ratio and a decrease of Pause and might reflect a neurovegetative alteration of lung function in response to medetomidine.[24] Tidal volume, PIF, and PEF recorded by BWBP do not correspond exactly to real volumes and flows and need to be considered as pseudovolumes or pseudoflows. However, if variations of box pressure are not influenced by changes of temperature or humidity, the comparison of V_T, PIF, and PEF throughout the protocol remains valuable.[7] Anesthesia further decreased V_T and PIF, whereas PEF and Penh did not change significantly. Penh recorded within 3 minutes after extraction of the bronchoscope was significantly increased, which depended on one hand on the PEF to PIF ratio that increased and on the other hand on an increase

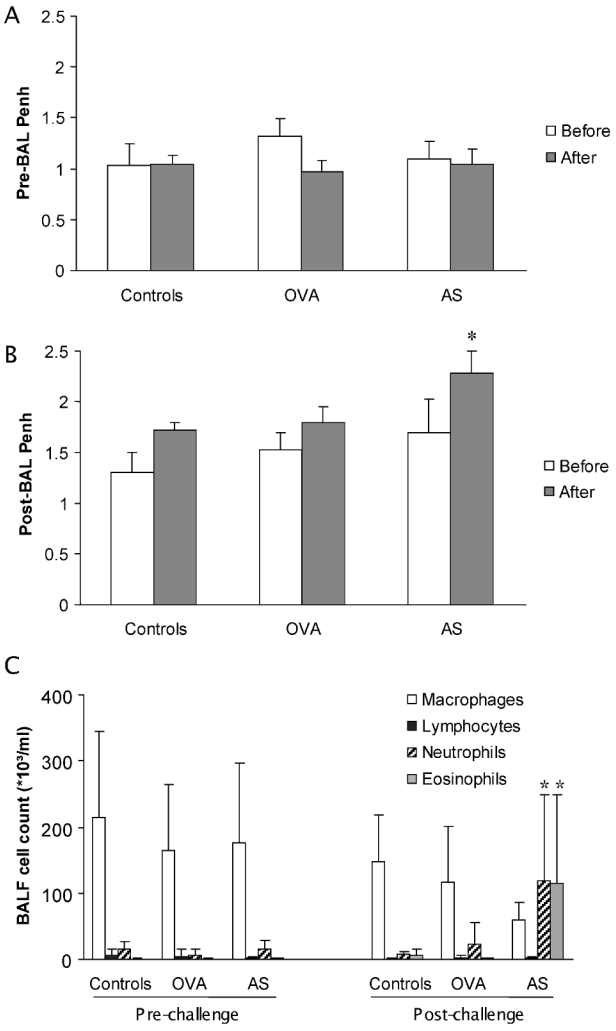

Fig 1. **(A)** Enhanced pause (Penh) recorded 24 hours before broncholaveolar lavage in 6 healthy (controls), 6 ovalbumin-sensitized (OVA), and 6 *Ascaris suum*–sensitized (AS) cats before and after a placebo (controls) or allergen (OVA or AS) challenge. Data are shown as means ± SD. **(B)** Penh recorded immediately after bronchoalveolar lavage in 6 healthy (controls), 6 OVA, and 6 AS cats before and after a placebo (controls) or allergen (OVA or AS) challenge. An asterisk (*) indicates a significant difference from respective prechallenge value ($P < .05$). **(C)** Differential cell count of bronchoalveolar lavage fluid of 6 healthy (controls), 6 OVA, and 6 AS cats before and after a placebo (controls) or allergen (OVA or AS) challenge. Data are shown as means ± SD. An asterisk (*) indicates a significant difference from respective pre-exposure and control-values ($P < .05$).

of Pause. This increase of Penh was indicative of an airflow limitation that might be due either to bronchoconstriction or to remaining lavage fluid within the airways.

A decrease of FEV_1 in human patients has been recorded immediately after BAL and has been identified in some studies as bronchoconstriction,[13,15,16,25] whereas one study associated it with residual lavage fluid.[14] Recovery of FEV_1 was reported to occur within 30–120 minutes after BAL.[15,25] If a decrease in FEV_1 in human patients cannot directly be compared with pulmonary resistance (R_L) and even less with Penh, each variable might nevertheless quantify airflow limitation, thereby allowing careful comparisons. In the present study, further measurements after BAL were not performed because sedation was reversed immediately after the last BWBP measurement. Because the animals started moving in the plethysmograph as soon as they woke up, no representative data could be acquired. Some measurements that were performed within 2–4 hours after BAL indicated absence of persisting airflow limitation, but a lower respiratory rate than in nonsedated animals (data not shown).

