

ORIGINAL ARTICLE

Asthma and Rhinitis

Efficacy of air cleaners in asthmatics allergic to cat in ALYATEC® environmental exposure chamber

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Abstract

Background: Air cleaners have been promoted for respiratory allergic disease prevention, but there is no clear clinical proof of their efficacy in allergic asthma.

Objective: To examine the efficacy of a new air cleaner on early and late asthmatic responses in cat-allergic patients.

Methods: This randomized, cross-over, double-blind placebo-controlled study enrolled 24 cat-asthmatic patients with GINA 1 asthma. At baseline, participants were exposed to 40 ng/m³ of airborne cat allergen for a maximum of 2 hours in ALYATEC® environmental exposure chamber (EEC). All participants were subsequently randomized into two groups that were exposed to cat allergen, either with active then placebo air cleaners or with placebo then active air cleaners with a 3-week interval in the EEC. This study was registered under number (NCT03928561).

Results: Fewer patients experienced an EAR with active air cleaners (seven patients; 29.17%) than placebo (21 patients; 87.50%). The response incidence was lower with active than with placebo air cleaners. A Cox model demonstrated a significant treatment effect (hazard ratio, 0.10; $P = .002$). Active air cleaners also prevented late asthmatic response: four patients (16.67%) had a late asthmatic response with active air cleaners compared to 11 patients (45.83%) with placebo (Prescott test $P = .002$). Active air cleaners also decreased the maximal severity of bronchial response (FEV1 decrease of 17.24% with active vs 25.62% with placebo air cleaners; $P = .001$).

Conclusions: Our present results demonstrated that Intense Pure Air XL® air cleaners significantly prevented early and late asthmatic responses among cat-allergic asthmatics during cat allergen exposure in the ALYATEC® EEC.

KEYWORDS

air cleaners, cat-allergic asthma, environmental exposure chamber

1 | INTRODUCTION

Cat allergen is among the most important perennial indoor allergens and a common cause of IgE-mediated allergic disease worldwide. It affects 10%-30% of atopic patients with allergic rhinoconjunctivitis, with or without asthma, and an even greater proportion in areas

such as Scandinavia, which do not have a high mite prevalence.¹ The major cat allergen *Felis domesticus* 1 (Fel d 1) is primarily present in the cat's sebaceous glands, the basal squamous epithelial cells of the skin,² and the salivary and perianal glands.^{3,4} The Fel d 1 allergen is found in the highest amounts in households with cats, and the concentration correlates with the number of cats in a home. However,

this allergen can also be carried on clothes and shoes and brought into homes and schools without cats, where it may persist for months to years.^{5,6} Thus, it is difficult to avoid cat allergen exposure in the natural environment. Moreover, pets are major contributors to endotoxin in homes. In people sensitized to cat and exposed to cat allergens may enhance the association of endotoxin with asthma and wheeze.⁷

Patients with high concentrations of cat allergen-specific IgE carry a higher risk of asthma-associated rhinoconjunctivitis symptoms.^{8,9} In the United States, cat sensitization accounts for 29.30% of asthma cases.¹⁰ Despite the obvious cause of their asthma, patients are often unwilling to acknowledge the relationship between their symptoms and the presence of the cat and thus refuse to remove the offending pet from their homes. Approximately 30% of cat-sensitized allergic asthmatic patients have a cat at home.¹¹ Although removing the animal from the home is the most commonly recommended measure, the emotional impact makes this difficult. Some studies of cat immunotherapy demonstrate significant improvement after 12 months of treatment.¹² However, further supporting studies are needed.¹³

Physical methods of reducing cat allergen exposure at home represent another possible solution that requires further investigation. The American Academy of Allergy, Asthma & Immunology Indoor Allergen Committee states that sufficient evidence indicates that air filtration reduces indoor levels of ambient particulates that might trigger disease processes.¹⁴ However, only limited clinical field studies demonstrate that air cleaners significantly decrease airborne cat allergen^{11,15} and have significant clinical effects.¹⁶ Cat allergen is a very good model to assess the efficacy of air cleaner, because it is the most difficult aeroallergen to be reduced since 20% of airborne Fel d 1 is carried in particles <5 µm.¹⁷ Mite allergy is more prevalent than cat allergy. However, if an air cleaner reduced significantly airborne Fel d 1, most likely it will reduce significantly airborne mite allergen since more than 90% of airborne Der p 1 and Der p 2 are carried on particles more than 10 µm.¹⁸

Bronchial allergen challenges appear to be the best prerequisite for determining whether a drug might be effective in a field study.¹⁹ In recent decades, since the first cat room exposures²⁰ multiple environment exposure chambers (EEC) have been developed to help with drug development.²¹ Advantages of EECs include a shorter time frame for the dose-finding process, avoiding the confounding effects of rescue medications and using smaller numbers of subjects than are required in natural exposure studies.²² The ALYATEC EEC is a new-generation chamber that provides standardized and controlled allergenic and non-allergenic exposure, located in the Strasbourg University Hospital within 3 minutes of the intensive care unit. It has previously been used for validation studies with mite²³ and cat allergen extracts in patients with asthma.

In the present study, we aimed to perform the first assessment of the clinical efficacy of the Intense Pure AIR XL[®] air cleaner with regard to early and/or late asthmatic response in cat-allergic patients with asthma.

2 | METHODS

2.1 | Patients

This study enrolled 24 adults (13 women and 11 men) with a history of cat-allergic asthma. The inclusion criteria were as follows: controlled intermittent asthma (step 1 treatment, only under short-acting beta 2 agonist as needed, according to GINA Guideline 2016) with or without association with cat allergy-related rhinoconjunctivitis; sensitization to cat allergen extract as defined by skin prick test for cat extract with a wheal diameter of ≥3 mm greater than negative control (ALK, Hørsholm, Denmark) and specific IgE anti-Fel d 1 ≥ 0.7 kU/L (ImmunoCAP, Thermofischer), FEV1 ≥ 70% of the predicted value; no cat exposure at home or outside of the home during the study; positive methacholine challenge test performed using an AeroDoseur DTF-Atomisor ATO-AD 12 as previously published²³ and early asthmatic response during baseline cat allergen exposure.

2.2 | Study design

We designed a single-centre, double-blind, placebo-controlled, cross-over study that was conducted outside of the pollen season. ALYATEC[®] recruited all subjects for this study. They were all outpatients, previously registered in site's database, which comprised patients sensitized to different aeroallergens based on positive skin prick tests. The enrolment period lasted 2 months. Among 63 eligible patients for the study, only 41 were selected, 22 declining to participate (Figure 1).

The study lasted 3 months for each patient and included a screening period, two exposure visits in the EEC with active or placebo air cleaners and a follow-up visit. The screening period comprised a screening visit including skin prick test for a panel of nine common allergens: *Dermatophagoides pteronissinus*, *Dermatophagoides farinae*, *Aspergillus fumigatus*, *Alternaria*, cat, dog, timothy grass, birch, olive pollens (ALK, Hørsholm, Denmark) and Fel d 1-specific IgE assessment, methacholine challenge test and baseline airborne Fel d 1 exposure (Expo 1). The study design is presented in Figure 2.

Patients with early asthmatic response during baseline exposure were randomly allocated to one of two sequences: active air cleaners/placebo or placebo/active air cleaners. Randomization was balanced (1:1) between the two sequences. There was a 3-week wash-out period between the two exposures.

Written informed consent was obtained from the patients prior to study participation. This study was conducted in accordance with Good Clinical Practice, the principles of the Declaration of Helsinki and was registered at ClinicalTrials.gov (NCT03928561). The protocol received ethical approval with number RCB: 2017-A02731-52 from the Ethical Committee (Nord-Ouest II, France) and was performed according to applicable local regulatory requirements.

2.3 | Conditions of allergen exposure

The ALYATEC[®] EEC is located inside the University Hospital of Strasbourg, France. It has a volume of 147 m³ (area = 65 m²),