Examination of our data indicates that bronchoscopy and BAL induced transient airflow limitation in healthy cats and these data are in agreement with an earlier report where arterial blood gas tension decreased immediately after BAL in healthy cats and returned to baseline values within 60 minutes.[26]

After sensitization of the cats assigned to the OVA- and AS-sensitized groups, all animals were nebulized either with saline (controls) or allergens (OVA and AS) 48 hours before performing bronchoscopy and BAL. Chest radiographs 24 hours before bronchoscopy demonstrated a significant increase of the attributed score in the OVA- and the AS-sensitized cats. Penh recorded the same day did not differ between groups or from results obtained at test 1 (Fig 1A). A slight but nonsignificant increase in respiratory rate was noted in the AS-sensitized group, as well as increased lung sounds on auscultation. Post-BAL Penh values recorded in AS-sensitized cats were significantly higher than during test 1 (Fig 1B). Although somewhat subjective, the score evaluating dyspnea during and within 3 minutes after bronchoscopy, as well as the bronchoscopy score evaluating macroscopic signs of lower airway inflammation, were significantly increased in the OVA- and AS-sensitized cats. The differential cell count of BAL fluid of the AS-sensitized cats showed a significant increase of neutrophils and eosinophils (Fig 1C), suggesting a repeatable allergic response to inhaled AS antigens,[22] which was not the case for the cats challenged with OVA. These findings might be compared with reports on OVA-sensitized rodents, where a decreased inflammatory response occurs after repeating the allergic stimulus,[27,28] whereas AS-sensitized cats are reported to maintain their hypersensitivity response.[22]

An increase in pulmonary resistance occurs immediately after allergen exposure in feline experimental asthma.[22] Because measurement of pulmonary resistance requires general anesthesia and tracheal intubation, repeated measurements may not be performed and to our knowledge data recorded at 24 hours after challenge have not been reported. If the functional response of a cat to an inhaled allergen is similar to that of a human asthmatic,[29] it might be possible that at 24 hours after challenge, Penh has come back to baseline and that only bronchial hyperreactivity would persist. Because we do not have representative BWBP records immediately after AS challenge or data regarding bronchial reactivity, the present hypothesis remains to be proven.

The decrease in FEV_1 in humans undergoing bronchoscopy immediately after BAL is reported to be more pronounced in asthmatic than in healthy patients[13,25] and can be correlated with pre-BAL airway hyperreactivity.[13] These observations suggest that changes of lung function occurring after BAL depend on the intensity of lower airway inflammation. Experimentally induced asthmatic cats as

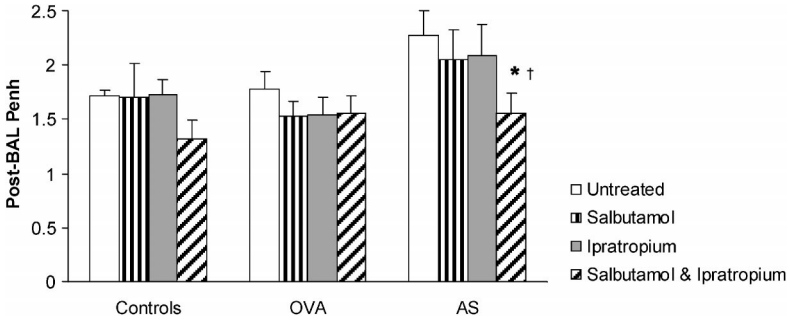

Fig 2. Enhanced pause recorded immediately after bronchoalveolar lavage in 6 healthy (controls), 6 ovalbumin-sensitized (OVA), and 6 *Ascaris suum*–sensitized (AS) cats after challenge without preventive bronchodilator treatment (Untreated) and with preventive bronchodilator treatment. An asterisk (*) indicates a significant difference from AS Untreated value; a dagger (†) indicates a significant difference from AS salbutamol value and from AS ipratropium value ($P < .05$).

well as clinical feline patients presenting bronchopulmonary disease[2] have been demonstrated to be hyperreactive.[22,30] The hypothesis that post-BAL Penh reflects lower airway inflammation is supported by the positive and significant correlation established between this variable and BAL fluid neutrophil count, bronchoscopy, and dyspnea score. In the present study, the radiography score, respiratory rate, and Penh recorded 24 hours before BAL might be considered as potential predictors of post-BAL airflow limitation. However, none of these variables could be correlated with post-BAL Penh. In clinical cases, where symptoms are likely to be more pronounced than in the experimental cats in this study, a significant and positive correlation between baseline pulmonary resistance measured under anesthesia and clinical and radiographic scores has been described.[2] Although less specific than lung function assessment by measurement of pulmonary resistance and dynamic compliance, BWBP bears an advantage as a noninvasive method of determination of respiratory function and might therefore be helpful in detecting at-risk patients.