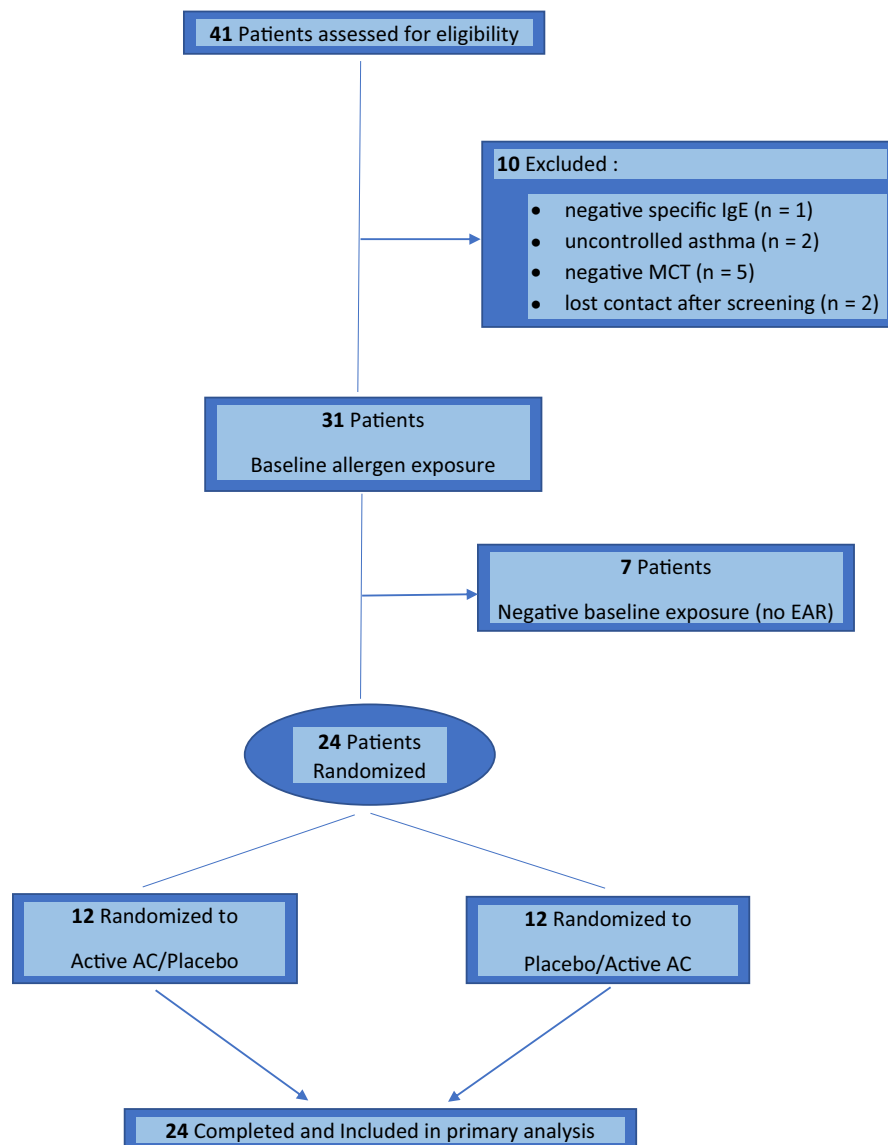


FIGURE 1 Flow diagram. AC, air cleaner; EAR, early asthmatic response; MCT, methacholine challenge test

with 20 seats, and provides a homogenous distribution of allergen for each subject. The EEC was conceived as a clean room, constructed with low-emitting, non-adherent, easily-cleaned materials. All details concerning the airflow system, environmental conditions (endotoxins and VOCs levels), airborne particles and allergens have been published elsewhere.²³ Patients were asked to wear protective coverall with integrated socks before entering the EEC and during the 2-hours exposure in order to avoid contamination with outside allergens and with inside allergens when getting out of the EEC. Moreover, patients were also asked to wear headsets connected to a music program to reduce the noise difference between placebo air cleaners (without filters) and active air cleaners.

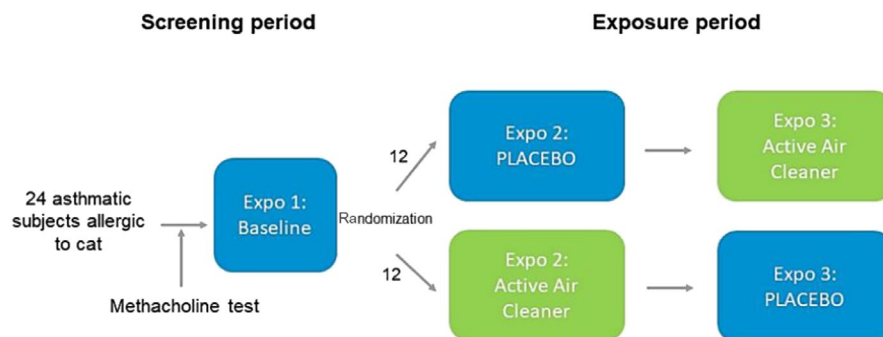
All exposure challenges were performed using the same batch of lyophilized cat allergen extract (100 000 SQ-U; Stallergenes), diluted in saline. These extracts have been approved by the French drug regulatory agency (ANSM). The nebulization was initiated before the subject entered the EEC, in order to reach the plateau of Fel d 1 aeroallergen.

Then, a continuous nebulization was required after the subjects entered the EEC and lasted 2-hours maximum during exposures.²³

The patients entered the EEC after 30 minutes of air cleaners activity, which was the time required for allergen filtration. A preliminary technical study showed that 30 minutes after the start of air cleaners (using H13 filters), there were significant decreases in the number of particles in the EEC ($P < .005$) and the Fel d 1 concentration. Patients were exposed to Fel d 1 allergen for a maximum of 2 hours and exited the EEC as soon as a 20% drop in FEV1 was observed. The Fel d 1 allergen concentration was determined using ELISA (Indoor Biotechnologies), and the results were expressed in ng/m³. The detection limit was 0.40 ng Fel d 1/mL, and the interassay coefficient of variation was 7.50%.

2.4 | Patients monitoring assessments (before, during and after exposure)

All participants completed online Total Ocular Symptoms Score (TOSS) and Total Nasal Symptoms Score (TNSS) questionnaires,²⁴

FIGURE 2 Study design chart

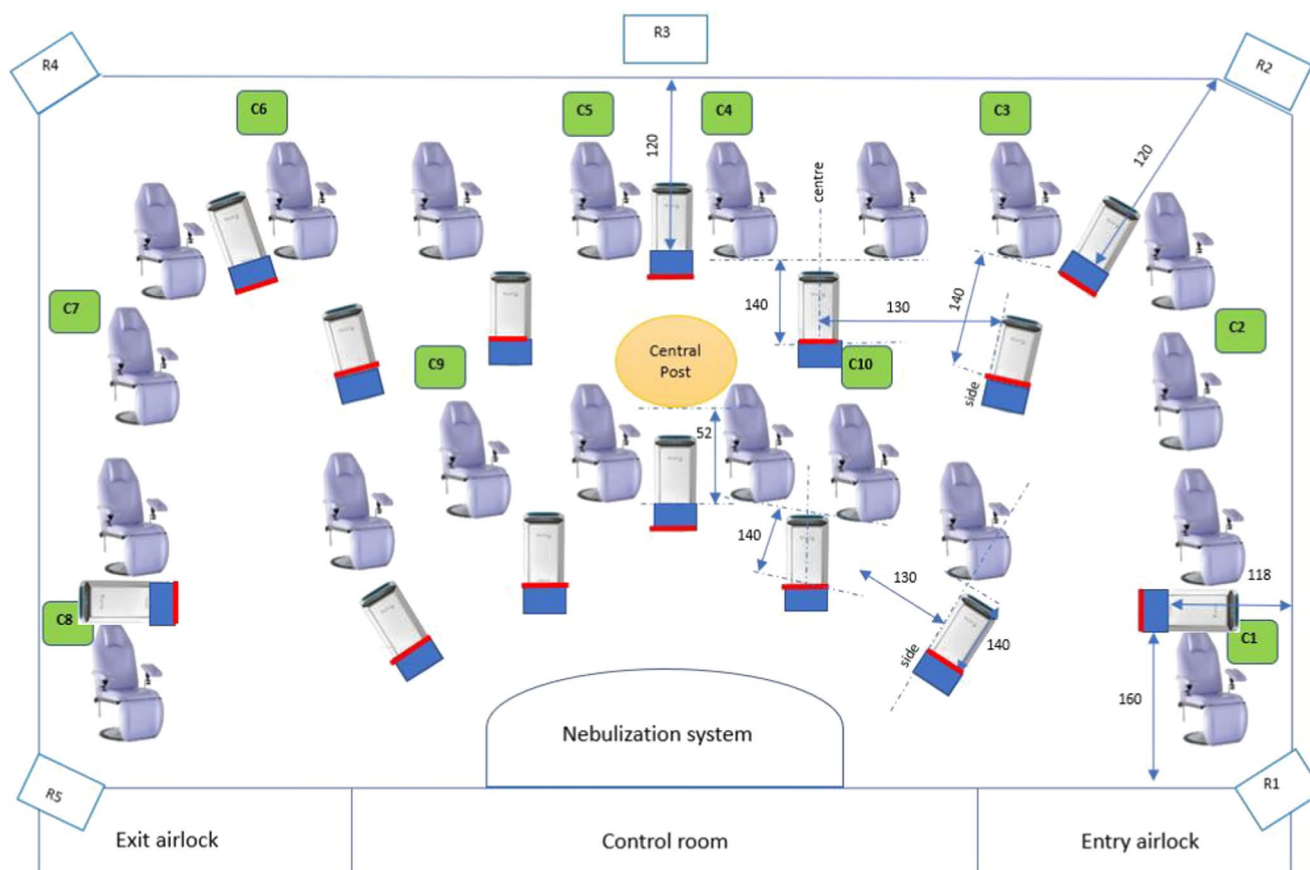
rating their symptom severity on a scale of 0-3, as well as the rhinitis visual analogue scale (VAS)²⁵ at 20-minute intervals during exposure in the EEC and hourly for 6 hours post-exposure. A positive response for rhinitis was defined as a TNSS ≥ 6 or a 23-mm increase in rhinitis VAS. A positive conjunctivitis response was defined as a TOSS ≥ 3 . At home, patients continued to complete self-assessed questionnaires during the 24 hours following exposures.

Online pulmonary function measurements were taken every 10 minutes during the 2 hours of allergen exposure and every 30 minutes for 6 hours post-exposure on ALYATEC site. Pulmonary function was assessed at home by peak expiratory flow measurement every hour before bedtime and early in the morning.

Analyses included the best value obtained from consecutive spirometry measurements.

An early asthmatic response (EAR) was defined as a 20% drop in FEV1 during 2 hours of exposure, compared to the baseline value. When an EAR occurred, the patient exited the EEC and treated with two puffs of inhaled salbutamol and then remained under supervision for at 6 hours, since a possible late asthmatic response (LAR) was expected. LAR was defined as a 15% drop in FEV1 and or 20% in PEF occurring between 3 and 12 hours after allergen challenge.²⁶

The patients were not allowed to take any antihistamines for the 7 days prior to exposures. Topical corticosteroids were stopped for 7 days before exposures, short-acting β_2 -agonist treatment for

**FIGURE 3** Distribution of air cleaners in the environmental exposure chamber (EEC). Air cleaners were distributed all around the EEC to perform homogeneous air filtration. The distances between each air cleaner, and between each air cleaner and the EEC wall, are indicated in centimeters. R1-R5 correspond to different recovery zones, and C1-C10 correspond to particle counters located every two seats

8 hours and long-acting β_2 -agonist treatment for 24 hours prior to allergen exposures. No other immunomodulatory drugs were used by the patients.

2.5 | Air cleaners

In this study, we tested the Intense Pure Air XL[®] air cleaner PU6020FO model (Rowenta[®]). This device has been on the European market since March 2015 and conforms to European Commission standards. In this study, HEPA filters H12 were replaced with H13 filters, which allowed better particle filtration. The air cleaner air-flow was 360 m³/h.

Prior to the patients' exposure, technical tests were performed to verify the reproducibility of exposures with Fel d 1 in the EEC. The mean value was 37.10 ng/m³ with an interassay CV of 9.10% (n = 12). The ALYATEC EEC has been designed as a clean room with full renewed air ventilation. Knowing that one air cleaner was able to process 62.5 m³, the volume of EEC (147 m³) and the mixing rate (six times) in the EEC, a number of 14 air cleaners were calculated. Air cleaners were located at a precise distance, permitting homogenous repartition within the EEC (Figure 3). The same location of the air cleaners was used during the whole clinical study.