The use of inhaled bronchodilators in cats is under investigation in preclinical and clinical tests,[a,x,11,31] but knowledge is still poor about the appropriate choice of a pharmacologic agent and its dosing. Use of inhaled rather than injected anticholinergic or β-adrenergic drugs considerably reduces systemic adverse effects and a pMDI with a spacing chamber and a facemask might easily be applied to a majority of feline patients. In our opinion, the taste of the propellant used for the pMDI seems to play an important role in acceptance of this nebulization method.

We selected salbutamol as β-adrenergic agonist because this agent is frequently used as a rescue bronchodilator in humans. Inhaled ipratropium bromide has been compared with intramuscular administration of atropine and was significantly more efficient in preventing bronchoconstriction after bronchoscopy in human patients.[16]

The choice of the dose of salbutamol used in the present study was essentially based on recommendations made by other authors for cats.[a,3,31] Because the advised dosages for salbutamol in cats correspond to those for a human adult, we also used the human dosages for ipratropium and the combination of salbutamol + ipratropium. This might ex-

Table 2. Chest radiography score and bronchoscopy score of control cats (n = 6), ovalbumin-sensitized cats (OVA, n = 6), and *Ascaris suum*–sensitized cats (AS, n = 6) before inhalation challenge (pre-exposure), after inhalation challenge without bronchodilator treatment (postexposure), and after inhalation challenge with salbutamol, ipratropium bromide, and a combination of salbutamol and ipratropium bromide (Salb/Iprat). Data are medians with ranges.

Variable	Treatment	Controls	OVA	AS
Chest radiography score	Pre-exposure	1.5 (0–3)	1 (0–2)	1 (1–1)
	Postexposure	3 (2–4)	2.5 (1–4)†	4 (1–6)†
	Salbutamol	2 (1–5)	2.5 (1–6)†	3.5 (0–7)†
	Ipratropium	2 (0–6)	2.5 (1–7)†	2.5 (1–7)†
	Salb/Iprat	3 (1–4)	3 (1–5)†	4 (1–5)†
Bronchoscopy score	Pre-exposure	0 (0–1)	0 (0–1)	1 (0–2)
	Postexposure	0.5 (0–1)	1.5 (0–2)†	2 (0–3)*†
	Salbutamol	0 (0–0.5)	2 (0–3)†	2 (0–3)*†
	Ipratropium	0.5 (0–2)	2 (0–3)*†	2 (1–3)†
	Salb/Iprat	1 (0.5–4)	2 (0–3)†	1 (1–2)
Post-BAL dyspnea score	Pre-exposure	0 (0–2)	0 (0–1)	0.5 (0–1)
	Postexposure	1 (1–2)	1 (1–2)	2 (0–2)†
	Salbutamol	1 (0–1)	1 (0–1)	1 (1–2)
	Ipratropium	1 (1–1)	1 (0–1)	1 (0–2)
	Salb/Iprat	1 (1–2)	1 (1–1)	1 (1–2)

* Significantly different from respective control ($P < .05$).

† Significantly different from respective pre-exposure value ($P < .05$).

Table 3. Coefficients of correlation between enhanced pause (Penh) recorded after bronchoalveolar lavage (Penh Post-BAL) and prelavage respiratory variables; radiography, bronchoscopy, and dyspnea scores; and cytology of bronchoalveolar lavage fluid (BALF) in 18 cats (6 healthy, 6 ovalbumin-sensitized, and 6 *Ascaris suum*–sensitized) before (pre-exposure) and after (postexposure) inhalation challenge and after inhalation challenge with preventive salbutamol, ipratropium, and salbutamol + ipratropium (Salb/Iprat) treatment.