2.6 | Statistical analysis

All statistical analyses were performed using SAS[®] guide Enterprise software (SAS Institute). Missing data were not replaced. Continuous variables were described as the numbers of observed data, mean, standard deviation of normally distributed and median (interquartile range). Categorical variables were described as the effective and percentage in each category. For inferential statistics, *P* values below .05 were considered statistically significant. Tests were two-tailed.

The main judgment criterion was the instantaneous hazard of having an EAR after allergen exposures. We used a Cox model adjusted for the treatment group and accounting for the cross-over design. Results were expressed as hazard ratio and 95% confidence interval (CI) with placebo as reference. The Prescott test was performed to assess whether there was a difference between the active and placebo devices. The incidence of EAR was estimated in a general linear model with the natural logarithm of duration of presence in the EEC as an offset term and is expressed for 1000 person*minute. The subject was classified according to the "preferred" period (ie, if they did not develop the bronchial response solely for this period). The proportion was compared to what was expected assuming no difference between groups.

In the absence of information on the bronchial response with air cleaners, a convenient sample of 24 subjects was to be included.

3 | RESULTS

3.1 | Patients

Among 41 screened patients, 31 underwent baseline exposure, of whom 24 were randomized into one of the two sequence groups. All 24 of these patients underwent exposures 2 and 3 and completed the end-of-study visit (Figure 1). The ITT population and the PP population were identical; therefore, the results are presented for the ITT population. The safety analysis was conducted among the 31 patients who underwent baseline exposure.

The mean patient age was 30.50 years, and the age range was 22-62 years. No formal tests were performed to compare the treatment sequence groups, but the demographic characteristics were similar between groups. All patients had at least one additional sensitization. All patients had a GINA step 1 treatment. The mean FEV1 (percentage of the predicted value) was 96.34% (Table 1).

Patients	Active air cleaners/placebo (n = 12)	Placebo/active air cleaners (n = 12)	Total (n = 24)
Age (y), Mean (SD)	30.50 (12.66)	30.42 (11.27)	30.46 (11.72)
Gender, Female, n (%)	5 (41.67)	8 (66.67)	13 (54.17)
Skin prick test mean wheal diameter (mm), Mean (SD)	6.50 (1.43)	5.92 (1.22)	6.21 (1.33)
FEV1% mean of predicted value, Mean (SD)	95.88 (11.32)	96.81 (9.69)	96.34 (10.32)
Specific IgE Fel d 1 (U/L), Median (Q1;Q3)	12.15 (3.32; 29.50)	5.77 (1.24; 25.50)	10.07 (2.32; 25.95)
Pauci-sensitized (2-3), n (%)	3 (25)	2 (16.67)	5 (20.84)
Poly-sensitized (>3), n (%)	9 (75)	10 (83.34)	19 (79.17)
Methacholine PD ₂₀ (μg), Median (Q1;Q3)	157.10 (86.95; 1033.45)	149.32 (73.01; 1262.46)	152.86 (75.67; 1077.30)

TABLE 1 Baseline demographic and clinical characteristics of the patients

Note: There was no difference between sequences between the two groups (*P* = .22).

Abbreviations: FEV1, forced expiratory volume-one second; IQR, interquartile range.

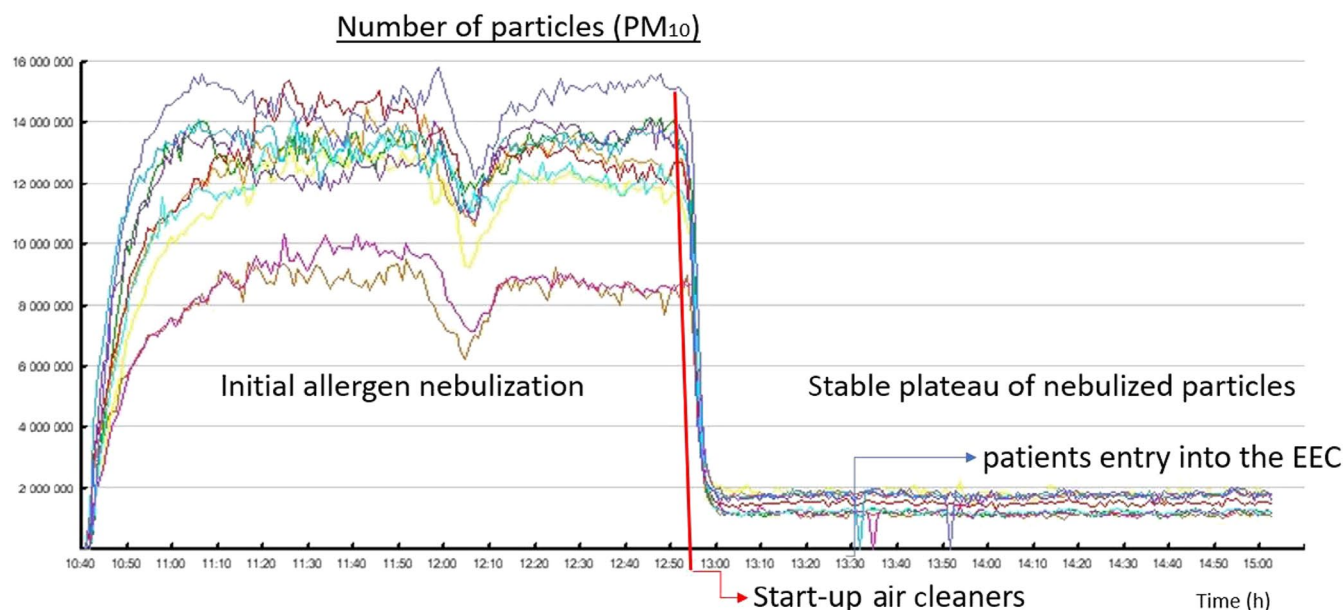


FIGURE 4 Particle number curves during nebulization in the EEC. Fel d 1 nebulization was initiated 2 h before patient entry into the EEC to obtain a stable particles numbers plateau. When the active air cleaners are turned on, the number of particles dramatically decreased to reach a stable low plateau. Each colored curve corresponds to a particle counter ($n = 10$). Fel d 1 concentrations also decreased significantly

3.2 | Efficiency of air cleaners to decrease airborne Fel d 1

With active air cleaners, the mean Fel d 1 airborne concentration decreased from 36.30 ng/m^3 with an interassay CV of 10% ($n = 4$) to 4.70 ng/m^3 with an interassay CV of 35% ($n = 4$; Figure 4). With the PCB air cleaners, the mean airborne Fel d 1 concentration did not decrease and stayed at 37.10 ng/m^3 with an interassay CV of 8.20% ($n = 4$).

3.3 | Frequency of early and late asthmatic responses with air cleaners

Fewer patients experienced an early asthmatic response when exposed to active air cleaners (seven patients; 29.17%) than when exposed to placebo (21 patients; 87.50%; Table 2). The incidence of response was lower with active than with placebo air cleaners. If 1000 patients had been followed during 10 minutes, 2.8 events would be expected in the active air cleaners group compared to 14.3 in the placebo group (Table 3). A Cox model demonstrated a significant treatment effect, with a hazard ratio of 0.10 (95% CI 0.02;0.43, $P = .002$; Figure 5).

Active air cleaners also prevented late asthmatic response upon exposure to airborne cat allergen. Only four patients (16.67%) had a late asthmatic response in the chamber when exposed to active air cleaners, compared to 11 patients (45.83%) when exposed to placebo (Prescott test $P = .002$).

3.4 | Severity of bronchial response

Active air cleaners decreased the maximal severity of the bronchial response, assessed by the maximal drop in FEV1 while the

patient was in the EEC. When exposed to active air cleaners, the maximal severity of the bronchial response was an FEV1 decrease of 17.24%, compared to a FEV1 decrease of 25.62% with placebo ($P = .001$).

3.5 | Effect on rhinitis and conjunctivitis

Active air cleaners did not demonstrate efficacy on rhinitis VAS ($P = .812$), TNSS ($P = .752$), nor TOSS ($P = .052$) scores.

4 | DISCUSSION

Our present study is the first to use an environmental exposure chamber to demonstrate that air cleaners reduced early and late asthmatic responses to airborne Fel d 1 in cat-allergic patients. For several decades, portable air cleaners have been used to reduce exposure to indoor pollutants.¹⁴ Various types of filters have been marketed, including high-efficiency particulate air HEPA filters, electrostatic precipitators (ESPs) or powered electronic filters (EACs), ion generators, and composite filters comprising activated carbon.¹⁴ Shaughnessy et al²⁷ demonstrated that air cleaners with HEPA filters are more effective for removing indoor particles than electronic filter systems, ionizers and ozone generators. In our present study, we tested a new air cleaner: the Intense Pure Air XL[®] equipped with a HEPA (H13) filter and a charcoal filter. We found that the use of air cleaners in a 147-m^3 room yielded a significant decrease in airborne Fel d 1 to $<5 \text{ ng/m}^3$. A high number of air cleaners were used in this study to compensate for the high air exchange rate of the EEC, but this modelization corresponds to natural home environment with only one air cleaner in a room

TABLE 2 Early and late responses to allergen exposure

	EAR%	LAR%	EAR or LAR%	EAR and LAR%	Neither EAR nor LAR%
Active air cleaners	29.1 (7/24)	16.6 (4/24)	37.5 (9/24)	8.3 (2/24)	62.6 (15/24)
Placebo air cleaners	87.5 (21/24)	45.8 (11/24)	100 (24/24)	33.3 (8/24)	0 (0/24)
P	<.0001	.01	<.0001	.03	<.0001

Note: Descriptive statistics by air cleaners' effect in the intention-to-treat population.

Abbreviations: EAR, early asthmatic response; LAR, late asthmatic response. At baseline, all patients had an EAR.

TABLE 3 Occurrence of early asthmatic response (EAR)

	Exposures 2 and 3	
	Placebo air cleaners	Active air cleaners
EARn (%)		
No EAR	17 (70.83)	3 (12.50)
EAR	7 (29.17)	21 (87.50)
Nb event	7	21
Incidence for 1000 person-min		
Person-min	2485	1465
Incidence rate (95% CI) ^a	2.817 (1.343, 5.909)	14.334 (9.346, 21.985)

Note: Descriptive statistics by group in the intention-to-treat population.