		Penh Post-BAL				
		Pre-exposure	Postexposure	Salbutamol	Ipratropium	Salb/Iprat
Prelavage respiratory variables	RR	0.25	0.27	−0.23	−0.20	−0.36
		NS	NS	NS	NS	NS
	Penh	0.01	0.17	−0.26	−0.19	0.28
		NS	NS	NS	NS	NS
Scores	Radiography	0.07	−0.36	−0.23	−0.02	−0.49
		NS	NS	NS	NS	NS
	Bronchoscopy	0.45	0.62	−0.1	−0.29	−0.26
		NS	*	NS	NS	NS
	Post-BAL dyspnea	0.10	0.56	0.35	0.28	−0.32
		NS	*	NS	NS	NS
BALF cytology	Macrophages (cells/mL)	−0.20	−0.1	0.01	−0.31	−0.12
		NS	NS	NS	NS	NS
	Neutrophils (cells/mL)	0.01	0.55	0.21	0.1	−0.07
		NS	*	NS	NS	NS
	Eosinophils (cells/mL)	0.05	0.1	0.03	0.12	0.08
		NS	NS	NS	NS	NS

RR, respiratory rate; NS, not significant.
* $P < .05$.

plain why only the combined treatment had a significant effect in preventing BAL-induced increase of Penh in the AS-sensitized cats (Fig 2). Because this treatment provided 200 μg of salbutamol and 40 μg of ipratropium, its efficiency is likely to be higher than that of 200 μg of salbutamol or 40 μg of ipratropium given alone. Our findings suggest that bronchoscopy-induced increase of Penh is at least partially due to bronchoconstriction and might be modulated in cats suffering from lower airway inflammation. The results obtained in control and OVA-sensitized cats are less clear because only the salbutamol + ipratropium treatment tended to decrease post-BAL Penh in the control group, whereas all treatments tested tended to be efficient in the OVA-sensitized group. Further investigations with higher dosages of the drugs should allow identification of an optimal dose.

The dyspnea score attributed during each bronchoscopy suggests that all bronchodilators tested prevented bronchoconstriction in the OVA- and AS-sensitized cats. However, this study aimed to assess the effect of bronchoscopy and BAL in healthy and in allergen-challenged cats before testing the potential effect of bronchodilators. Therefore, we proceeded in a step-by-step manner and consequently, attribution of the dyspnea score was not performed in a blind manner and needs to be interpreted with caution.

The correlation analyses performed between post-BAL Penh and various respiratory variables also suggest that the bronchodilator treatments tested were efficient. The positive and significant correlations observed after exposure (test 2) between post-BAL Penh, endoscopy score, dyspnea score, and BAL fluid neutrophil count were not found after bronchodilator treatments.

Footnotes

[a] Rozanski, EA, Hoffman AM. Lung function and inhaled albuterol in cats with asthma. J Vet Intern Med 1999;13:259 (abstract)
[b] Cats, Harlan, Horst, The Netherlands
[c] Barometric whole-body plethysmograph, Buxco Electronics, Sharon, CO
[d] Air Control Industries Ltd, Somerset, UK
[e] Influx model A9HDAI08, Caché Instrumentation Ltd, Wakefield, UK
[f] Differential pressure transducer, Emka Technologies, Paris, France
[g] Amplifier AC264, Emka Technologies, Paris, France
[h] IOX Software, Emka Technologies, Paris, France
[i] Ovalbumin (chicken egg), Sigma Chemical Co, St Louis, MO
[j] *Ascaris suum* antigen, Greer Laboratories Inc, Lenoir, NC
[k] Titer Max, Alexis Corporation, Lausen, Switzerland
[l] Ultraneb Devilbiss 2000, Devilbiss Healthcare Inc, Somerset, PA
[m] Docsalbuta, Docpharma, Heverlee, Belgium
[n] Atrovent, Boehringer Ingelheim, Bruxelles, Belgium
[o] Combivent, Boehringer Ingelheim, Bruxelles, Belgium
[p] Aerokat, Trudell Medical International, London, Ontario, Canada
[q] Domitor, Pharmacia Animal Health, Puurs, Belgium
[r] Diprivan, Zeneca, Destelbergen, Belgium
[s] Linisol 1%, Braun Medical, Diegem, Belgium
[t] Fujinon EB-4105, ONYS s.a., Brussels, Belgium
[u] Antisedan, Pharmacia Animal Health, Puurs, Belgium
[v] Cytospin 2, Shandon Inc, Pittsburgh, PA
[w] Statview, version 5, SAS Institute Inc, Cary, NC
[x] Kirschvink N, Hirt R, Delvaux F, et al. Bronchoprotective effects of inhaled salmeterol, fenoterol and oxitropium in healthy cats. J Vet Intern Med 2003;17:747 (abstract)

Acknowledgment

N. Kirschvink and F. Delvaux are supported by the grant Région wallonne DGTRE, Nomur, Belgium.

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