Abbreviation: CI, confidence interval.

^aIncidence rate for 1000 person-min.

up to 80 m³. Notably, the amount of Fel d 1 that was continuously nebulized during 2 hours was dramatically higher than the levels emitted by a cat in a room, which is reportedly around 14 ng/m³ carried on a wide range of particles and with a flow far lower than that in the EEC.^{11,17,28}

Other items seem to show that exposure to airborne Fel d 1 in the EEC corresponded to natural exposure. In houses with cats detected airborne Fel d 1 concentrations vary from 0.7 to 38 ng/m³. Within minutes after a cat enters a room, the Fel d 1 concentration sharply increases from 30 to 90 ng/m³. The particle size of the major cat allergen Fel d 1 plays an important role in determining respiratory allergic responses. In homes with cats, most of the allergen is carried on particles of >10 µm; however, a substantial portion (around 25%) is carried on particles of <5 µm. In a house with a cat and without disturbance, the mean airborne Fel d 1 concentration is reportedly 14 ng/m³.^{3,11,15,17} In a house with a cat, it takes approximately 40 minutes for a cat-allergic person to develop asthma symptoms (unpublished). In the EEC, with a Fel d 1 concentration of 40 ng/m³ and with 10 L of ventilation per minute, the cumulative inhaled dose of Fel d 1 will be 16 ng in 40 minutes. This dose is close to the early asthmatic response-inducing doses during individual challenge tests, where the MMAD was 10.30 µm with a value of 13.50 ng of Fel d 1.²⁸ In ALYATEC's EEC, the MMAD of the Fel d 1-carrying particle was 10.20 µm as measured with a cascade impactor (n = 3; data not shown), yielding a mean value of 38.20 ± 4.30 ng/m³ of Fel d 1. Thus, the exposure to cat allergen in our EEC corresponded to the natural exposure in terms of both the cumulative Fel d 1 dose and the particle size distribution.²⁸

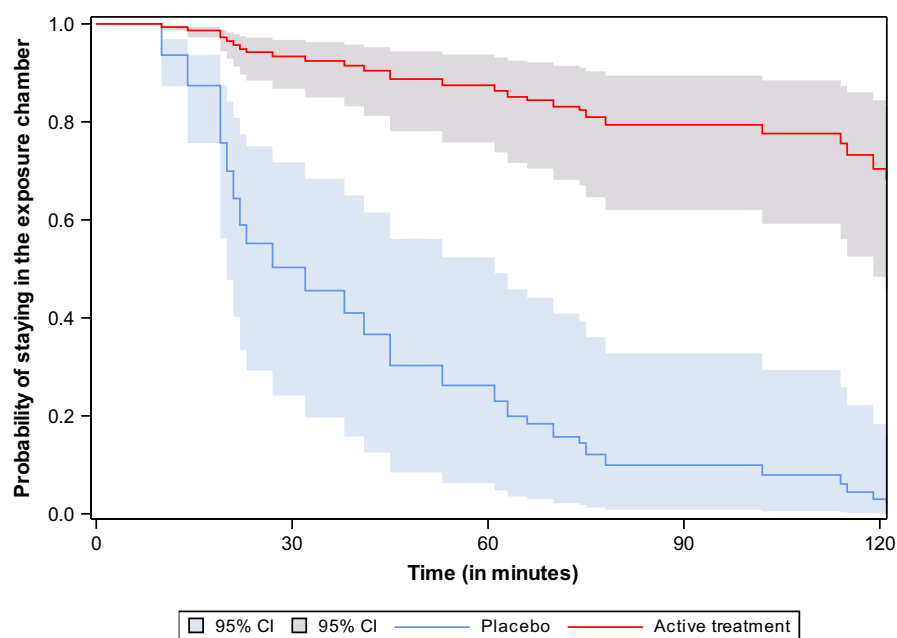


FIGURE 5 Time to early asthmatic response. Mean survival curves derived from the Cox model for cross-over studies. Intention-to-treat population incidence rate of 2.82 (1.34, 5.91) in the active air cleaner group versus 14.33 (9.35, 21.98) in the placebo group (hazard ratio, 0.10; $P = .002$)

TABLE 4 Time to early asthmatic response

Exposures 2 and 3		
	Air cleaner	Placebo
Time to early asthmatic response (in min)		
N	7	7
Mean (SD)	62.14 (30.59)	53.29 (45.53)
(Min;Max)	(23.00;121.00)	(10.00;120.00)
Median (Q1;Q3)	53.00 (45.00;74.00)	22.00 (20.00;102.00)

Note: Descriptive statistics by group—Subjects with EAR on treatment.

Since cat allergen is measurable in the air of dwellings housing a cat, even in the absence of the cat, air cleaners use appears to be a relevant method for reducing airborne cat allergen. Indeed, in the absence of cat, the use of a HEPA air cleaner and a HEPA vacuum cleaner reportedly yielded a significant reduction of airborne cat allergen in an uncarpeted apartment.¹¹ Using nasal air samples, Gore et al described a significant reduction in the quantity of inhaled Fel d 1 when an air cleaner was used in the presence of a cat.²⁹ The use of a HEPA air cleaner in the living room reduced airborne Fel d 1 levels by 70%-80% in seven homes with a cat, as compared to 30% in apartments containing higher levels of cat allergen.¹⁵ However, contradictory results have been reported in previous clinical studies of cat-allergic patients using HEPA air cleaners. Among asthmatic patients sensitized to cat and dog, Francis et al³⁰ found that the use of portable HEPA air filters reduced a combined asthma outcome (comprising at least a doubling dose in histamine hyperreactivity or a reduction treatment mounting of one-step change) in 10 of 15 patients. They found that airborne Fel d 1 concentrations were significantly reduced with the active air cleaners. In 24 pet-sensitized asthmatic children, lung function and airway hyperresponsiveness were monitored over a 6-month period outside of pollen season.³¹ During the intervention with air cleaners, higher amounts of airborne pet allergens were captured, but there were no changes in FEV₁, symptom scores, or medication use. Only PD20 adenosine improved with air cleaners. In contrast, among 35 adult cat-allergic patients, no clinical improvement was observed when using HEPA air cleaners (ie, with regard to nasal symptoms, PEF and chest symptoms, sleep disturbance and rescue medication use).³² However, there were no previously published data regarding the efficacy of air cleaners on early and late asthmatic responses during controlled cat allergen exposure.

In the present study, all patients were continuously exposed, at baseline exposure, to around 40 ng/m³ airborne Fel d 1, and experienced an early asthmatic response. The active air cleaners yielded a 62% decrease in early and late asthmatic response. These findings are similar to the results of clinical studies assessing the efficacy of anti-asthmatic drugs. Late asthmatic response frequency was reduced by 100% when 500 µg beclomethasone was administered 2 hours after an early asthmatic response with a mean FEV1 reduction of 70%, as compared to placebo and cromolyn sodium.³³ Another study using

400 µg of inhaled mometasone furoate twice a day for 4 days before allergen challenge reduced the magnitude of early and late asthmatic responses, with complete prevention of LAR.³⁴ Moreover, 800 µg of budesonide administered 2 hours after early asthmatic response showed a significant reduction in the magnitude of the LAR.³⁵ In mite-asthmatic patients, 1 year of immunotherapy treatment induced a 47% reduction in late asthmatic response.³⁶

In our present study, active air cleaners use did not impact rhinoconjunctivitis. It is not surprising that we did not observe significant changes in TOSS, TNSS scores and VAS rhinitis since bronchial symptoms occurred earlier than nasal and ocular symptoms (100 minutes). The patients left the EEC at the time of recording a FEV1 decrease, which corresponded to a mean time of 62 minutes (Table 4). Moreover, the questionnaires had high variability, and it appears that a large number of patients would be required to obtain a significant difference. To decrease the variability, we also compared the baseline-corrected AUC over time, but still found no statistical difference. This suggests that a statistically significant difference may have been obtained with more patients.

No severe adverse events were recorded in this study. One patient experienced a maximum FEV1 drop of 53% with no severe symptoms, and total reversibility was obtained within 14 minutes. Moreover, this patient did not experience any asthma response during exposure with active air cleaners compared to baseline and placebo, highlighting the clinical efficiency of air cleaners in terms of asthma response.

In conclusion, our study experimentally demonstrated the clinical efficacy of a new air cleaner, the Intense Pure Air XL, in a controlled environment, with regard to early and late asthmatic responses in cat-asthmatic patients. As air cleaners use becomes increasingly frequent, it was necessary to obtain objective data regarding the effect of air cleaners on allergic asthma. Moreover, ALYATEC EEC appears to be a good tool to assess the efficacy and benefice of such devices in asthmatic patients.

ACKNOWLEDGEMENTS

SOLADIS France for the statistical analysis.

CONFLICT OF INTERESTS

AG, AJ and FS are ALYATEC's employees. ND is cofounder and ALYATEC's employee. FdB is medical expert, cofounder and shareholder of ALYATEC. FdB reports grants from STALLERGENES GREER, grants from CHIESI and personal fees from ALK ABELLO, MUNDIPHARMA, NOVARTIS, and he is being part of board membership at STALLERGENES GREER, NOVARTIS, ALK ABELLO, MUNDIPHARMA, MEDAPHARMA, BOEHRINGER, ASTRAZENECA and CALOR.

DECLARATION

There are limited clinical field studies on air cleaner's efficacy in cat-allergic patients. This is the first study demonstrating the effect of

air cleaners on early and late bronchial responses in an environmental exposure chamber. Present data suggest improvement of asthma management for clinicians to advice patients using such devices in add-on therapy.

AUTHORS CONTRIBUTIONS

All authors reviewed the manuscript. AG provided supervision, interpreted the data and drafted the manuscript. FdB provided supervision, conceived and designed the study, interpreted the data. ND conceived and designed the study, interpreted the data. AJ interpreted the data, provide clinical study supervision. FC provided technical study supervision. FdB is the guarantor of the study.

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DATA AVAILABILITY STATEMENT

Data available on request from the authors

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